

VOLUME LXXVI, ISSUE 6, JUNE 2023

ISSN 0043-5147

E-ISSN 2719-342X

Wiadomości Lekarskie Medical Advances



Official journal of Polish Medical Association has been published since 1928



INDEXED IN PUBMED/MEDLINE, SCOPUS, EMBASE, EBSCO, INDEX COPERNICUS,
POLISH MINISTRY OF EDUCATION AND SCIENCE, POLISH MEDICAL BIBLIOGRAPHY

VOLUME LXXVI, ISSUE 6, JUNE 2023

ISSN 0043-5147

E-ISSN 2719-342X

Wiadomości Lekarskie Medical Advances



Official journal of Polish Medical Association has been published since 1928



ALUNA Publishing House



Memory of
dr Władysław
Biegański

Wiadomości Lekarskie is abstracted and indexed in: PUBMED/MEDLINE, SCOPUS, EMBASE, INDEX COPERNICUS,
POLISH MINISTRY OF EDUCATION AND SCIENCE, POLISH MEDICAL BIBLIOGRAPHY

Copyright: © ALUNA Publishing House.

Articles published on-line and available in open access are published under Creative Commons Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0) allowing to download articles and share them with others as long as they credit the authors and the publisher, but without permission to change them in any way or use them commercially.

The journal *Wiadomości Lekarskie* is cofinanced under Contract No.RCN/SN/0714/2021/1
by the funds of the Minister of Education and Science



Wiadomości Lekarskie Medical Advances

Editor in-Chief:

Prof. Władysław Pierzchała

Deputy Editor in-Chief:

Prof. Aleksander Sieroń

Statistical Editor:

Dr Lesia Rudenko

Managing Editor:

Agnieszka Rosa – amarosa@wp.pl

International Editorial Office:

Nina Radchenko (editor) – n.radchenko@wydawnictwo-aluna.pl

Polish Medical Association (Polskie Towarzystwo Lekarskie):

Prof. Waldemar Kostewicz – President PTL

Prof. Jerzy Woy-Wojciechowski – Honorary President PTL

International Editorial Board – in-Chief:

Marek Rudnicki Chicago, USA

International Editorial Board – Members:

Kris Bankiewicz	San Francisco, USA	George Krol	New York, USA
Christopher Bara	Hannover, Germany	Krzysztof Łabuzek	Katowice, Poland
Krzysztof Bielecki	Warsaw, Poland	Jerzy Robert Ładny	Białystok, Poland
Zana Bumbuliene	Vilnius, Lithuania	Henryk Majchrzak	Katowice, Poland
Ryszarda Chazan	Warsaw, Poland	Ewa Małecka-Tendera	Katowice, Poland
Stanislav Czudek	Ostrava, Czech Republic	Stella Nowicki	Memphis, USA
Jacek Dubiel	Cracow, Poland	Alfred Patyk	Göttingen, Germany
Zbigniew Gasior	Katowice, Poland	Palmira Petrova	Yakutsk, Russia
Mowafaq Muhammad Ghareeb	Baghdad, Iraq	Krystyna Pierzchała	Katowice, Poland
Andrzej Gładysz	Wrocław, Poland	Waldemar Priebe	Houston, USA
Nataliya Gutorova	Kharkiv, Ukraine	Maria Siemionow	Chicago, USA
Marek Hartleb	Katowice, Poland	Vladyslav Smiiianov	Sumy, Ukraine
Roman Jaeschke	Hamilton, Canada	Tomasz Szczepański	Katowice, Poland
Andrzej Jakubowiak	Chicago, USA	Andrzej Witek	Katowice, Poland
Peter Konturek	Saalfeld, Germany	Zbigniew Wszolek	Jacksonville, USA
Jerzy Korewicki	Warsaw, Poland	Vyacheslav Zhdan	Poltava, Ukraine
Jan Kotarski	Lublin, Poland	Jan Zejda	Katowice, Poland

Distribution and Subscriptions:

Bartosz Guterman prenumerata@wydawnictwo-aluna.pl

Graphic design / production:

Grzegorz Sztank www.red-studio.eu

Publisher:

ALUNA Publishing House
ul. Przesmyckiego 29,
05-510 Konstancin – Jeziorna
www.wydawnictwo-aluna.pl
www.wiadomoscilekarskie.pl
www.wiadlek.pl

CONTENTS

ORIGINAL ARTICLES

- Aidyn G. Salmanov, Volodymyr Artyomenko, Olena M. Susidko, Svitlana M. Korniyenko, Orusia A. Kovalyshyn, Oleksandr A. Voloshyn, Oleg V. Golyanovskiy
 CATHETER-ASSOCIATED URINARY TRACT INFECTIONS AFTER CAESAREAN SECTION IN UKRAINE: RESULTS A MULTICENTER STUDY (2020-2022) 1325
- Evangelos C. Fradelos, Maria Saridi, Vissarion Bakalis, Aikaterini Toska, Viktor Vus, Arndt Büssing, Kyriakos Souliotis
 MENTAL HEALTH, QUALITY OF LIFE, SPIRITUAL DRYNESS AND ACEDIA SYMPTOMS IN PATIENTS SUFFERING FROM CHRONIC DISEASES 1332
- Muhamad Arifin Parenrengi, Wihasto Suryaningtyas, Rifqi Aulia Destiansyah
 HYPERGLYCEMIA AS A PREDICTOR OF OUTCOME IN PAEDIATRIC SEVERE TRAUMATIC BRAIN INJURY PATIENTS UNDERWENT SURGERY: A SINGLE CENTER EXPERIENCE FROM EASTERN INDONESIA FROM 2017-2022 1342
- Olga Bilyayeva, Ivan Karol, Eugeniy Demianenko, Alina Gaidai, Yevhenii Kryzhevskiy, Polina Vakuliuk, Alexander Golub
 ORNIDAZOL-BASED APPLICATION SORBENT WITH NANO SILICA AND ITS ANTIMICROBIAL ACTIVITY 1347
- Sofia S. Bauman, Olga V. Sheshukova, Valentyna P. Trufanova, Iryna O. Kuz, Tetiana V. Polishchuk, Anna S. Mosienko, Kateryna S. Kazakova
 CYTOLOGIC CHARACTERISTIC OF THE CELLULAR COMPOSITION OF THE GUM MUCOUS MEMBRANE IN SCHOOL-AGE CHILDREN 1359
- Hayder Ch. Assad, Fadhil A. Rizij, Ayad A. Hussien, Zainab Hadi
 ACCEPTANCE OF THE COVID-19 VACCINE AND ITS RELATED FACTORS AMONG IRAQI ADOLESCENTS: A CROSS-SECTIONAL STUDY 1363
- Vlasta Vysochanska, Galina Koval
 MALASSEZIA COLONIZATION CORRELATES WITH THE SEVERITY OF SEBORRHEIC DERMATITIS 1371
- Sidrah Parvez, Ghizal Fatima, Farzana Mahdi, Najah R. Hadi, Jan Fedacko
 ASSESSMENT OF THE ASSOCIATION OF SEROTONIN TRANSPORTER GENE (5-HTTVNTR & 5-HTTLPR) POLYMORPHISM IN PATIENTS WITH FIBROMYALGIA SYNDROME 1378
- Taras V. Romaniv, Nadiya V. Skrypnyk, Ulyana V. Synko, Nataliia M. Voronych-Semchenko, Oleh V. Melnyk, Anna O. Hryb, Igor B. Boruchok
 THE ASSESSMENT OF COMPENSATION OF CARBOHYDRATE METABOLISM IN PATIENTS WITH TYPE 2 DIABETES MELLITUS WITH METABOLIC SYNDROME BEYOND THE LIMITS OF GLYCATED HEMOGLOBIN 1385
- Sergiy Stadnik, Olena Radchenko, Orest Komarytsia, Iryna Zhakun, Angelica Filipyuk, Nataliya Bek
 PECULIARITIES OF STRUCTURAL CHANGES IN THE BRAIN SUBSTANCE IN PATIENTS WITH ARRHYTHMIAS DEPENDING ON THE SEVERITY OF COGNITIVE DISORDERS 1391
- Grygoriy P. Griban, Olha S. Zablotska, Halyna A. Kolomoiets, Natalia A. Lyakhova, Iryna M. Nikolaieva, Iryna I. Shpak, Olena V. Lobova
 FAMILY INFLUENCE ON THE FORMATION OF CHILDREN'S MOTIVATION FOR A HEALTHY LIFESTYLE 1400

- Viktoriia Rudnyk, Nataliia Chaplynska, Liubov Skrypnyk
BRONCHIECTASIS IN ADULT PATIENTS: CLINICAL PECULIARITIES AND APPROACHES TO THE TREATMENT 1406
- Tetiana Miyer, Anna Klim-Klimaszewska, Svitlana Palamar, Olga Kotenko, Hennadii Bondarenko, Liudmyla Nezhyva, Yurii Savchenko
CAUSES OF ANXIETY DURING PLAY AS A FACTOR OF NEGATIVE IMPACT ON THE HEALTH OF PRESCHOOL AND SCHOOL CHILDREN 1413
- Iryna Yu. Karpiuk, Tetiana K. Obeziuk, Maryna O. Demydenko, Iryna Yu. Zakharova, Olena V. Pidvalna, Oleksandr Ye. Salamakha, Iryna A. Holovanova
IMPACT OF MOTOR ACTIVITY ON THE DYNAMICS OF INTELLECTUAL WORKING CAPACITY AND MENTAL COGNITIVE PROCESSES IN STUDENTS 1422
- Ivan M. Okhrimenko, Vadym V. Barko, Lesia V. Vavryk, Vadym D. Chornous, Svitlana S. Okhrimenko, Yurii V. Aleksandrov, Larysa M. Onishchuk
THE IMPACT OF PROFESSIONAL STRESS ON THE MENTAL HEALTH OF LAW ENFORCEMENT OFFICERS 1428
- Oleksandr O. Sabirov, Zoia V. Syrovatko, Viktoriia M. Yefremenko, Nataliia Ye. Havrylova, Olena K. Syrotynska, Anna Yu. Chekhovska, Oleksandr D. Mokhunko
DYNAMICS OF STUDENTS' PHYSICAL WELL-BEING INDICATORS DURING QUARANTINE RESTRICTIONS 1436
- Yulia G. Kolenko, Tetiana O. Timokhina, Olesya V. Lynovytska, Olena V. Cherkasova, Ilona S. Semenova
INDICATORS OF DENTAL HEALTH AND LOCAL IMMUNITY IN YOUNG ADULTS WHO HAVE SUFFERED FROM CORONAVIRUS INFECTION 1443
- Kostiantyn V. Prontenko, Ivan M. Okhrimenko, Olena O. Yevdokimova, Kateryna R. Mannapova, Volodymyr M. Filonenko, Luliia L. Tverdokhvalova, Liliia O. Bondarenko
PECULIARITIES OF FORMATION OF CADETS' PSYCHOLOGICAL RESILIENCE AND PHYSICAL READINESS FOR COMBAT STRESS 1450
- Oleksii V. Tymoshenko, Zhanna H. Domina, Valerii V. Trotsenko, Serhii V. Sembrat, Andrii O. Artiyushenko, Oleksandr A. Tomenko, Romana R. Sirenko
DEVELOPMENT OF COORDINATION ABILITIES IN 6-10 YEARS OLD BOYS WITH POSTURAL DISORDERS 1457
- Mykhailo F. Khoroshukha, Grygoriy P. Griban, Anatolii I. Bosenko, Natalia A. Lyakhova, Alla M. Harlinska, Pavlo P. Tkachenko, Anna A. Bondar
INFLUENCE OF SEROLOGICAL MARKERS OF BLOOD GROUPS UPON THE DEVELOPMENT OF VISUAL MEMORY IN HIGH SCHOOLERS AND STUDENTS 1464
- Borys P. Savchuk, Inga V. Yehorova, Oksana V. Vintoniak, Ruslan M. Kotenko, Nadiya O. Fedchyshyn, Svitlana Yu. Nesterova, Halyna V. Bilavych
EMOTIONAL INTELLIGENCE AS A FACTOR IN STRENGTHENING THE STUDENTS' MENTAL HEALTH DURING THE COVID-19 PANDEMIC 1470
- Andrii A. Borysenko, Anna M. Antonenko, Vasyl Aleksiiichuk, Mykola Kondratiuk, Igor Pelo
COMPARATIVE HYGIENIC ASSESSMENT OF THE POTENTIAL DIQUAT HAZARD TO THE POPULATION WHEN CONSUMING AGRICULTURAL CROPS TREATED WITH THE REGLONE AIR 200 SL FORMULATION USING DIFFERENT APPLICATION TECHNOLOGIES (UAV, AERIAL, HIGH-CLEARANCE ROD SPRAYER TREATMENT) 1478

Volodymyr O. Korshnyak, Julia V. Bovt, Oleksandr R. Pulyk, Oleksandr M. Stoyanov
MINE-BLAST TRAUMA AS A FACTOR IN THE EARLY DEVELOPMENT OF VASCULAR DISEASES OF THE BRAIN 1485

REVIEW ARTICLES

Ruzhena Matkivska, Inga Samborska, Oleksandr Maievskyi
EFFECT OF SCORPION VENOM TOXINS ON STRUCTURAL AND FUNCTIONAL PARAMETERS OF INTERNAL ORGANS,
INCLUDING KIDNEYS (REVIEW) 1491

CASE STUDIES

Oleksandr Pulyk, Myroslava Hyryavets, Vladyslava Ahij
CHRONIC MIGRAINE. CASE REPORT 1499

CATHETER-ASSOCIATED URINARY TRACT INFECTIONS AFTER CAESAREAN SECTION IN UKRAINE: RESULTS A MULTICENTER STUDY (2020-2022)

DOI: 10.36740/WLek202306101

Aidyn G. Salmanov^{1,2}, Volodymyr Artyomenko³, Olena M. Susidko⁴, Svitlana M. Korniyenko³, Orusia A. Kovalyshyn⁵, Oleksandr A. Voloshyn^{1,6}, Oleg V. Golyanovskiy^{1,6}

¹SHUPYK NATIONAL HEALTHCARE UNIVERSITY OF UKRAINE, KYIV, UKRAINE

²INSTITUTE OF PEDIATRICS, OBSTETRICS AND GYNECOLOGY OF THE NATIONAL ACADEMY OF MEDICAL SCIENCES OF UKRAINE, KYIV, UKRAINE

³ODESA NATIONAL MEDICAL UNIVERSITY, ODESA, UKRAINE

⁴DOCTOR NIKOLAEV MEDICAL CENTER, DNIPRO, UKRAINE

⁵LVIV MEDICAL INSTITUTE, LVIV, UKRAINE

⁶KYIV REGIONAL MATERNITY HOSPITAL, KYIV, UKRAINE

ABSTRACT

The aim: To obtain the first national estimates of the current prevalence rate of catheter-associated urinary tract infections (CAUTIs) after caesarean section (CSEC) and antimicrobial resistance of causing pathogens in Ukraine.

Materials and methods: Prospective multicentre surveillance was conducted from January 2020 to December 2022 in 15 women hospitals of Ukraine. Definitions of CAUTIs were adapted from the CDC/NHSN. Antibiotic susceptibility was done by the disc diffusion test as recommended by European Committee on Antimicrobial Susceptibility Testing guidelines.

Results: A total of 15,892 catheterized women undergoing primary CSEC and 13.6% CAUTI were identified. The most common uropathogen was *Escherichia coli*, *Proteus mirabilis*, and *Enterococcus* species followed by *Providencia stuartii* and *Pseudomonas aeruginosa*. Many uropathogens isolated from CAUTI cases were found to be multidrug resistant.

Conclusions: This study showed that CAUTIs in catheterized women undergoing primary CSEC in Ukraine is a common occurrence and many cases are caused by pathogens that are resistant to antibiotics. Optimizing the management and empirical antimicrobial therapy may reduce the burden of CAUTIs in catheterized women undergoing primary CSEC, but prevention is the key element.

KEY WORDS: catheter-associated urinary tract infection, cesarean section, antimicrobial resistance, pathogens, Ukraine

Wiad Lek. 2023;76(6):1325-1331

INTRODUCTION

Catheter Associated Urinary Tract Infection (CAUTI) is one of the most common healthcare-associated infections (HAI) accounting for up to 40% of all hospital acquired infections [1]. According to literature, eighty percent of these are associated with the use of urinary catheters [2]. In Ukraine, fourteen percent of HAIs are associated with the use of urinary catheters [3]. Risk of infection is about 5-10% with each day of indwelling catheterization [4, 5] [and 1-3% with each insertion in intermittent catheterization [6]. CAUTIs have a high impact in terms of morbidity, mortality, and costs.

CAUTIs can be associated with Cesarean section (CSEC). CSEC is one of the most common surgical procedures performed in the both developed and developing coun-

tries [7]. The rate of CSEC has seen a soar in the past few decades, varying from 0.4% to as high as 44.1% across the world [8-11]. Among the European Union Member States, CSEC were most frequent in Cyprus (54.8 %), Romania (44.1%), Bulgaria (43.1%), Poland (39.3%) and Hungary (37.3%) [9]. Similarly, high CSEC rates have been reported in the USA, Australia and China, where 32%, 32.4% and 41% of births are by CSEC, respectively [8, 10, 12]. The reported rates of caesarean section are 3.3% in Africa, 33.7% in Latin America, 27.3% in Asia and 40.5% in China with an average of 15.9% [11, 13]. CSEC in Ukraine accounts for up to 23% of all births [14]. Over the past two decades, along with significant improvements in clinical obstetric care in many countries, the incidence rate of CAUTIs after CSEC remains an important issue.

Current guidelines for management of CAUTIs recommend the use of antibiotics for both treatment and postoperative infections. However, the growing antimicrobial resistance is limiting their use in Ukraine. Resistant CAUTI is becoming more and more pressing for medical specialists worldwide. In the available literature, studies on antimicrobial resistance of causing pathogens of CAUTIs after CSEC are limited. Monitoring of the prevalence of causing pathogens of CAUTIs after CSEC and antimicrobial resistance is necessary to enhance our knowledge of its epidemiology.

Incidence rates of CAUTI after CSEC and antimicrobial resistance of causing pathogens in Ukraine are currently unknown. This creates problems as well for physicians and as infection control professionals in hospitals of Ukraine. The prevalence of and causative agents of most CAUTIs after CSEC among female in-patients have not been studied in Ukraine. This was the basis for this study.

THE AIM

The aim of this study was to obtain the first national estimates of the current prevalence rate of CAUTIs after CSEC and antimicrobial resistance of causing pathogens in Ukraine.

MATERIALS AND METHODS

STUDY DESIGN, SETTINGS AND PARTICIPANTS

This a prospective multicenter cohort study was based on surveillance data for CAUTIs done in 15 women hospitals (located in Odessa, Ivano-Frankivsk, Vinnytsia, Volyn, Rivne, Chernivtsi, Lviv, Poltava, Cherkasy, Zhytomyr, Chernihiv, Dnipropetrovsk, and Kyiv, Ukraine) from 13 Ukrainian regions over 36 months period from 1st January, 2020 to 31st December, 2022. We compiled list of the 18 women medical centers. However, only 15 hospitals agreed to take part in our study. This study included fifty hemodynamically stable women without any therapeutic or surgical complications who underwent bladder catheterization after caesarean section. All participants were comparable in terms of indication for caesarean section, type of caesarean section, anaesthesia and same operating surgeon. All participants were local residents. Exclusion criteria: (a) Associated medical problem (e.g. Pregnancy Induced Hypertension or chronic hypertension, Gestational Diabetes Mellitus or Overt Diabetes Mellitus, Renal Disease etc.), (b). Surgical complication or previous Caesarean section, (c) Rupture of membranes > 4 hours, (d) Pre-existing UTI; (e) Patients with CAUTI present on admission and other

infections of the urinary tract. All patients received the antibiotic ceftriaxone intravenously for prophylaxis.

DEFINITION

CAUTI was evidenced by urine microscopy and culture and sensitivity done in urine sample. CAUTIs were defined according to the published CDC definition ((1) use of an indwelling foley for more than two consecutive days, (2) catheter in place on day of or day prior to event, (3) two or more symptoms concerning for CAUTI and (4) urine culture with no more than two species of organism of which at least one is a bacterium of $\geq 10^5$ CFU/mL) [Centers for Disease Control and Prevention (CDC). Urinary Tract Infection (Catheter-Associated Urinary Tract Infection [CAUTI] and Non-Catheter-Associated Urinary Tract Infection [UTI]) and Other Urinary System Infection [USI] Events, 2019.].

MICROBIOLOGICAL METHODS

Urine of all patients was sampled immediately before and 24 hours, and 48 hours post-surgery (cesarean section) and subjected to routine and microscopy examination and culture and sensitivity. Urine was collected as per the guidelines described earlier for culture and sensitivity with aseptic precautions and was transported immediately to the laboratory in a sterile container. The significant bacteriuria was 10^5 cfu/ml was taken into consideration while confirmation as CAUTI. The identification and antibiotic sensitivity was done by the disc diffusion test as recommended by European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines.

DATA COLLECTION

The data were collected using socio-demographic and clinical data sheets. These were all extracted from the patient's medical records in these units and daily observations of the nurses. The Infection control nurse collected all the details like name of the patient, age, date of catheterization, laboratory reports during her daily rounds. All data were collected using the Urinary Tract Infection (UTI) Checklist. It is scrutinized for the signs and symptoms as per CDC/NHSN criteria for confirmation as CAUTI. Caesarean section procedure was performed by conventional manner in all cases. The time of onset of surgery was designated as zero hour. The duration of surgery was defined as interval between the onset of surgery till completion of skin closure, measured by standard clock. The duration of hospital stay was defined as the time from onset of surgery to the hospital discharge. Discom-

Table I. Distribution of catheter-associated urinary tract infections (CAUTIs) after caesarean section (CSEC) procedures in the participating hospitals

Hospital	No. of CSEC procedures	CAUTIs (n/%)	95% CI
A	1,149	157/13.7	12.3 – 14.7
B	1,242	133/10.7	9.8 – 11.6
C	1,128	127/11.3	10.4 – 12.2
D	1,083	186/17.2	16.1 – 18.4
E	982	112/11.4	10.4 – 12.4
G	1,123	176/15.7	14.6 – 16.8
H	988	93/9.4	8.5 – 10.3
I	1,022	131/12.8	11.8 – 13.9
J	996	117/11.7	10.7 – 12.7
K	1,087	168/15.5	14.4 – 16.6
L	988	122/12.3	11.3 – 13.3
M	979	163/16.6	15.4 – 18.8
N	1,007	159/15.8	14.7 – 16.9
O	989	186/18.8	17.6 – 20.0
P	1,129	138/12.2	11.2 – 13.2
Total	15,892	2,168/13.6	13.3 – 13.9

CI, confidence interval

fort at first voiding was defined as burning, urging and difficulty at voiding. The time of first voiding was defined into two ways; First, as the time interval between removal of urinary catheter and first spontaneous voiding. Second, as the time interval from the onset of surgery and first spontaneous voiding. The time of first ambulation was defined as interval between onset of surgery and the time patient first ambulated. Method of voiding was noted in the form of use of bedpan or bathroom. Febrile morbidity due to UTI and postoperative urinary retention was also noted.

ETHICS

Ethical approval was obtained from the ethics committee of the Shupyk National Healthcare University of Ukraine, including the aim of the study and confirmation that all data collected, will be kept confidential and used for scientific research only. Informed consent was obtained from the study participants. Women who did not give informed consent for this study were excluded. The Study complies with the Declaration of Helsinki.

STATISTICAL ANALYSIS

Data entry and statistical analysis were done using EXCEL and SPSS 10.0 statistical software package. Data were presented using descriptive statistics in the form of frequencies and percentages. Results were compared and analysed using unpaired student t-test. In this study

all statistical analyses were two-sided and significance was set at $P < 0.05$.

RESULTS

PREVALENCE OF CAUTI

In this study total 15,892 catheterized women undergoing primary CSEC without any medical complication or pre-existing Urinary Tract Infections were included from January 2020 to December 2022. Total numbers of catheterized days were 63,568. Catheterization days ranged from 2 days to 9 days. During the study period applying CDC/NHSN methods of detection, a total of 2,168 CAUTIs were identified from 15,892 CSEC procedures. The prevalence of CAUTIs after CSEC in Ukraine was 13.6% [95% confidence interval (CI) 13.3-13.9].

The CAUTIs cases after CSEC in the participating hospitals varied significantly. This study showed that the situation with CAUTI after CSEC in Ukraine varies greatly by region. Lower CAUTIs percentages were reported by Ukrainian regions in the east and west while higher percentages were reported in the central region, north, and south of Ukraine. In terms of regions, fluctuations of the indicator values were observed – from the smallest in Volyn and Rivne region to the largest in Odessa, Lviv, Poltava region, and in Kyiv. Distribution of a catheterized women with CAUTIs undergoing primary CSEC delivery admitted to the women's hospitals of Ukraine are presented in Table I.

Table II. Characteristics of participants with catheter-associated urinary tract infections (CAUTI) after caesarean section (CSEC) in Ukraine (2020-2022)

Variables	Number of participants (n)	CAUTI		95% CI
		n	%	
Age of participants				
≤20	936	95	10.1	9.1 – 11.1
21-25	1,218	161	13.2	12.2 – 14.2
26-30	2,336	316	13.5	12.8 – 14.2
31-35	2,983	362	12.1	11.5 – 12.7
36-40	3,874	570	14.7	14.1 – 13.3
41-45	2,811	381	13.6	12.9 – 14.3
46-50	978	152	15.5	14.3 – 16.7
≥51	756	131	17.3	15.9 – 18.7
Total	15,892	2,168	13.6	13.3 – 13.9

CI, confidence interval

Table III. Distribution of microorganisms (n=2,168) identified in catheter-associated urinary tract infections (CAUTIs) after caesarean section (CSEC) in catheterized women in Ukraine (2020-2022)

Microorganisms	All isolates	Percentages, %
<i>Gram-positive cocci</i>	692	27,3
<i>Staphylococcus aureus</i>	91	13,1
<i>Coagulase-negative staphylococci</i>	162	23,4
<i>Enterococcus species</i>	265	38,3
<i>Streptococcus species</i>	108	15,6
<i>Other Gram-positive cocci</i>	66	9,5
<i>Gram-negative bacilli</i>	1,559	71,9
<i>Enterobacteriales</i>	1,196	76,7
<i>Escherichia coli</i>	421	35,2
<i>Citrobacter species</i>	91	7,6
<i>Enterobacter species</i>	103	8,6
<i>Klebsiella pneumoniae</i>	89	7,4
<i>Proteus mirabilis</i>	274	22,9
<i>Serratia marcescens</i>	59	4,9
<i>Providencia stuartii</i>	159	13,3
<i>Gram-negative non-fermentative bacilli</i>	363	23,3
<i>Acinetobacter species</i>	34	9,4
<i>Pseudomonas aeruginosa</i>	157	19,8
<i>Stenotrophomonas maltophilia</i>	72	3,3%
<i>Fungi</i>	17	0,8
<i>Candida species</i>	17	0,8
Total	2,168	100

The CAUTI rates were 5.8% [95% CI 5.6 – 6.0] after elective cesarean delivery and 7.8% [95% CI 7.6 – 8.0] after urgent CSEC. None of the patients died as a result of CAUTIs after CSEC procedure. The median time the duration of catheterized period for all CAUTIs was four days. The median age of women included in this study was 30 years (range 20–51). Characteristics of a catheterized women with CAUTI undergoing primary CSEC

delivery admitted to the women's hospitals of Ukraine are presented in Table II.

ANTIBIOTIC PROPHYLAXIS

In our study 100% of women for whom information was collected were given antimicrobial prophylaxis. In most hospitals (12/15) the first choice of antibiotic

agent was ceftriaxone. A further three hospitals used cefazoline or cefotaxim. Of 15,892 CSEC delivery participants who underwent chart review, 11,872 (74.7%) were prescribed combination ceftriaxone and metronidazole postpartum.

CAUSING PATHOGENS OF CAUTI

In this study a total of 2,971 different bacterial strains were isolated from 2,168 a catheterized women are with CAUTIs undergoing primary CSEC delivery. Causative microorganisms were recorded for all of the CAUTIs. Of all CAUTIs 37% (803/2,168) were reported to be polymicrobial. Gram-negative bacilli make up 71.9% and 31.9% gram-positive cocci from of all isolates. The most commonly identified pathogen were *Escherichia coli* (19.4%), *Proteus mirabilis* (12.6%), and *Enterococcus* species (12.2%). Other pathogens included Coagulase-negative staphylococci (7.5%),

Providencia stuartii (7.3%), *Pseudomonas aeruginosa* (7.2%), *Streptococcus* species (5%), *Enterobacter* species (4.8%), *Staphylococcus aureus* (4.2%), *Citrobacter* species (4.2%), *Klebsiella pneumoniae* (4.1%), *Stenotrophomonas maltophilia* (3.3%), *Serratia marcescens* (2.7%), *Acinetobacter* species (1.6), and *Candida* species (0.8%). Distribution of microorganisms identified in CAUTIs after CSEC in catheterized women in Ukraine shown in Table III.

ANTIMICROBIAL RESISTANCE

Bacterial uropathogens isolated from patients with CAUTI after CSEC revealed the presence of multidrug resistant pathogens. Imipenem was the single best antibiotic for all pathogens except *P. aeruginosa* where Amikacin was the drug of choice. The *Acinetobacter* species also showed very high resistance to all antibiotics except Imipenem. The overall proportion of extended spectrum beta-lactamases (ESBL) production among *Enterobacteriales* was 21.7%. The prevalence of ESBL production among *E. coli* isolates was significantly higher than in *K. pneumoniae* (29.7%, vs 13.8%). Resistance to third-generation cephalosporins was observed in 10.5% *K. pneumoniae* and *E. coli* 14.7% isolates. Methicillin resistance was observed in 9.1% of *S. aureus* (MRSA) and 7.5% CoNS (MRSE). Vancomycin resistance was observed in 5.7% of isolated enterococci (VRE). In this study carbapenem resistance was identified in 11.8% of *P. aeruginosa* isolates.

DISCUSSION

This study presents the first prospective multicenter cohort study for current prevalence of CAUTIs in catheter-

ized women undergoing primary CSEC and antimicrobial resistance of responsible pathogens in Ukraine. Our study showed that CAUTIs in catheterized women undergoing primary CSEC in Ukraine is a common occurrence. The prevalence of CAUTIs after CSEC in Ukraine was 13.6%. The situation with CAUTI after CSEC in Ukraine varies greatly by region. The most common uropathogens were *E. coli* (19.4%), *P. mirabilis* (12.6%), and *Enterococcus* spp. (12.2%) followed by CoNS (7.5%), *P. stuartii* (7.3%) and *Paeruginosa* (7.2%) from the cases of CAUTI. Our study showed that CAUTIs after CSEC in women in Ukraine were significantly associated with pathogens resistant to antibiotics. Many uropathogens isolated from CAUTI cases in Ukraine were found to be multidrug resistant. These findings correlate with various other studies [15, 16] where multidrug resistant uropathogens were isolated. Increase in the antibiotic resistance amongst the uropathogens indicates that they are hospital acquired and thus difficult to treat. This will be more dangerous if infection prevention practices are not followed during care of the catheterized patients. Possibly, higher incidence rate of CAUTIs after CSEC in Ukraine were significantly associated with many risk factors and antimicrobial resistance of responsible pathogens.

CSEC is a standard obstetric procedure initially recognized as a life-saving intervention to reduce maternal and fetal mortality. The rate of CSES has seen a soar in the past few decades. Urinary catheter (UC) can keep the bladder empty during CSEC procedure, preventing bladder injury and avoiding postoperative urinary retention [17, 18]. Most UTIs acquired in the hospital are associated with a urinary catheter, which is a tube inserted into the bladder through the urethra to drain urine. Therefore, catheters should only be used for appropriate indications and should be removed as soon as they are no longer needed. According to literature, the conventional time for UC removal is immediately after or within 12–24 h of CSEC [19]. Previous studies have reported that delayed UC removal following CSEC could reduce urinary urgency, decrease the incidence of urinary retention, and avoid recatheterization [17, 20]. However, growing evidence has demonstrated that early UC removal after CSEC can reduce the occurrence of UTI, contribute to early ambulation and reduce the length of hospital stay [21]. Onile et al. suggested that UC should be removed immediately after CSEC to minimize the risk of UTI [22]. However, Pandey et al. suggested that routine use of an indwelling UC during CSEC was unscientific and unnecessary, and use of an indwelling UC should be based on the prenatal physical condition of the pregnant woman [23]. Taken together, these studies indicate that the optimal time for UC removal following CS remains debatable [24].

Due to CAUTIs there is increase in the hospital stay of the patient along with increase in the use of higher antibiotics. Multiple risk factors can affect the occurrence of CAUTI. These include quality of aseptic technique, duration of catheterization, appropriate hand hygiene and care of catheter. They directly reflect on the quality care of the hospital. CAUTIs occur with high incidence if preventive protocols are not maintained. The most common practices shall include hand hygiene, close drainage system, aseptic method for insertion and catheter care along with daily need assessment with evidence-based observations. Our study showed moderate to high resistance in few uropathogens which is a concern for all in Ukraine.

Given of the rapidly developing antimicrobial resistance, the policy of antibiotic use for CAUTIs after CSEC treatment in each region should be determined depending on local data on resistance to antimicrobials. The chances of transmission of these multi drug resistant are high if health care workers do not follow

preventive practices meticulously [25]. Optimizing the management and empirical antimicrobial therapy may reduce the burden of UTIs, but prevention is the key element. This investigation provides valuable data as a first study for national surveillance of CAUTIs and potential comparison with data from other countries.

CONCLUSIONS

Our study showed that CAUTIs in catheterized women undergoing primary CSEC in Ukraine is a common occurrence and many cases are caused by pathogens that are resistant to antibiotics. Given of the rapidly developing antimicrobial resistance, the policy of antibiotic use for CAUTIs after CSEC treatment in each region should be determined depending on local data on resistance to antimicrobials. Optimizing the management and empirical antimicrobial therapy may reduce the burden of CAUTIs in catheterized women undergoing primary CSEC, but prevention is the key element.

REFERENCES

- Gastmeier P, Kampf G, Wischnewski N et al. Prevalence of nosocomial infections in representative German hospitals. *J Hosp Infect.* 1998;38(1):37-49. doi: 10.1016/s0195-6701(98)90173-6.
- Wagenlehner FM, Naber KG. Hospital-acquired urinary tract infections. *J Hosp Infect.* 2000;46(3):171-81. doi: 10.1053/jhin.2000.0821.
- Salmanov A, Shcheplov D, Svyrydiuk O et al. Epidemiology of healthcare-associated infections and mechanisms of antimicrobial resistance of responsible pathogens in Ukraine: a multicentre study. *J Hosp Infect.* 2023;131:129-138. doi: 10.1016/j.jhin.2022.10.007.
- Tissot E, Limat S, Cornette C et al. Risk factors for catheter-associated bacteriuria in a medical intensive care unit. *Eur J Clin Microbiol Infect Dis.* 2001;20(4):260-2. doi: 10.1007/s100960100480.
- World Health Organization. World Health Statistics 2009. <http://who.int/whosis/whostat/2009/en/index.html>. [date access 14.02.2023].
- Pandey D, Mehta S, Grover A et al. Indwelling Catheterization in Caesarean Section: Time To Retire It! *J Clin Diagn Res.* 2015;9(9):QC01-4. doi: 10.7860/JCDR/2015/13495.6415.
- WHO Statement on Caesarean Section Rates. https://apps.who.int/iris/bitstream/handle/10665/161442/WHO_RHR_15.02_eng.pdf?sequence=1 [date access 14.02.2023].
- Kawakita T, Landy HJ. Surgical site infections after cesarean delivery: epidemiology, prevention and treatment. *Matern Health Neonatol Perinatol.* 2017; 3: 12. doi: 10.1186/s40748-017-0051-3.
- Eurostat. Caesarean births in the EU Member States. <https://ec.europa.eu/eurostat/web/products-eurostat-news/-/DDN-20191217-1> [date access 14.02.2023].
- Li Z, Zeki R, Hilder L, Sullivan EA. Australia's mothers and babies 2011. Perinatal statistics series no. 28. Cat. no. PER 59. Canberra: AIHW National Perinatal Epidemiology and Statistics Unit. 2013. <https://www.aihw.gov.au/getmedia/265f3a72-1ea2-4bff-8a44-b16ca55d00f4/15639.pdf.aspx?inline=true>. [date access 14.02.2023].
- Lumbiganon P, Laopaiboon M, Gülmezoglu AM et al. Method of delivery and pregnancy outcomes in Asia: the WHO global survey on maternal and perinatal health 2007-08. *Lancet.* 2010;375(9713):490-9. doi: 10.1016/S0140-6736(09)61870-5.
- Betran AP, Merialdi M, Lauer JA et al. Rates of caesarean section: analysis of global, regional and national estimates. *Paediatr Perinat Epidemiol.* 2007;21:98-113. doi:10.1111/j.1365-3016.2007.00786.x.
- Villar J, Carroli G, Zavaleta N et al. Maternal and neonatal individual risks and benefits associated with caesarean delivery: multicentre prospective study. *BMJ.* 2007;335(7628):1025. doi: 10.1136/bmj.39363.706956.55.
- Salmanov AG, Vitiuk AD, Ishchak OM et al. Surgical site infection after cesarean section in Ukraine: results a multicenter study. *Wiad Lek.* 2021;74(4):934-939. doi: 10.36740/WLek202104123.
- Raka L, Mulliqi-Osmani G, Berisha L et al. Etiology and susceptibility of urinary tract isolates in Kosova. *Int J Antimicrob Agents.* 2004;23(1):S2-5. doi: 10.1016/j.ijantimicag.2003.09.009.
- Sabir S, Ahmad Anjum A, Ijaz T et al. Isolation and antibiotic susceptibility of E. coli from urinary tract infections in a tertiary care hospital. *Pak J Med Sci.* 2014;30(2):389-92.

17. El-Mazny A, El-Sharkawy M, Hassan A. A prospective randomized clinical trial comparing immediate versus delayed removal of urinary catheter following elective cesarean section. *Eur J Obstet Gynecol Reprod Biol.* 2014;181:111-4. doi: 10.1016/j.ejogrb.2014.07.034.
18. Cantone D, Pelullo CP, Cancellieri M et al. Can antenatal classes reduce the rate of cesarean section in southern Italy? *Women Birth.* 2017;30(2):e83-e88. doi: 10.1016/j.wombi.2016.09.004.
19. Meshawy A, Ghanem E, Meshawy E et al. Early versus delayed removal of indwelling urinary catheter after elective cesarean delivery: systematic review and meta-analysis of randomized controlled trials. *J Matern Fetal Neonatal Med.* 2020;33(16):2818-2825. doi: 10.1080/14767058.2018.1557142.
20. Nakawuki AW, Nekaka R, Ssenyonga LVN et al. Bacterial colonization, species diversity and antimicrobial susceptibility patterns of indwelling urinary catheters from postpartum mothers attending a Tertiary Hospital in Eastern Uganda. *PLoS One.* 2022;17(1):e0262414. doi: 10.1371/journal.pone.0262414.
21. Basbug A, Yuksel A, Ellibeş et al. Early versus delayed removal of indwelling catheters in patients after elective cesarean section: a prospective randomized trial. *J Matern Fetal Neonatal Med.* 2020;33(1):68-72. doi: 10.1080/14767058.2018.1487394.
22. Onile TG, Kuti O, Orji EO et al. A prospective randomized clinical trial of urethral catheter removal following elective cesarean delivery. *Int J Gynaecol Obstet.* 2008;102(3):267-70. doi: 10.1016/j.ijgo.2008.04.020.
23. Pandey D, Mehta S, Grover A et al. Indwelling Catheterization in Caesarean Section: Time To Retire It! *J Clin Diagn Res.* 2015;9(9):QC01-4. doi: 10.7860/JCDR/2015/13495.6415.
24. Hou D, Jia Y, Han A et al. Effect of urinary catheter removal at different times after caesarean section: A systematic review and network meta-analysis. *Eur J Obstet Gynecol Reprod Biol.* 2023;280:160-167. doi: 10.1016/j.ejogrb.2022.12.002.
25. Salmanov A, Shchekhlov D, Artyomenko V et al. Nosocomial transmission of multi-drug-resistant organisms in Ukrainian hospitals: results of a multi-centre study (2019-2021). *J Hosp Infect.* 2022;132:104-115. doi: 10.1016/j.jhin.2022.12.008.

We thank the participating hospitals and the infection control community for their diligent efforts in performing the prevalence surveys of CAUTIs after CSEC. The findings and conclusions in this study are those of the authors.

ORCID and contributorship:

Aidyn G. Salmanov: 0000-0002-4673-1154^{A,C,F}
 Volodymyr Artyomenko: 0000-0003-2490-375X^{B-D,F}
 Olena M. Susidko: 0000-0002-4840-0033^{B-D,F}
 Svitlana M. Korniyenko: 0000-0003-3743-426X^{B-D,F}
 Orusia A. Kovalyshyn: 0000-0002-9710-0694^{B-D,F}
 Oleksandr A. Voloshyn: 0000 0002- 6586- 5449^{B-D,F}
 Oleg V. Golyanovskiy: 0000-0002-5524-4411^{B-D,F}

Conflict of interest:

The Authors declare no conflict of interest

CORRESPONDING AUTHOR

Aidyn G. Salmanov

Shupyk National Healthcare University of Ukraine
 9 Dorohozhytska St., 04112 Kyiv, Ukraine
 tel: +380667997631
 e-mail: mozsago@gmail.com

Received: 09.01.2023

Accepted: 16.05.2023

A - Work concept and design, **B** - Data collection and analysis, **C** - Responsibility for statistical analysis, **D** - Writing the article, **E** - Critical review, **F** - Final approval of the article

ORIGINAL ARTICLE

MENTAL HEALTH, QUALITY OF LIFE, SPIRITUAL DRYNESS AND ACEDIA SYMPTOMS IN PATIENTS SUFFERING FROM CHRONIC DISEASES

DOI: 10.36740/WLek202306102

Evangelos C. Fradelos¹, Maria Saridi¹, Vissarion Bakalis¹, Aikaterini Toska¹, Viktor Vus², Arndt Büssing³, Kyriakos Souliotis^{4,5}

¹UNIVERSITY OF THESSALY, LARISSA, GREECE

²INSTITUTE FOR SOCIAL AND POLITICAL PSYCHOLOGY NAES OF UKRAINE, KYIV, UKRAINE

³UNIVERSITY OF WITTEN/HERDECKE, HERDECKE, GERMANY

⁴UNIVERSITY OF PELOPONNESE, CORINTH, GREECE

⁵HEALTH POLICY INSTITUTE, ATHENS, GREECE

ABSTRACT

The aim of the present study is to examine mental health, quality of life, acedia and spiritual dryness in patients suffering from chronic diseases.

Materials and method: Data were collected by special design instrument for the needs of the present study. Descriptive statistics and inferential statistics were applied and the analysis was carried out with IBM SPSS 26 and JASP 0.14.01.

Results: From the total of 210 participants, 106 (50.4%) were male, the mean age was 62.9 years, and the majority of them were diagnosed with type 2 diabetes. 50 (23.8%) of the participants suffer from anxiety and 39 (18.6%) from depression. In addition, 17.1% experience phases of spiritual dryness frequently or regularly. Physical quality of life component, was associated with the following variables: live from faith, psychological wellbeing, type of disease and age. This model can predict 31.1% of the variance. In terms of psychological wellbeing, the variables living arrangement, awe/gratitude, anxiety, and spiritual dryness can interpret 41.5% of the variance. When it comes to depression, we found that wellbeing, awe/gratitude are predictors of depressive symptoms, explaining at least 14.1% of the variance. Finally, anxiety can be predicted by wellbeing, awe/gratitude, and the type of the disease, interpreting 17.2% of the variance.

Conclusions: Patients suffering from chronic diseases are experiencing spiritual dryness and acedia symptoms, and those aspects can be associated with various domains of health and wellbeing.

KEY WORDS: chronic diseases; mental health; quality of life; spiritual dryness; acedia symptoms

Wiad Lek. 2023;76(6):1332-1341

INTRODUCTION

Chronic illness is defined as a condition that lasts a year or more and requires continued medical care and/or limitations of daily activities throughout a person's lifetime [1]. Chronic diseases include communicable diseases (e.g. AIDS,), non-communicable diseases (e.g. kidney failure, cancer, heart disease, diabetes mellitus, chronic lung diseases), chronic mental diseases (e.g. schizophrenia, depression), neurological disorders (e.g. epilepsy) and gradually worsening diseases (e.g. blindness, spinal cord atrophy) [1]. Several of these result in changes of self-image and, depending on the severity of disease, may threaten one's sense of power or competence and possible dependence on others. The decline in strength, fatigue, pain, alopecia, the side effects of the treatment drugs question the functionality of the body of the sufferers [2].

Chronic illness can affect the physical, psychological, social, and spiritual dimensions of a patient's life [3]. Spirituality and mental health are linked, and many people find that their spiritual beliefs and practices have a positive impact on their emotional and mental well-being [4] and these are thus utilized as a resource to cope. Studies have shown that engaging in spiritual practices, such as prayer, meditation, or attending religious services, can help reduce stress, lower blood pressure, and improve overall health. These observations are often found in healthy people, and cannot easily transferred to all patients with different chronic diseases, independently from cultural or religious context. In addition, having a sense of purpose and meaning in life, which is one specific aspect of the multidimensional construct spirituality, may to play

a role in mental health and resilience [3]. Some spiritual practices and beliefs can help individuals find this sense of purpose and connect with something greater than themselves, which can lead to greater overall well-being [5].

On the other hand, spiritual distress refers to a state of lack of inner peace and connectedness to loved ones, an inability to accept what is happening, find meaning in life, and hope for the future [3]. Such spiritual struggles are connected with low mental health [6]. Spiritual dryness refers to a feeling of heaviness, emptiness, or disconnectedness towards God or the Sacred that can arise when one's spiritual practice or beliefs are not providing the sense of fulfillment and purpose they once did]. Main predictors are low perception of the Sacred in life and low sense of coherence on the one hand, and depressive symptoms and emotional exhaustion on the other hand [7]. This can be a source of stress and anxiety, which can contribute to poor mental health. In turn, poor mental health can exacerbate spiritual dryness, creating a vicious cycle. For example, depression and anxiety can make it difficult to connect with others and to feel a sense of purpose in life, which in turn can deepen feelings of spiritual emptiness [8,9]. In addition, one more term that is linked to spiritual dryness is acedia [10]. The definition of this term ranges from the lack of care to the lack of care for spiritual matters. Often, the term has been used with depression and described as weariness, listlessness, boredom, ennui, meaninglessness, despair, despondency, and anhedonia, indicating the link to depression [10]. Acedia is considered to be a contribution factor of spiritual dryness, with symptoms of spiritual/emotional fatigue, tiredness or even boredom [11].

Despite the fact that spirituality and spiritual needs have been thoroughly investigated [12-14], the relationship between spiritual dryness, acedia, mental health, and quality of life of patients suffering from chronic diseases was rarely addressed. One paper addressed these perceptions in the specific group of Seventh-day Adventists [11]. In addition, there is a lack of instruments to assess those concepts in the Greek language.

THE AIM

Thus, the aim of the present study is to assess the validity of the Greek version of instruments addressing of spiritual dryness and acedia on the one hand, and the resources Awe and Gratitude and Transformative Spirituality on the other hand. These indicators of spiritual and mental health were addressed in patients suffering from chronic diseases.

MATERIALS AND METHODS

STUDY PARTICIPANTS

From June 2022 to August 2022, individuals from the Greek region of Larissa took part in an anonymous survey with standardized measures using the convenience sample approach. Participants were recruited during their routine check-up at an outpatient healthcare facility. To be eligible for the study, participants had to be Greek-speaking and at least 18 years old, as well as have been diagnosed with at least one chronic health condition.

ETHICS

The study was approved from the ethics committee of Nursing Department n. ND 806.10.06.2022.

MEASURES

The survey included fundamental sociodemographic inquiries on gender, age, nationality, religious affiliation, and the degree of perceived pressure. The Greek version of the measures used in the survey will be described below. To create the Greek language version, a bilingual researcher translated the original English version, which was then reviewed and adjusted by another bilingual researcher. After back-translating it into English, any inconsistencies were corrected. Seven nursing and medical experts were invited to comment on how well the items fit within the context of Greek culture in order to assess the content validity of the items. Next, the tool's cognitive assessment was conducted utilizing the feedback of ten chronic patients who met the inclusion requirements (those over 18 years old, and fluent in Greek) in order to examine the tool's clarity and readability of the questions.

SPIRITUAL DRYNESS

The Spiritual Dryness Scale (SDS) was developed as a measure to assess a specific form of spiritual struggle [15]. The scale consists of six items that demonstrate good internal consistency (Cronbach's $\alpha = 0.87$). Specific statements make reference to the perceptions of God's distance, that one's prayers are not heard, as well as the feelings of spiritual emptiness, spiritual exhaustion, and being abandoned by God. The components of the instrument were designed with religious people's everyday experiences in mind. We added one more item (SDS0) to this study to address the question of "deep longing for God". A Likert scale with response options ranging from not at all (1) to regularly (5) was used by

participants to rate their responses. The SDS scores are the mean scores and reflect the perceived frequency of these perceptions [15].

AWE AND GRATITUDE

The seven-item Awe/Gratitude scale (GrAw-7)), which has high psychometric qualities (Cronbach's alpha = 0.82), was used to measure the perceptions of standing still in wondering awe with subsequent feelings of gratitude [16]. It is regarded as an indicator of experienced spirituality. The experiential elements of being affected and touched by specific events and/or places, nature-related reactions to suspending daily tasks, and the ensuing feelings of awe and gratitude are clearly the focus of this measure. The particular statements are, "I stop and then think of so many things for which I'm really grateful," "I stop and am captivated by the beauty of nature," "I pause and stay spellbound at the moment," and "In certain places, I become very quiet and devout." The scoring system for each item was a 4-point scale: 0, never; 1, seldom; 2, often; and 3, regularly [16].

TRANSFORMATORY ASPECTS OF SPIRITUALITY

To address transformatory aspects of spirituality, the 26-item Franciscan Spirituality questionnaire (FraSpir) was used. It differentiates four topics: "Living from the Faith/Searching for God" as the intentional and experiential aspect of spirituality, and "Peaceful Attitude/Respectful Treatment"; "Commitment to the Disadvantaged and Creation"; and "Attitude of Poverty" as the behavioral consequences of transformation [17]. Their primary version's internal reliability coefficient Cronbach's alpha ranges from 0.79 to 0.97 [14]. Each item was rated on a five-point scale from 0 (does not apply at all) to 4 (applies very much). 11 items from the scale's Living from the Faith/Searching for God subscale were employed in the current study [17].

ACEDIA SYMPTOMS

In order to evaluate Acedia symptoms in a broader context, we used items that had previously been used in a study among religious brothers and sisters. Ten items were utilized, of which two were meant to be informative items ("My prayer life is rich and fulfilling," "In prayer I am focused and present before God"), while the other eight discussed the experiences of challenges in prayer life (in terms of inattentiveness and distance) and overbearing spiritual demands (in terms of perceived overcharging demands referred to

God). Examples of the former topic include: "I am more passive in prayer and without any inner involvement," "My prayer life doesn't excite me so much anymore," "I really enjoy only a little in my spiritual life," "I don't really care whether I find God in prayer or not", while the latter topic was addressed by items such as "What God asks of me is more than I can give", "What God asked of me is just too much", "I really don't know what God wants from me", "Somehow, everything got too much for me". In this paper, a reliability analysis of these items will be provided. On a Likert scale, the possible responses were not at all (1), rarely (2), occasionally (3), fairly often (4) and regularly (5) [18].

MENTAL HEALTH

The Patient Health Questionnaire-2 (PHQ-2) and the Generalized Anxiety Disorder-2 (GAD-2) questionnaires were created as ultra-short depression and anxiety screening tools that might be used in epidemiological studies [16-18]. Two questions make up the PHQ-2, which has been shown to be sensitive and specific for identifying depressive disorders. The two-question GAD-2 questionnaire also seems to have acceptable accuracy for identifying post-traumatic stress disorder, generalized anxiety disorder, panic, and social anxiety. Each item in both questionnaires asks respondents to rank on a four-point scale ranging from "0 = not at all" to "3 = nearly every day". PHQ-2 and GAD-2 total scores are determined by summing the results of the two questions, yielding a score for each questionnaire ranging from 0 to 6, with a higher score indicating a more severe mental health condition. On both the PHQ-2 and GAD-2 scales, the optimal cut-point is 3 based on receiver-operating characteristic curve analysis [19-21].

WELLBEING

The 5-item WHO-Five Well-being Index (WHO-5) was used to measure psychological wellbeing (Bech et al., 2003). The representative items are "I have felt cheerful and in good spirits" or "My daily life has been filled with things that interest me." A 6-step grading scale, from at no time (0) to all the time (5), was used to rate the intensity of feelings over the past two weeks (5). The reported WHO-5 total scores here correspond to a 100% level [0-100], where scores under 50 are signs of diminished wellbeing [22].

QUALITY OF LIFE

The 12-question SF-12 health survey questionnaire was used. It was designed as a shorter substitute for

Table I. Demographic characteristics of the sample (n=210)

		Frequency	Percent %
Gender	Male	106	50,4
	Female	104	49,5
Age (Mean±SD)			62.9±12.7
Area Of Residence	Rural	7	3,3
	Semi-Urban	28	13,3
	Urban	175	83,3
Marital Status	Single	6	2,8
	Married	181	86,1
	Divorced	1	0,4
	Widowed	22	10,4
Living Alone	Yes	29	13,8
	No	181	86,1
Educational Level	Elementary	39	18,5
	Junior High School	56	26,6
	High School	50	23,8
	Student	2	0,9
	University	63	30,0
	Occupation	Unemployed	1
Occupation	Household	20	9,5
	Freelancer	26	12,3
	Private	44	20,9
	Public	24	11,4
	Pension	95	45,2
	Health Status	More Or Less Healthy	3
Acute		2	0,9
Chronic		51	24,2
Mental		18	8,5
Neurological		5	2,3
Pain		9	4,2
Cnacer		14	6,6
Diabetes Type II		108	51,4
Type Disease	Diabetes	108	51,4
	Other	102	48,5
Duration Of Disease (Mean±SD)			20.8±13.2

Translation and validation of Spiritual Dryness, Awe and Gratitude, Franciscan Spirituality Questionnaire (FraSpir) and Acedia scales.

the SF-36 questionnaire, which is utilized in large-scale studies, particularly when the outcomes of interest are general physical and mental health rather than the distinctive diagram comprised of the eight scales of the SF-36 [23]. All 12 questions have previously been employed to assess the total physical and mental components (PCS-12 and MCS-12). The validity of the Greek version was determined in a study using a stratified representative sample (n = 1,005) of a healthy Greek population [24].

STATISTICAL ANALYSIS

Descriptive statistics (frequency, mean values, and standard deviations) and inductive statistics were used to examine the data in order to provide answers to all of the research questions. With the use of SPSS 26.0 and JASP, analyses of variance (ANOVA), independent t-tests, first-order correlations (Spearman rho), regressions, internal consistency (Cronbach's coefficient), and confirmatory factor analyses were performed.

Table II. Scales of the study descriptive statistics

	Mean	SD	Min	Max
Under pressure	55.11	15.64	10.00	90.00
SF-12 physical component scale 12 (PCS12)	50.01	8.15	22.98	60.66
SF-12 mental component scale 12 (MCS12)	51.11	7.95	27.34	62.85
wellbeing	60.70	14.42	8.00	100.00
Depression	2.33	1.00	0.00	4.00
Anxiety	2.29	0.99	0.00	4.00
Awe Gratitude	75.77	16.79	28.54	99.90
Live from the Faith	1.93	0.69	0.40	4.00
Spiritual Dryness	2.75	0.77	1.00	4.83
Acedia	2.76	0.66	1.00	4.25
Acedia Subscale Excessive Spiritual Demands	2.705	0.732	1.000	4.750
Acedia Subscale Difficulties Prayer Life	2.819	0.683	1.000	4.250

Table III. Differences between T2D and other chronic conditions

	Group	Mean	SD	t-test	p
Under pressure	Diabetes	58.05	13.68	2.847	0.005
	other	52.01	16.99		
PCS12	Diabetes	51.32	6.09	2.195	0.029
	other	48.79	9.56		
MCS12	Diabetes	51.55	6.55	0.744	0.458
	other	50.70	9.09		
wellbeing	Diabetes	59.18	12.51	-1.577	0.116
	other	62.31	16.10		
Depression	Diabetes	2.39	1.05	1.220	0.224
	other	2.19	0.86		
Anxiety	Diabetes	2.38	1.04	1.756	0.081
	other	2.09	0.86		
Awe Gratitude	Diabetes	74.39	14.15	-1.225	0.222
	other	77.23	19.16		
Live from the Faith	Diabetes	1.87	0.56	-1.286	0.200
	other	2.00	0.79		
Spiritual Dryness	Diabetes	2.95	0.46	3.988	<0.001
	other	2.53	0.96		
Acedia	Diabetes	2.94	0.31	4.306	< 0.001
	other	2.56	0.85		
Acedia Subscale Excessive Spiritual Demands	Diabetes	2.91	0.30	4.513	< 0.001
	other	2.48	0.95		
Acedia Subscale Difficulties Prayer Life	Diabetes	2.97	0.43	3.482	< 0.001
	other	2.65	0.84		

RESULTS

From the total of 210 participants, 106 (50.4%) were male, the mean age was 62.9 years, and the majority of them were diagnosed with type 2 diabetes. Detailed demographic and health related characteristics are presented in table I.

Forward and backward translation procedure was performed in order to obtain the Greek version of the instruments. Test – retest reliability was performed to examine the stability of the instruments overtime. High and strong correlation was observed between two administrations ($p < 0.001$) indicating the stability

Table IV. Pearson's Correlations between quality of life , mental health and spirituality measures

Variable		Under pressure	PCS12	MCS12	wellbeing	Depression	Anxiety	Awe Gratitude	Live from the Faith	Spiritual Dryness	Acedia	Excessive Spiritual Demands
PCS12	Pearson's r	-0.120	-									
	p-value	0.093	-									
MCS12	Pearson's r	-0.159	0.283	-								
	p-value	0.026	< .001	-								
wellbeing	Pearson's r	-0.228	0.500	0.597	-							
	p-value	< .001	< .001	< .001	-							
Depression	Pearson's r	0.112	-0.076	-0.299	-0.334	-						
	p-value	0.158	0.360	< .001	< .001	-						
Anxiety	Pearson's r	0.179	-0.065	-0.376	-0.348	0.811	-					
	p-value	0.024	0.435	< .001	< .001	< .001	-					
Awe Gratitude	Pearson's r	-0.002	0.016	0.224	0.119	0.216	0.218	-				
	p-value	0.977	0.829	0.002	0.084	0.006	0.006	-				
Live from the Faith	Pearson's r	-0.137	-0.189	-0.068	0.056	0.151	0.121	0.245	-			
	p-value	0.047	0.008	0.343	0.421	0.057	0.128	< .001	-			
Spiritual Dryness	Pearson's r	0.261	0.008	0.042	-0.288	-0.013	-0.014	-0.103	-0.557	-		
	p-value	< .001	0.915	0.560	< .001	0.871	0.862	0.138	< .001	-		
Acedia	Pearson's r	0.428	-0.103	0.057	-0.207	-0.022	0.052	0.023	-0.375	0.710	-	
	p-value	< .001	0.152	0.431	0.003	0.785	0.516	0.736	< .001	< .001	-	
Excessive Spiritual Demands	Pearson's r	0.433	-0.081	0.068	-0.165	-0.077	-0.009	0.012	-0.354	0.679	0.940	-
	p-value	< .001	0.257	0.343	0.017	0.331	0.907	0.866	< .001	< .001	< .001	-
Difficulties Prayer Life	Pearson's r	0.366	-0.112	0.037	-0.225	0.024	0.083	0.033	-0.348	0.649	0.931	0.752
	p-value	< .001	0.119	0.610	0.001	0.760	0.298	0.637	< .001	< .001	< .001	< .001

of the scales over time. Finally, confirmatory factor analysis performed to verify the factor structure of the instruments. Based on the results of the confirmatory factor analysis for the Spiritual Dryness Scale, it was determined that the Greek version of the SDS was appropriate. The comparative fit index (CFI) was 0.957, the goodness of fit index (GFI) was 0.924, and the standardized root mean square residual (SRMR) was 0.028. Confirmatory factor analysis results revealed that the Greek version of Awe and Gratitude scale suited the data fairly well. The comparative fit index (CFI) was 0.807, the goodness of fit index (GFI) was 0.851, and the standardized root mean square residual (SRMR) 0.070. According to the findings of the confirmatory factor analysis for the Franciscan Spirituality Questionnaire (FraSpir), the Greek version had a fair fit. The comparative fit index (CFI) was 0.795, the goodness of fit index (GFI) was 0.805 and the standardized root mean square residual (SRMR) was 0.071. Results of a confirmatory factor analysis of Acedia Scale showed that the Greek version had a satisfactory fit. The comparative fit index (CFI) was 0.958, the goodness of fit index (GFI) was 0.925, and the standardized root mean square residual (SRMR)

was 0.042. Results of a confirmatory factor analysis of Wellbeing scale showed that the Greek version had a satisfactory fit. The comparative fit index (CFI) was 0.950, goodness of fit index (GFI) was 0.927, and the standardized root mean square residual (SRMR) was 0.042.

Regarding the scale's descriptive statistic, we can observe that participants are reporting average quality of life as the mean scores of SF12 are slightly above 50, which is considered to be the mean value of the theoretical range. Similarly, the mean values of the depression and anxiety scales are above the value 2, that is the mean of the theoretical range. While taking into consideration the cut-off value of 3 on those scales 50 (23.8%) of the participants suffer from anxiety and 39 (18.6%) from depression. In addition, 17.1% experience phases of spiritual dryness frequently or regularly. Detailed descriptive statistics of the scales are presented in table II.

Bivariate analysis revealed that type 2 diabetes patients are reporting better physical quality of life compared to other chronic patients, more spiritual dryness, and more acedia symptoms. A Detailed bivariate analysis is presented in table III.

Table V. Predictors of Quality of life and Mental health

		Coefficients					
Model		Unstandardized	Standard Error	Standardized	t	p	
Physical Quality of life component	(Intercept)	59.200	4.878		12.136	< .001	
	Live from the Faith	-4.363	0.884	-0.360	-4.933	< .001	
	wellbeing	0.151	0.043	0.268	3.512	< .001	
	Type disease -T2D reference category						
	Other chronic conditions	-2.897	1.037	-0.199	-2.794	0.006	
	Age	-0.093	0.045	-0.168	-2.064	0.041	
F(4,140)=17.231, adR2=31.1%, p<0.001							
Mental Quality of life component	(Intercept)	18.983	5.518		3.440	< .001	
	wellbeing	0.252	0.039	0.450	6.397	< .001	
	Living alone yes reference category						
	No	5.125	1.391	0.238	3.686	< .001	
	Anxiety	-1.941	0.480	-0.280	-4.040	< .001	
	Awe Gratitude	0.077	0.031	0.169	2.513	0.013	
	Spiritual Dryness	2.183	0.936	0.157	2.333	0.021	
	F(5,139)=21.424, adR2=41.5%, p<0.001						
Depression	(Intercept)	2.913	0.527		5.528	< .001	
	wellbeing	-0.027	0.006	-0.327	-4.424	< .001	
	Awe Gratitude	0.013	0.005	0.207	2.792	0.006	
F(2,155)=13.920, adR2=14.1%, p<0.001							
Anxiety	(Intercept)	3.026	0.515		5.879	< .001	
	wellbeing	-0.026	0.006	-0.321	-4.380	< .001	
	Awe Gratitude	0.017	0.005	0.264	3.486	< .001	
	Type disease -T2D reference category						
	Other chronic conditions	-0.352	0.164	-0.164	-2.141	0.034	
F(3,154)=12.361, adR2=17.2%, p<0.001							

In order to examine the relationship between mental health and quality of life and spirituality measures, we performed correlations between the scales. A few significant and moderate correlations were observed. The detailed results of the Pearson correlation test are presented in table IV.

Finally, in order to examine possible predictors of quality of life and mental health, linear regression analysis with the stepwise method was performed. Regarding the physical quality of life component, we observed that live from faith, wellbeing, type of disease, and age can predict 31.1% of the variance. Regarding mental quality of life component wellbeing, living arrangement, awe gratitude, anxiety, and

spiritual dryness can interpret 41.5% of the variance. When it comes to depression, we found that wellbeing, awe and gratitude are predictors of depression, explaining 14.1% of the variance. Finally, anxiety can be predicted by wellbeing, awe, gratitude, and the type of the disease, interpreting 17.2% of the variance (Table V).

DISCUSSION

The aim of this study was to examine the mental health and quality of life of patients suffering from chronic conditions, as well as the possible effect that spiritual aspects can have on those domains. According

to our results, to live from the faith, wellbeing, type of disease, age, living alone, anxiety, awe gratitude, and spiritual dryness can have an important impact on physical and mental quality of life of chronic patients. Regarding mental health wellbeing, the type of disease and awe gratitude can impact the mental health of patients.

The chronicity of the disease is a particularly stressful situation and causes fear and uncertainty about the outcome of the disease and the new living conditions. In addition to negative emotions and physical problems, chronic disease causes mainly pain, weakness, and fatigue, as well as limitation and changes in daily habits and side effects from medication. As patients are challenged to cope with the new situation caused by the disease, recovery and adaptation strategies are developed [25]. According to our results, patients are reporting high levels of QoL, and almost one in five patients are reporting poor mental health. This result is in opposition to various studies in the international literature [26]. Although a recent study in Greece among hemodialysis patients also reported good levels of QoL among the patients, the variety of results can be attributed to cultural factors as well as the family structure and enhanced social support that patients can have in other cultures [27]. In the present study, 23.8% of the participants suffered from anxiety and 18.6% from depression. The percentages for the prevalence of depression and anxiety vary among studies on the emotional burden of chronic conditions [28-31]. An explanation that could be given is the different diseases, the different family and social environments, and the support that individuals get from them. Also, one could say that the acceptance of the new lifestyle varies from study to study and from disease to disease. Finally, we must be aware that the amount of information that patients have about their chronic health problem and the perceptions they have about their illness contribute to their better adaptation to it.

According to our results, aspects of spirituality, spiritual dryness, and acedia were found to be related to aspects of mental health and wellbeing. This result is in accordance with recent studies, which conclude that spirituality plays an important role in improving physical and mental health. Researchers argue that maintaining spirituality and religiosity can improve health and wellbeing. In addition, spirituality can help individuals maintain hope, meaning, purpose, and a sense of peace. Patients spiritual/religious practices and beliefs can help them cope with chronic illness [31]. It is worth mentioning, however, that this is a deeply subjective concept, that is mentioned in an

internal system of values and beliefs. Also, it is worth mentioning that the Greek population, as measured, is characterized at a rate of almost too much to be very religious and close to God.

This study revealed that diabetic patients are reporting better QoL and more spiritual dryness and acedia symptoms compared to other chronic conditions. This is a conflicting study that opposes studies in the international literature that report poor QoL in diabetic patients compared to controls [32]. Yet our rest sample is composed of individuals suffering from other health conditions, some of which are serious and life-threatening, such as cancer. Previous studies conclude that diabetes can alter not only physical health but also social, psychological, and spiritual health and wellbeing. As stated above, patients who can maintain a sense of purpose in life, productivity, and reason for living are usually reported to have better health outcomes [33].

Despite the fact that this study provided important information regarding physical, mental, and spiritual aspects of health, it has some limitations. The cross-sectional design of the study doesn't allow a deeper understanding of the effect that spirituality can have on physical and mental health. The sample of the present study was a convenience sample and came from a single center, which was in fact in regional Greece, and therefore the results cannot be generalized to the entire population of Greek patients suffering from chronic diseases. By extension, it remains important to evaluate the association between mental health, spirituality, and QoL in a larger sample of patients in a more representative sample.

CONCLUSIONS

Patients suffering from chronic diseases are experiencing spiritual dryness and acedia symptoms, and those aspects can be associated with various domains of health and wellbeing. Spirituality helps patients cope with symptoms and reduced functioning while still maintaining overall well-being. Finding meaning in life is equally important for mental resilience and developing recovery methods and strategies, and this can be achieved through spirituality. For many people, religion and spirituality are central to their lives. These axes should be considered during its design to provide care to these patients, as there is considerable evidence in the literature to support this. Spiritual orientation can offer a sense of destination in life while providing a multitude of coping strategies for stressor situations and ultimately leading to self-empowerment for dealing with stress, even adapting to disease.

REFERENCES

1. Martin CM. Chronic disease and illness care: adding principles of family medicine to address ongoing health system redesign. *Can Fam Physician*. 2007 Dec;53(12):2086-91. PMID: 18077734; PMCID: PMC2231531.
2. Van Wilder, L., Pype, P., Mertens, F. et al. Living with a chronic disease: insights from patients with a low socioeconomic status. *BMC Fam Pract* 22, 233 (2021). <https://doi.org/10.1186/s12875-021-01578-7>
3. Klimasiński M, Baum E, Praczyk J, Ziemkiewicz M, Springer D, Cofta S, Wieczorowska-Tobis K. Spiritual Distress and Spiritual Needs of Chronically Ill Patients in Poland: A Cross-Sectional Study. *Int J Environ Res Public Health*. 2022 May 1;19(9):5512. doi: 10.3390/ijerph19095512. PMID: 35564907; PMCID: PMC9101665.
4. Fradelos EC, Tzavella F, Koukia E, Papathanasiou IV, Alikari V, Stathoulis J, Panoutsopoulos G, Zyga S. Integrating chronic kidney disease patient's spirituality in their care: health benefits and research perspectives. *Mater Sociomed*. 2015 Oct;27(5):354-8. doi: 10.5455/msm.2015.27.354-358. Epub 2015 Oct 5. PMID: 26622206; PMCID: PMC4639341.
5. Brown DR, Carney JS, Parrish MS, Klem JL. Assessing spirituality: The relationship between spirituality and mental health. *Journal of spirituality in mental health*. 2013 Apr 1;15(2):107-22.
6. Büssing A, Kerdar SH, Akbari ME, Rassouli M. Perceptions of Spiritual Dryness in Iran During the COVID-19 Pandemic. *J Relig Health*. 2021 Oct;60(5):3347-3371. doi: 10.1007/s10943-021-01360-0. Epub 2021 Jul 29. PMID: 34327572; PMCID: PMC8321505.
7. Wilt JA, Exline JJ, Pargament KI. Daily measures of religious/spiritual struggles: Relations to depression, anxiety, satisfaction with life, and meaning. *Psychology of Religion and Spirituality*. 2022 Aug;14(3):312.
8. Büssing A, Baumann K, Jacobs C, Frick E. Spiritual dryness in Catholic priests: Internal resources as possible buffers. *Psychology of Religion and Spirituality*. 2017 Feb;9(1):46.
9. Farahani AS, Kerdar SH, Ashrafzadeh H, Büssing A, Mehrnoush N, Akbari ME, Karami M, Tajalli S, Mojen LK, Rassouli M. The predictors of spiritual dryness among Iranian cancer patients during the COVID-19 pandemic. *Front Psychol*. 2023 Jan 20;13:1024009. doi: 10.3389/fpsyg.2022.1024009. PMID: 36743631; PMCID: PMC9895950.
10. Irving TD. Acedia and the Evagrius Antidotes to Pastoral Burnout. https://scholar.smu.edu/cgi/viewcontent.cgi?article=1005&context=theology_ministry_etds.
11. Büssing A, Starck L, van Treeck K. Experience of Spiritual Dryness and Acedia Symptoms in Seventh-Day Adventists. *J Relig Health*. 2021 Apr;60(2):1261-1280. doi: 10.1007/s10943-020-01092-7. Epub 2020 Nov 2. PMID: 33136232; PMCID: PMC7997817.
12. Büssing A, Koenig HG. Spiritual Needs of Patients with Chronic Diseases. *Religions*. 2010;1:18-27. <https://doi.org/10.3390/rel1010018>
13. Drutchas A, Anandarajah G. Spirituality and coping with chronic disease in pediatrics. *RI Med J* (2013). 2014 Mar 3;97(3):26-30. PMID: 24596927.
14. Unantenne N, Warren N, Canaway R, Manderson L. The strength to cope: spirituality and faith in chronic disease. *J Relig Health*. 2013 Dec;52(4):1147-61. doi: 10.1007/s10943-011-9554-9. PMID: 22083464.
15. Büssing A, Gunther A, Baumann K, Frick E, Jacobs C. Spiritual dryness as a measure of a specific spiritual crisis in catholic priests: Associations with symptoms of burnout and distress. *Evid Based Complement Alternat Med*. 2013:246797. <https://doi.org/10.1155/2013/246797>.
16. Büssing A, Recchia DR, Baumann K. Validation of the gratitude/awe questionnaire and its association with disposition of gratefulness. *Religions*. 2018;9:117. <https://doi.org/10.3390/rel9040117>.
17. Büssing A, Recchia DR, Dienberg T. Attitudes and behaviors related to Franciscan-inspired spirituality and their associations with compassion and altruism in Franciscan brothers and sisters. *Religions*. 2018;9:324. <https://doi.org/10.3390/rel9100324>.
18. Büssing A. Geistliche Trockenheit bei Seelsorgern und Ordens-Christen. In: Büssing A, Dienberg T, eds. *Geistliche Trockenheit - empirisch, theologisch, in der Begleitung*. Münster: Aschendorff; 2019, p.79-103. (in German).
19. Kroenke K, Spitzer RL, Williams JB, Monahan PO, Löwe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Ann Intern Med*. 2007 Mar 6;146(5):317-25. doi: 10.7326/0003-4819-146-5-200703060-00004. PMID: 17339617.
20. Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care*. 2003 Nov;41(11):1284-92. doi: 10.1097/01.MLR.0000093487.78664.3C. PMID: 14583691.
21. Tsaras K, Papathanasiou IV, Mitsi D, Veneti A, Kelesi M, Zyga S, Fradelos EC. Assessment of Depression and Anxiety in Breast Cancer Patients: Prevalence and Associated Factors. *Asian Pac J Cancer Prev*. 2018 Jun 25;19(6):1661-1669. doi: 10.22034/APJCP.2018.19.6.1661. PMID: 29938451; PMCID: PMC6103579.
22. Bech P, Olsen LR, Kjoller M, Rasmussen NK. Measuring well-being rather than the absence of distress symptoms: A comparison of the SF-36 Mental Health subscale and the WHO-Five well-being scale. *International Journal of Methods in Psychiatric Research*. 2019;12(2):85-91. <https://doi.org/10.1002/mpr.145>
23. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992;30(6):473-483. doi: 10.1097/00005650-199206000-00002.
24. Kontodimopoulos N, Pappa E, Niakas D, Tountas Y. Validity of SF-12 summary scores in a Greek general population. *Health Qual Life Outcomes*. 2007;5:55. doi: 10.1186/1477-7525-5-55.

25. Petrie KJ. Coping with chronic illness. In: Llewellyn CD, Ayers S, McManus C et al., eds. The Cambridge handbook of psychology, health and medicine Cambridge University Press; 2019, p.110-114.
26. Megari K. Quality of Life in Chronic Disease Patients. Health Psychol Res. 2013 Sep 23;1(3):e27. doi: 10.4081/hpr.2013.e27.
27. Fradelos E. Predictors of quality of life in chronic kidney disease: The contribution of spirituality. Archives of Hellenic Medicine. 2020;37(2):227-36.
28. Uhlenbusch N, Löwe B, Härter M, Schramm C, Weiler-Normann C, Depping MK. Depression and anxiety in patients with different rare chronic diseases: A cross-sectional study. PloS one. 2019 Feb 20;14(2):e0211343.
29. Tarar ZI, Zafar MU, Farooq U, Ghous G, Aslam A, Inayat F, Ghouri YA. Burden of depression and anxiety among patients with inflammatory bowel disease: results of a nationwide analysis. International Journal of Colorectal Disease. 2022 Feb 1:1-9.
30. Smith KJ, Peterson MD, O'Connell NE, Victor C, Liverani S, Anokye N, Ryan JM. Risk of depression and anxiety in adults with cerebral palsy. JAMA neurology. 2019 Mar 1;76(3):294-300.
31. Lucette A, Ironson G, Pargament KI, Krause N. Spirituality and Religiousness are Associated With Fewer Depressive Symptoms in Individuals With Medical Conditions. Psychosomatics. 2016 Sep-Oct;57(5):505-13. doi: 10.1016/j.psych.2016.03.005.
32. Al-Shehri AH, Taha AZ, Bahnassy AA, Salah M. Health-related quality of life in type 2 diabetic patients. Ann Saudi Med. 2008 Sep-Oct;28(5):352-60. doi: 10.5144/0256-4947.2008.352.
33. Jafari N, Farajzadegan Z, Loghmani A, Majlesi M, Jafari N. Spiritual well-being and quality of life of Iranian adults with type 2 diabetes. Evid Based Complement Alternat Med. 2014;2014:619028. doi: 10.1155/2014/619028.

ORCID and contributionship:

Evangelos C. Fradelos: 0000-0003-0244-9760^{A,B,C,D,F}

Saridi Maria: 0000-0002-9008-824X^{B,D,F}

Vissarion Bakalis: 0000-0003-0834-8557^{B,D,F}

Aikaterini Toska: 0000-0002-6888-3394^{B,D,F}

Viktor Vus: 0000-0002-1042-5323^{B,D,F}

Arndt Büssing: 0000-0002-5025-7950^{A,D,F}

Kyriakos Souliotis: 0000-0003-1624-9444^{A,D,F}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Evangelos C. Fradelos

Gaiopolis Campus,
Larissa – Trikala Ring Road,
41500, Larissa, Greece
e-mail: efradelos@uth.gr

Received: 15.11.2022

Accepted: 30.05.2023

A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

ORIGINAL ARTICLE

HYPERGLYCEMIA AS A PREDICTOR OF OUTCOME IN PAEDIATRIC SEVERE TRAUMATIC BRAIN INJURY PATIENTS UNDERWENT SURGERY: A SINGLE CENTER EXPERIENCE FROM EASTERN INDONESIA FROM 2017-2022

DOI: 10.36740/WLek202306103

Muhamad Arifin Parenrengi, Wihasto Suryaningtyas, Rifqi Aulia Destiansyah

UNIVERSITAS AIRLANGGA, SURABAYA, INDONESIA

ABSTRACT

The aim: Traumatic Brain Injury (TBI) remains a significant health burden worldwide. This study aimed to describe, determine and recommendation concerning the impact of hyperglycemia on paediatric TBI.

Materials and methods: Paediatric trauma patients with severe TBI event were identified and admitted to our Dr. Soetomo General Hospital, Surabaya, the regional Trauma Center of East Java, Indonesia between calendar year of 2017 and 2022. Our institutions trauma database was utilized to select the patient included in this study. Patients with GCS ≤ 8 who underwent neurosurgical interventions were included to the study. Neurosurgical interventions are craniotomy for clot evacuation and decompressive craniectomy. We excluded patients with GCS > 8 and/or treated with conservative therapy (no surgery needed). Data collected for analysis as independent variables included patient age, admission GCS score and admission serum glucose score, mechanism of injury, type of intracranial lesion and type of surgery. Outcome of the patients included was examined at discharge which sub-grouped by Glasgow Outcomes Scale (GOS) score. Independent variables were entered into the logistic model in a stepwise fashion with a significant cutoff of $p < 0,05$.

Results: Patients with worse neurological outcomes (GOS score 1-2) had a mean serum glucose value of over 200 mg/dL. Patients who died (GOS score of 1) had higher mean admission glucose values ($226.44 \pm 62,00$) than the patients who had survived with a GOS score of 3 (139.80 ± 10.87), 4 (87), or 5 (134). Patients who resulted in a vegetative state (GOS score of 2) had higher mean admission serum glucose values than patients who were discharged with a GOS score of 5 (205.14 ± 36.17 vs. 134; $p = 0.003$).

Conclusions: Hyperglycaemia in paediatric TBI patients that underwent neurosurgical intervention is associated with worse outcomes, even mortality. We believe that prospective evaluation of glucose normalization in the context of acute management of paediatric head injuries is both appropriate and necessary for the next study.

KEY WORDS: Paediatric TBI, hyperglycemia, craniotomy, GOS, mortality

Wiad Lek. 2023;76(6):1342-1346

INTRODUCTION

Traumatic Brain Injury (TBI) vestiged a significant health burden worldwide. Severe TBI subsidized ominously to morbidity and even mortality number in paediatric patients [1]. Secondary brain insults, including ischemia, acidosis and electrolyte imbalance might have a noteworthy role in consequences following TBI event in patients [2]. Both the adult and paediatric trauma literature has evaluated the relationship between hyperglycemia and outcomes after TBI. A definite relation existed in adult patients between hyperglycemia, severity of head injury and outcome from TBI [3]. Impact of hyperglycemia on TBI outcomes is less visible, and with several recently conducted studies presented a clear relationship between hyperglycemia and deprived

neurologic outcome, and some study presented no affiliation. Up to the present time, no studies appraised the clout of glucose regulation on neurologic outcomes afterward TBI event, and the need for glucose normalization in acute setting remains controversial.

Prognosticators for severe injury due to various and non-specific complaints amid TBI in paediatric patients who underwent craniotomy procedure is necessary. Age, Glasgow Coma Scale (GCS) score, accidental hypothermia, and coagulation disorders are reported to be independent prognostic factors for mortality [4]. This retrospective analysis provided descriptive information about patient characteristics at admission and their relationship to outcomes in paediatric TBI who underwent craniotomy procedure.

Table I. Patient's characteristic

	Characteristics	n	%
Age	<1 yo	1	4.3
	1 – 3 yo	3	13
	4 – 6 yo	5	21.7
	7 – 9 yo	1	4.3
	10 – 12 yo	2	8.7
	13 – 15 yo	8	34.8
	16 – 18 yo	3	13
Sex	Male	20	87
	Female	3	13
Mechanism of Injury	MVA*	12	52.2
	Pedestrian	4	17.4
	Fall	6	26.1
	Assault	1	4.3
Intracranial lesion type	EDH*	12	52.2
	SDH*	6	26.1
	ICH*	8	34.8
	Depressed Fracture	6	26.1
	Isolated Brain Edema	2	8.6
Single or multiple lesion	Single	12	52.2
	Multiple	11	47.8
Type of surgery	Craniotomy Evacuation	21	91.3
	Decompressive Craniectomy Only	2	8.7

* MVA: Motor Vehicle Accident; EDH: Epidural Hemorrhage; SDH: Subdural Hemorrhage; ICH: Intracerebral Hemorrhage

THE AIM

The aim of this study is to describe and determine whether hyperglycemia at the time of admittance on severe paediatric TBI patients who endured craniotomy procedure would have a negative connotation with neurologic outcome. We postulated that hyperglycemia would exhibit a strong relationship with mortality, hence, glucose control for pediatric TBI should be among the foremost attention and highly recommended.

MATERIALS AND METHODS

PATIENTS DATA

Paediatric trauma patients with severe TBI event were identified and admitted to our Dr. Soetomo General Hospital, Surabaya, the regional Trauma Center of East Java, Indonesia between calendar year of 2017 and 2022. Our institutions trauma database was utilized to select the patient included in this study. Patients with GCS \leq 8 who underwent neurosurgical interventions were included to the study. Neurosurgical

interventions are craniotomy for clot evacuation and decompressive craniectomy. We excluded patients with GCS $>$ 8 and/or treated with conservative therapy (no surgery needed). Data collected for analysis as independent variables included patient age, admission GCS score and admission serum glucose score, mechanism of injury, type of intracranial lesion and type of surgery. Outcome of the patients included was examined at discharge which sub-grouped by Glasgow Outcomes Scale (GOS) score.

STATISTICAL ANALYSIS

Descriptive statistics utilized to evaluate all included patient's data. One-way analysis of variance was used for comparison of hyperglycemia and outcome of patients. Independent t-test used for samples included to compare between admission blood glucose and outcome of the patients. All serum glucose presented as mean \pm SD. Independent variables were entered into the logistic model in a stepwise fashion with significant cutoff of $p < 0.05$. SPSS 24 was used for all data analysis.

Table II. Glasgow Outcome Scale Score Categories

GOS	Clinical Status	n	%	Serum glucose (mg/dL)	
				Mean	SD
1	Death	9	39.1	226.44	62.00
2	Vegetative; dependent for all activities	7	30.4	205.14	36.17
3	Severe deficit; conscious but requires extensive support	5	21.7	139.80	10.87
4	Moderate deficit; requires some assistance with daily activities	1	4.3	87.00	-
5	Minimal deficit; good neurologic outcome	1	4.3	134	-

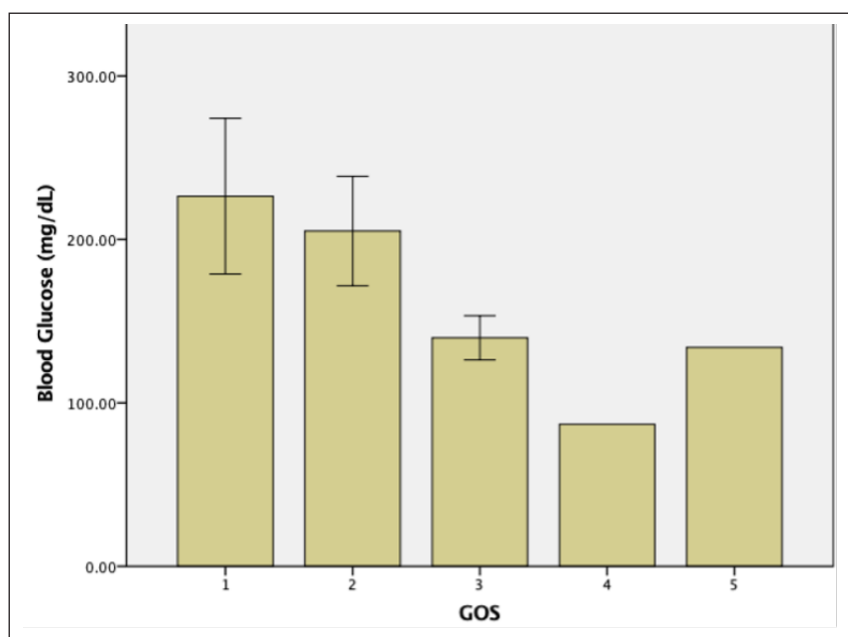


Fig.1. Mean admission serum glucose versus Glasgow Outcome Scale (GOS) score

RESULTS

98 paediatric trauma patients were admitted to our Trauma Center in calendar year 2017 until 2022. From 98 patients, 23 patients had GCS \leq 8 and endured craniotomy procedure. All patients had a serum glucose value logged at the time of admission. 20 of 23 were male patients (87%) and 3 were female patients (13%). Head injury resulted in death in 9 patients of our study. From those who deceased, seven had admission serum glucose values over 200 mg/dL. Median age of all studied patients was 9.58 years, male dominating over female in almost all age level. Motor vehicle accident (MVA) recorded as the most causal number of the injuries (52,2%). Other mechanisms of injury were pedestrian (17,4%), falls (26,1%) and other mechanisms of injury (4,3%) (Table I).

Epidural hemorrhage (EDH) had the greatest number of intracranial injuries with 12 cases (52.2%). Other categories were subdural hemorrhage (SDH) (6 cases, 26.1%), intracerebral hemorrhages (ICH) (8 cases, 34.8%), depressed fracture (6 cases, 26.1%) and isolated brain edema (2 cases, 8,6%). In several cases, there were multiple intracranial lesions suffered by the patients. There were 2 kinds of surgery that designated for paediatric TBI cases in this study,

craniotomy evacuation of hemorrhage (21 cases, 81.3%) and decompressive craniectomy only cases (2 cases, 8.7%).

Patients with worse neurological outcomes (GOS score 1-2) had mean serum glucose value more than 200 mg/dL at admission serum glucose (Figure 1). Patients who deceased (GOS score of 1) had ominously higher mean admission glucose values ($226.44 \pm 62,00$) than the patients who had survived after neurosurgical intervention, with a GOS score of 3 ($139.80 \pm 10,87$), 4 (87), or 5 (134) with p value was < 0.05 for each. Furthermore, patients who unremitting an injury resulting in a vegetative state (GOS score of 2) had significantly higher mean admission serum glucose values than patients who were settled with a GOS score of 5 (205.14 ± 36.17 vs. 134; $p = 0.003$) (Table II).

DISCUSSION

The result of our study confirmed prior research that presented an association between poor neurologic outcome and elevated admission serum glucose levels after traumatic brain injury [5]. In addition, hyperglycaemia is a previously documented independent risk factor for mortality in adult patients with traumatic brain injury [6]. Furthermore, study

by Fanchiang *et al.* mentioned that postoperative glucose was an independent predictor of outcomes [7]. Our study extends the concept of admission hyperglycaemia being an independent predictor of head injury related morbidity and mortality number that have a neurosurgical intervention to a robust paediatric population [8].

We also aware of a clear relationship between admission hyperglycaemia and succeeding mortality in our study population, and our finding is that all study patients with an admission serum glucose over 300mg/dL died is majorly captivating. Although threshold values have been regarded in association with mortality in adults TBI, we are insensible of any prior research documenting a threshold value for admission glucose in children that is consistently associated with morbidity and mortality.

The effectuate of hyperglycaemia after TBI event is multifactorial, consistent with its role in the physiologic stress response. Numerous theories as to the aetiology of hyperglycaemia following head trauma have been proposed. The release of catecholamines in response to traumatic brain injury is well documented, as is stimulated hepatic gluconeogenesis and glycogenolysis in response to catecholamine release. Decreased glucose utilization associated with cortisol release by adrenal glands, increased growth hormone leading to increased lipolysis and insulin antagonism are the complementary elements of the stress response and may further increase serum glucose [9]. Glucose intolerance has also been documented in association with head injury [10]. The predominance of any of these mechanisms of hyperglycaemia has not been accustomed, and it is probable that they function synergistically.

Distinguishing the cause and effect relationship between hyperglycaemia and poor outcome after TBI remains difficult. Study by Orellana *et al* have implied that hyperglycaemia may reflect the extent of the disease, in this case is traumatic brain injury [11]. However, Shukla *et al* implied that hyperglycaemia exacerbates the impact of ischemia and hypoxia, ultimately resulting in worse outcome after a variety of insults [12]. Although the epiphenomenon of hyperglycaemia after head injury is widely recognized, clarification of the cause-and-effect relationship of hyperglycaemia to outcome from head injury would greatly benefit patient care.

Preceding studies have shown worse neurologic outcomes in the existence of hyperglycaemia after head injury in adults and have advised advocated prospective evaluation of early, aggressive glycaemic control as a potential determinant for refined outcomes [13]. Our result of significantly higher serum glucose level in patient with higher GOS is in conjunction with the latest research which substantiated a reduction in mortality in critically ill patients [14]. Regarding insulin usage in hyperglycaemic-head-injured children, argued against such treatment due to most cases being only a transient hyperglycaemia [15]. However, this study is the only study indicating no relationship between hyperglycaemia and neurologic prognosis. Subsequent studies, including our study, had used standard outcome measures to substantiate a negative association between hyperglycaemia and neurologic outcome after neurosurgical interventions in severe paediatric TBI cases. Furthermore, we demonstrated hyperglycaemia as an independent predictor of mortality in paediatric traumatic brain injury patients as the majority of our fatal cases had over than 200 g/dL serum glucose. Study by Sharma *et al.* stated that currently there are insufficient data to support insulin treatment and does not address the issue whether glucose above 200 mg/dL should be treated. Insulin administration in such circumstances may be dangerous and should be initiated with caution [16]. Recently, Agus *et al.* published a randomized open trial study (HALF-PINT) protocol for the relevance of tight glycemic control for children undergoing intensive care in the needs to be assessed formally before being accepted into standard practice [17].

CONCLUSIONS

In conclusion, paediatric patients with TBI were showed increasing serum glucose levels. Hyperglycaemia in paediatric TBI patients that underwent neurosurgical intervention was associated with worse outcome, even mortality. Our findings assembled on the current evidence that neurologic outcomes were associated with hyperglycaemia. We believed that prospective evaluation of glucose regulation in the context of acute management of paediatric head injuries is both appropriate and necessary for the next study.

REFERENCES

1. Bandyopadhyay S, Kawka M, Marks K et al. Traumatic Brain Injury-Related Pediatric Mortality and Morbidity in Low- and Middle-Income Countries: A Systematic Review. *World Neurosurg.* 2021;153:109-130.e23. doi:10.1016/j.wneu.2021.06.077.
2. Dey S, Kumar R, Tarat A. Evaluation of Electrolyte Imbalance in Patients With Traumatic Brain Injury Admitted in the Central ICU of a Tertiary Care Centre: A Prospective Observational Study. *Cureus.* 2021;13(8):e17517. doi:10.7759/cureus.17517.
3. Chen S, Liu Z. Effect of hyperglycemia on all-cause mortality from pediatric brain injury: A systematic review and meta-analysis. *Medicine (Baltimore).* 2020;99(48):e23307. doi:10.1097/MD.00000000000023307.
4. Trimble DJ, Parker SL, Zhu L et al. Outcomes and prognostic factors of pediatric patients with a Glasgow Coma Score of 3 after blunt head trauma. *Childs Nerv Syst.* 2020;36(11):2657-2665. doi:10.1007/s00381-020-04637-z.

5. El-Kheir MMA, Attia SM, Ahmed MES et al. Hyperglycemia as Prognostic Factor in Pediatric Traumatic Brain Injury in Emergency Hospital Mansoura University. *Egypt J Hosp Med.* 2022;87(1):2139–2146.
6. Chen CH, Hsieh YW, Huang JF et al. Predictors of In-Hospital Mortality for Road Traffic Accident-Related Severe Traumatic Brain Injury. *J Pers Med.* 2021;11(12):1339. doi:10.3390/jpm11121339.
7. Fanchiang S-P, Indraghanty A, Liu H et al. Post-Traumatic Brain Injury (TBI) Blood Sugar (BG) and its Relation to Inpatient Rehabilitation Outcome. *Archives of Physical Medicine and Rehabilitation,* 2023;104(3):e44. doi: 10.1016/j.apmr.2022.12.127.
8. Seyed Saadat SM, Bidabadi E, Seyed Saadat SN et al. Association of persistent hyperglycemia with outcome of severe traumatic brain injury in pediatric population. *Childs Nerv Syst.* 2012;28(10):1773-1777. doi:10.1007/s00381-012-1753-5.
9. Rizoli SB, Jaja BN, Di Battista AP et al. Catecholamines as outcome markers in isolated traumatic brain injury: the COMA-TBI study. *Crit Care.* 2017;21(1):37. doi:10.1186/s13054-017-1620-6.
10. Shi J, Dong B, Mao Y et al. Review: Traumatic brain injury and hyperglycemia, a potentially modifiable risk factor. *Oncotarget.* 2016;7(43):71052-71061. doi:10.18632/oncotarget.11958.
11. Orellana RA, Coss-Bu JA. Metabolic alterations in the critically ill child. *Pediatr Med.* 2021;4:1–17.
12. Shukla V, Shakya AK, Perez-Pinzon MA et al. Cerebral ischemic damage in diabetes: an inflammatory perspective. *J Neuroinflammation.* 2017;14(1):21. doi:10.1186/s12974-016-0774-5.
13. Hermanides J, Plummer MP, Finnis M et al. Glycaemic control targets after traumatic brain injury: a systematic review and meta-analysis. *Crit Care.* 2018;22(1):11. doi:10.1186/s13054-017-1883-y.
14. Chao M, Wang CC, Chen CPC et al. The Influence of Serious Extracranial Injury on In-Hospital Mortality in Children with Severe Traumatic Brain Injury. *J Pers Med.* 2022;12(7):1075. doi:10.3390/jpm12071075.
15. Rostami E. Glucose and the injured brain-monitored in the neurointensive care unit. *Front Neurol.* 2014;5:91. doi:10.3389/fneur.2014.00091.
16. Sharma D, Jelacic J, Chennuri R et al. Incidence and risk factors for perioperative hyperglycemia in children with traumatic brain injury. *Anesth Analg.* 2009;108(1):81-89. doi:10.1213/ane.0b013e31818a6f32.
17. Agus MS, Hirshberg E, Srinivasan V et al. Design and rationale of Heart and Lung Failure - Pediatric INSulin Titration Trial (HALF-PINT): A randomized clinical trial of tight glycemic control in hyperglycemic critically ill children. *Contemp Clin Trials.* 2017;53:178-187. doi:10.1016/j.cct.2016.12.023.

ORCID and contributionship:

Muhammad Arifin Parenrengi: 0000-0002-1327-8955 ^{A,E,F}

Wihasto Suryaningtyas: 0000-0002-1187-3777^{A,E,F}

Rifqi Aulia Destiansyah: 0000-0001-8933-8785^{A-D}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Muhammad Arifin Parenrengi

Universitas Airlangga

Jl. Airlangga No.4 – 6, Surabaya, Indonesia

tel: +6281333888007

e-mail: muhammad.arifin@fk.unair.ac.id

Received: 06.11.2022

Accepted: 24.05.2023

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

ORNIDAZOL-BASED APPLICATION SORBENT WITH NANO SILICA AND ITS ANTIMICROBIAL ACTIVITY

DOI: 10.36740/WLek202306104

Olga Bilyayeva¹, Ivan Karol¹, Eugeniy Demianenko², Alina Gaidai³, Yevhenii Kryzhevskiy¹, Polina Vakuliuk^{3,4}, Alexander Golub^{3,5}

¹SHUPYK NATIONAL HEALTHCARE UNIVERSITY OF UKRAINE, KYIV, UKRAINE

²CHUIKO INSTITUTE OF SURFACE CHEMISTRY NAS OF UKRAINE, KYIV, UKRAINE

³NATIONAL UNIVERSITY OF KYIV-MOHYLA ACADEMY, KYIV, UKRAINE

⁴POLISH ACADEMY OF SCIENCES, INSTITUTE OF AGROPHYSICS, WARSAW, POLAND

⁵JUSTUS LIEBIG UNIVERSITY, GIESSEN, GERMANY

ABSTRACT

The aim: To investigate the effect of application sorbent based on ornidazole with nanosilicon in experiment and clinic.

Materials and methods: In order to study the effectiveness of the Ornidasil application sorbent for the treatment of purulent wounds, we conducted an experimental study in rats. Also, we studied the effectiveness of the Ornidasil in the clinic for the treatment of patients with diabetic foot syndrome and to prevent the suppuration of postoperative wounds in patients with purulent peritonitis in toxic and terminal stages.

Results: The formation of active substance complexes with hydroxylated matrices is due to hydrogen bonds between the oxygen atom of the silanol group of the silica surface and the hydrogen atom of the alcohol group of the ornidazole molecule. This promotes the gradual release of ornidazole from the surface of such a matrix into the wound exudate. Thus, on day 13, 9 experimental rats of group I healed completely, 11 rats had a small wound surface, complete healing occurred on day 15. We also investigated the effectiveness Ornidasil in the clinic. In the comparison group, postoperative wound suppuration occurred in 6 patients (31.6%), and in the main group - in 3 patients (12.5%).

Conclusions: A study of the effectiveness Ornidasil in the complex treatment of Diabetic foot syndrome showed that in the experimental groups, wound healing occurred 1.6 - 1.9 times faster. The use of polyurethane wound protector in combination with Ornidasil reduced the suppuration of postoperative wounds in patients of the main group by 2.5 times relative to patients in the comparison group.

KEY WORDS: ornidazole, nano silica, hybrid nanocomposites, quantum chemical calculations, in vivo therapeutic effect, clinical study

Wiad Lek. 2023;76(6):1347-1358

INTRODUCTION

Combined studies using quantum chemical calculations and IR spectroscopy have shown that the interaction of ornidazole with hydroxylated nano-silica is due to the formation of hydrogen bonds between the oxygen atom of the silanol group of the silica surface and the hydrogen atom of the hydroxyl group of the molecule.

The highest adsorption energy of the ornidazole molecule is inherent in hydroxylated silica (-87.5 kJ / mol). The ornidazole OH group is the most active in forming a hydrogen bond with the silanol group of the silica surface.

Comparison of the IR spectra of nanocomposites obtained after the release of the active substance (ornidazole) within 24 h, showed that the residual concentration of ornidazole on the surface according

to research and desorption kinetics is about 13%, indicating the possibility of prolonged action of the synthesized nanocomposite. Given the above, it can be assumed that the obtained nanocomposites can be further used as promising hybrid nanomaterials that prolong the action of traditional drugs.

This is confirmed by the comparison of the therapeutic effect of the nanocomposite with ornidazole immobilized on the surface of nanodispersed silica with the known long-acting drug Gentaxan in vivo, as well as comparative use in clinical studies.

The immobilisation of antimicrobial substances on the surface of inorganic carriers allows to design the modern nanohybrid materials of complex action, as this approach combines the therapeutic effect of the active ingredient with high adsorption capacity of the carrier,

such as silica [1]. One of the areas of improvement of these combined drugs is the creation of nanocomposite systems in which silica due to intermolecular interactions with the molecule of the active substance can affect the dynamics of its release. The interest in materials with programmed characteristics based on silica is due to the fact that they are non-toxic, biocompatible, biologically erosive and have a high adsorption capacity. That is why such materials allow to solve a number of topical interdisciplinary problems, primarily related to the development of modern forms of medicines and their delivery systems [1 - 3]. These properties also allow the active use of silica in medical and pharmaceutical practice and many other areas of human activity [4 - 6].

In particular, one of the promising areas of use of highly dispersed silica in modern pharmacology is its use as a carrier of drugs and disinfectants [7]. This is due to the fact that the immobilization of these compounds can improve their physicochemical properties, increase stability, reduce toxicity, change the bioavailability and kinetics of release of the active substance [8]. When creating hybrid nanocomposite systems, including on the basis of highly dispersed silica, it should be borne in mind that the specific properties of modified nanomaterials may be manifested as a result of their interaction with active centers occurring in the surface layer [9].

An important characteristic that plays a significant role in the use of silica in the biomedical field, as well as in the study of silica surface chemistry, are the large specific surface area of the carrier and the concentration of active groups [10,11]. In addition, in the case of hybrid nanocomposite materials for medical purposes, it should be borne in mind that the adsorption of antimicrobial compounds can be one of the effective ways to create long-acting drugs with controlled release of the active ingredient. In turn, all these features require detailed experimental studies, which should primarily relate to the interaction of silica (as a matrix) with specific biomolecules and / or drugs of different classes.

Due to the possibility of changes in certain physicochemical properties of the active ingredient when combined with a carrier matrix, as an active ingredient studied the known drug ornidazole (1-(2-hydroxy-3-chloropropyl)-2-methyl-5-nitroimidazole). It is a derivative of 5-nitroimidazole, has a heterocyclic structure, consists of a nitroimidazole nucleus and 2-hydroxy-3-chloropropyl group in position 1 and methyl group in position 2, soluble in water, ether, ethanol and chloroform [12]. The drug easily penetrates the blood-brain barrier [13], has antimicrobial action, and reduced bacterial resistance [14], low toxicity and optimal bioavailability [15].

The need to study in detail the intermolecular interaction of active drug components with nanomaterials

used as carriers is extremely important for managing pharmacokinetic processes, elucidation of pharmacological properties, creation of appropriate design of combined drug delivery nanosystems, etc. To this end, the authors in many studies are actively using not only experimental methods, but also the apparatus of quantum chemistry, in particular the method of DFT (Density Functional Theory) [16 - 18].

The use of molecular modeling methods revealed that the ability to penetrate target cells of the macroorganism, the peculiarities of drug transport during delivery *in vivo*, the kinetics of release of the active ingredient, etc., significantly affect not only the properties of the active substance but also the carrier characteristics [17]. Therefore, the combination of theoretical modeling and experimental studies *in vivo*, as well as clinical studies allows to rationally designing the composition and structure of nanoparticles of carriers while creating effective systems of controlled drugs delivery to target cells [16].

Promising today is the direction of designing modern nanocomposite drugs for the treatment of purulent wounds by immobilizing drugs on the matrices of sorbents that have the property of being a carrier of drugs. Immobilization of the drug reduces the side effects of the drug and promotes the prolongation of the therapeutic effect.

THE AIM

In view of the above, the aim of the study was to investigate the interaction of ornidazole with nanosilica using quantum chemical calculations, IR spectroscopy and to test the effectiveness and prolonged antimicrobial action of potential nanocomposite drugs *in vivo* and in clinical trials.

MATERIALS AND METHODS

Pyrogenic silica (A-300 «Sillard P») produced by the Kalush Research and Experimental Plant of the ISTC «Surface Chemistry» with a specific surface area of 300 m²/g (by low-temperature nitrogen adsorption by the BET method) was used as the initial matrix (5).

Ornidazole (1-(3-chloro-2-hydroxypropyl)-2-methyl-5-nitroimidazole) manufactured by Aarti Drugs Limited, India was used as the active substance. Immobilization of ornidazole was performed under constant stirring (500 rpm) for 20 min at a temperature of 20°C. Nanocomposite materials were obtained by immobilization of ornidazole on the surface of the hydroxylated matrix, so that the final content of active ingredient in dry nanocomposites was 0.184 mmol/g SiO₂, which is

much less than the number of adsorbable silanol groups on the surface of dispersed silica [19].

To confirm the presence of functional groups on the surface of matrices and the presence of ornidazole on the surface of nanocomposites synthesised on their basis after immobilization and after release of the active substance the method of IR spectroscopy with Fourier transform spectrometer Thermo Nicolet Nexus FT-IR (Nicolet, USA) in frequency range 500 - 4000 cm^{-1} was used. All samples were mixed with freshly calcined KBr at a mass ratio of 0.015: 0.3 [19].

The release of the active substance (ornidazole) from the surface of nanocomposites was carried out under static conditions in distilled water ($V = 100$ ml) at a temperature of 37 °C, the weight of the nanocomposite was 0.1 g. The duration of release was 24 hours.

To determine the most active centers for immobilization of the ornidazole molecule on hydroxylated and functionalized silica, the method of density functional theory (DFT) with functional B3LYP [12, 13] and basic set 6-31G (d, p) was used. GAMESS (US) program was used for calculations [14]. To take into account the dispersion effects of binding, which determine the formation of non-covalent intermolecular complexes, the energy variance of intermolecular interaction took into account the Grimme D3 variance correction [15, 16]. Given that the experiment was performed in aqueous solution, the effect of the solvent was described within the continuum approximation of the PCM (polarizable continuum model) [17]. The energy effect of complexation (adsorption) (ΔE) according to the reaction $A + B \rightarrow A \dots B$ was calculated by the formula: $\Delta E = E_{\text{tot}}(A \dots B) - (E_{\text{tot}}(A) + E_{\text{tot}}(B))$, where $E_{\text{tot}}(A)$ - the total energy of the ornidazole molecule taking into account the aqueous medium, $E_{\text{tot}}(B)$ is the total energy of the cluster that reproduces the surface, $E_{\text{tot}}(A \dots B)$ is the total energy of the intermolecular complex of ornidazole with the cluster.

Study of the prolongation of the therapeutic effect of nanocomposite drugs *in vivo*. In order to study the effectiveness of nanocomposite based on silica and immobilized on its surface ornidazole (Ornidasil) for the treatment of purulent wounds, we conducted an experimental study in rats. Thirty adult white male Vistar rats were used in the study. All experimental animals were in the same conditions, painful manipulations were performed under local infiltration anesthesia with 0.5% novocaine solution, animals were removed from the experiment by sodium thiopental overdose, in accordance with generally accepted ethical standards and recommendations.

In planning the presented study, they were guided by generally accepted domestic and international laws in accordance with the «General Ethical Principles of

Animal Experiments» (Ukraine, 2001), Order of the Ministry of Health of Ukraine № 281 of 01.11.2000, Law of Ukraine № 3447-IV «On Animal Protection from cruel treatment «of 21.02.2006, as well as in compliance with the basic provisions of the» Rules for the use of experimental animals «(1977), GCP 1996, the Council of Europe Convention for the protection of vertebrate animals used in experiments and other scientific purposes from 18.03.1986, EEC Directives № 609 from 24.11.1986, Order of the Ministry of Health of Ukraine № 373 from 22.07. 2005, Order № 95 of 16.02.2009, Order № 944 of 14.12.2009, Council of Europe Convention on Human Rights and Biomedicine (04.04.1997), Helsinki Declaration of the World Medical Association on the Ethical Principles of Medical Practice human research (1964–2000).

Study of the action of Ornidasil for the treatment of purulent wounds, compared with a known drug of prolonged action. In all experimental animals, a purulent wound was simulated according to the method [20]. The animals were divided into two groups. In the main group (group I) the study was performed on 20 rats, for them Ornidasil was used [21–22]. The comparison group (group II) consisted of 10 rats, for which was used the known application sorbent «Gentaxan», which includes: gentamicin sulfate, polymethylsiloxane, L-tryptophan and zinc sulfate [23].

Also, we studied the effectiveness of the «Ornidasil» application sorbent in the clinic for the treatment of patients with diabetic foot syndrome and to prevent the suppuration of postoperative wounds in patients with purulent peritonitis in toxic and terminal stages.

RESULTS

In the next stage of the study, nanocomposites based on hydroxylated silica matrix with immobilized ornidazole were created. The method of immobilization of ornidazole on the silica matrix used in this work is primarily simple. Another of its features is the weak fixation of the modifier on the matrix, which leads to the gradual release of the active ingredient from the surface of the carrier into the wet environment. The concentration of ornidazole chosen for immobilization was considered optimal on the grounds that the content of the active ingredient, according to previous studies [19] was sufficient for its antimicrobial action, and on the surface of nanosilica there were still enough free active centers may be involved in the adsorption of toxic wound destructs of polypeptide nature [24]. After immobilization of ornidazole, the presence of the active substance on the hydroxylated silica matrix was also identified by IR spectroscopy.

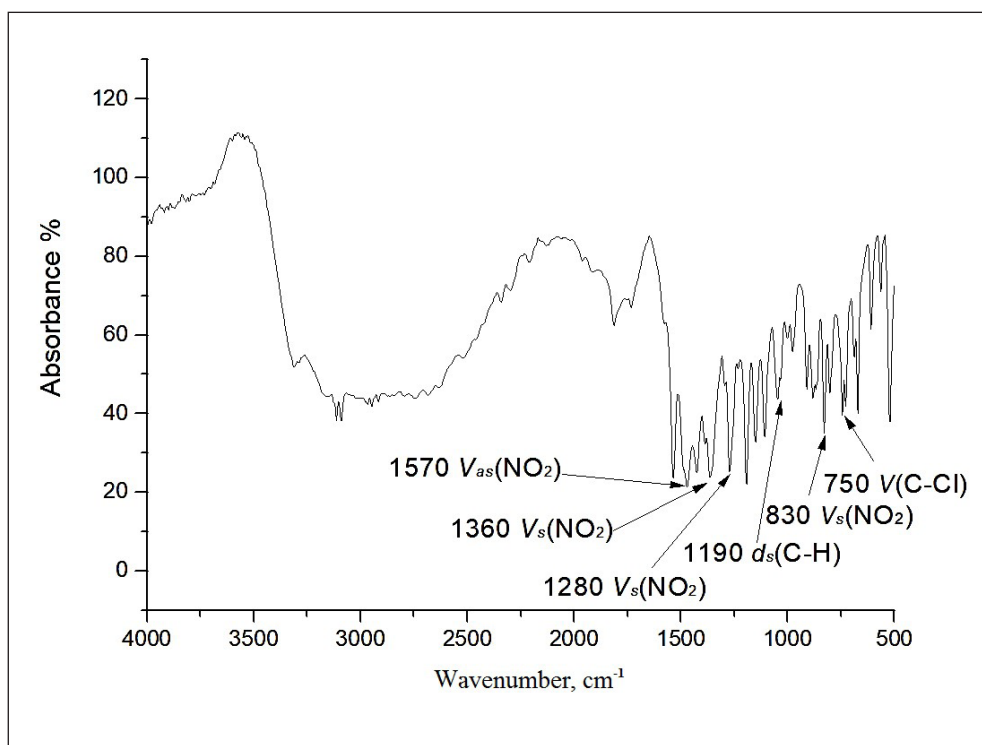


Fig. 1. IR-spectra of ornidazole.

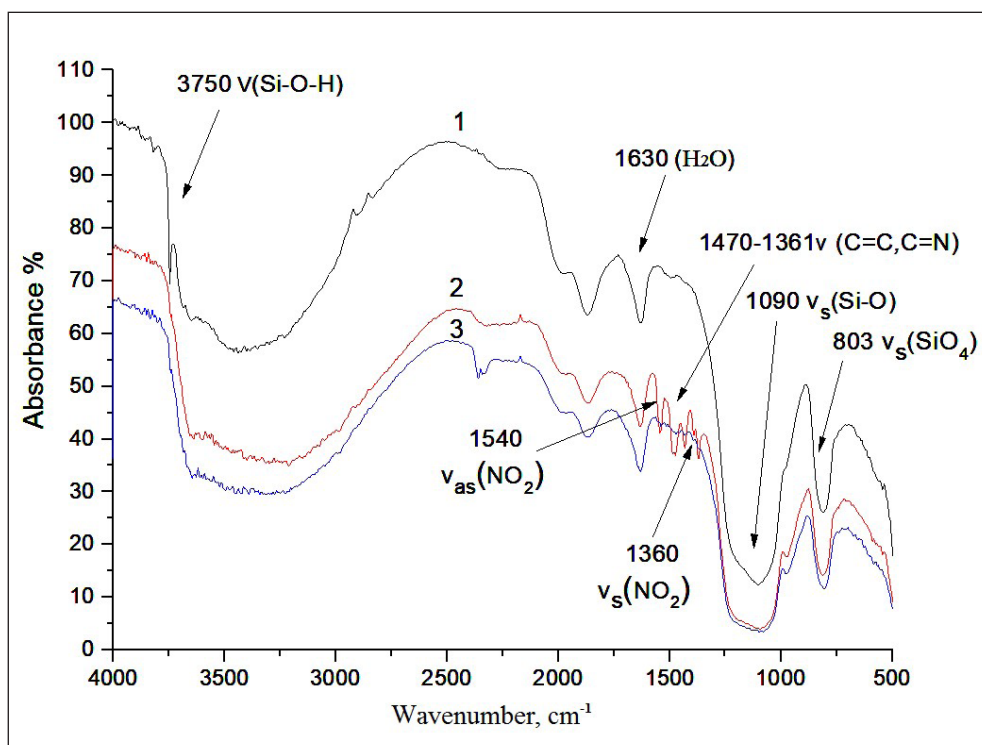


Fig. 2. IR-spectra of hydroxylated silica surface (1), nanocomposite based on silica and ornidazole immobilized on (2) and nanocomposite after ornidazole desorption by water during 24 h (3).

The spectrum of ornidazole contains a number of characteristic bands, the assignment of which is shown in Fig. 1.

The hydroxylated silica in the IR spectra (Fig. 2, curve 1) has a wide absorption band in the range 3200-3700 cm^{-1} due to the superposition of -OH stretching and adsorbed water molecules. Peak 3750 cm^{-1} corresponds to the free silanol groups. The peak at 1870 cm^{-1} belongs to the oscillations of the SiO_2 framework, present in all

spectra. The band at 1630 cm^{-1} refers to the deformation frequency of water molecules, the band 803 cm^{-1} corresponds to the symmetric vibration of the tetrahedron SiO_4 . The band at 970 cm^{-1} belongs to the stretching Si-O bond in $^\circ\text{Si-OH}$ groups.

In the spectrum of the nanocomposite (Fig. 2, curve 2), there were absorption bands at 1540 cm^{-1} , and 1360 cm^{-1} , corresponding to asymmetric and symmetric stretching of NO_2 group of ornidazole (Fig. 1). The series

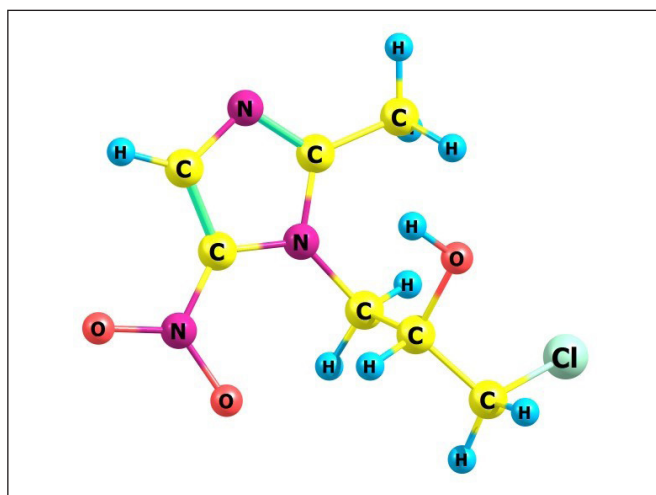


Fig. 3. Optimized structure of ornidazole conformer and its full energy.

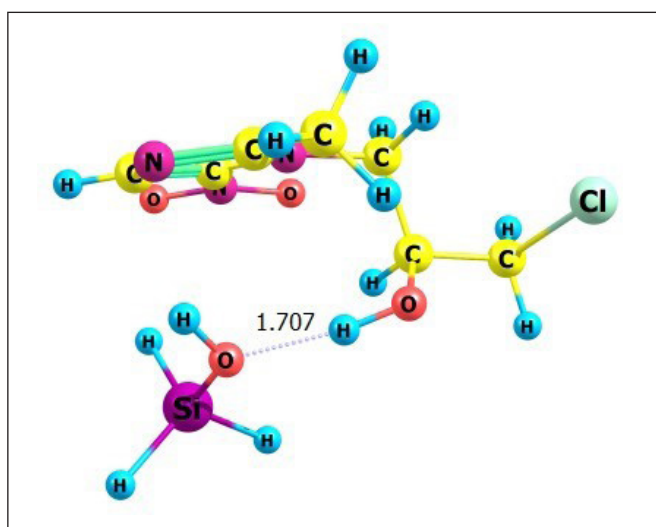


Fig. 4. Equilibrium structure of silanol and ornidazole intermolecular complex with lowest energy obtained in B3LYP-D3/6-31G(d,p) approximation. Here and then bond length is in Å [28].

of bands in the region $1470\text{--}1361\text{ cm}^{-1}$ belongs to the stretching of $\text{C}=\text{C}$ and $\text{C}=\text{N}$ bonds. After the water leaching process, the intensity of the characteristic peaks of ornidazole decreased significantly (Fig. 2, curve 3), which indicates a noticeable but not complete release of the active substance into solution. Confirmation of this fact is the study of desorption of ornidazole from the nanocomposite, which showed that after 24 h of leaching on the surface of the nanocomposite remains about 13% of the active substance (to be published).

The analysis of adsorption data raises the question of the structure of the sorption layer of the silica surface. It is also important to determine the most active adsorption centers of the ornidazole molecule relative to hydroxylated silica, the structure of ornidazole adsorption complexes on the surface, and to compare the energy of hydrogen bonds of ornidazole with water and

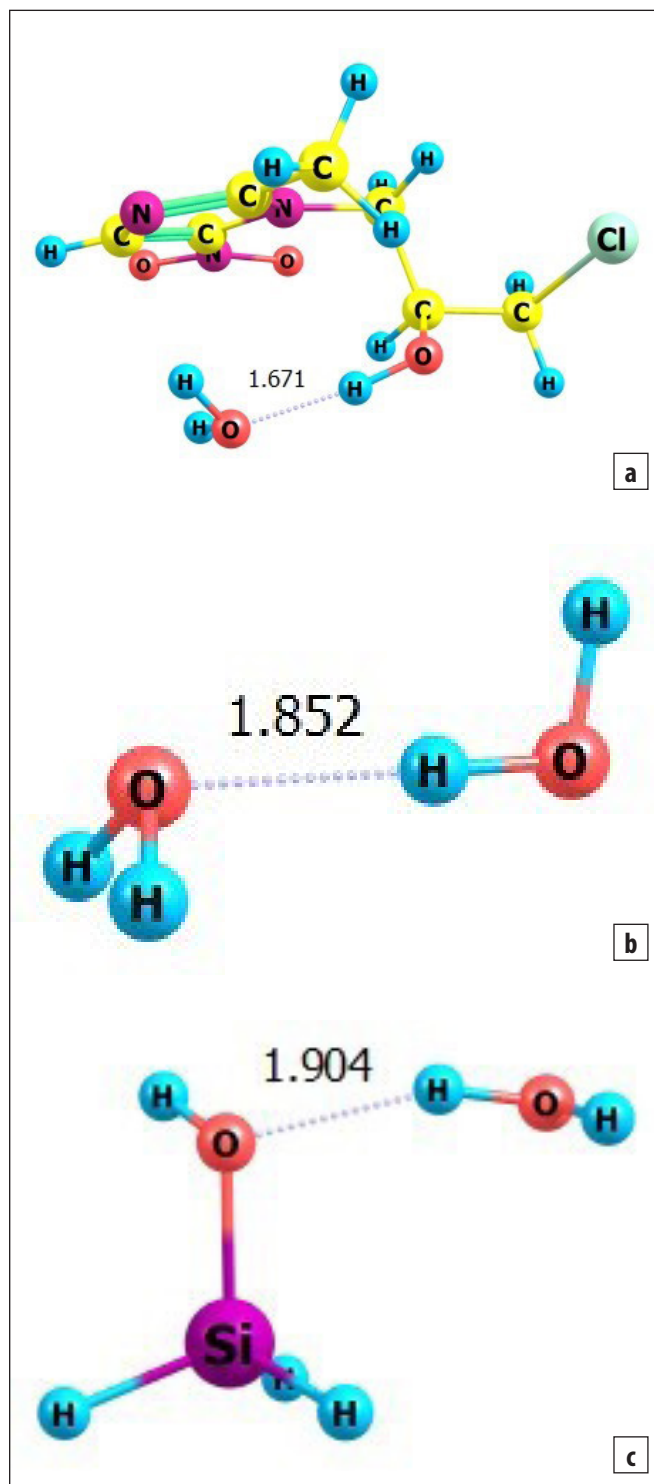


Fig. 5. Equilibrium structures of molecular complexes and their formation energies: a – water and ornidazole molecules, b – water dimer, c – water and silanol molecules [28].

silica molecules. Detailing of elementary processes at the level of intermolecular interactions allows a deeper interpretation of experimental data.

For quantum chemical modeling of physical sorption, the structure of the most probable conformer of the ornidazole molecule, which exists in aqueous solution,

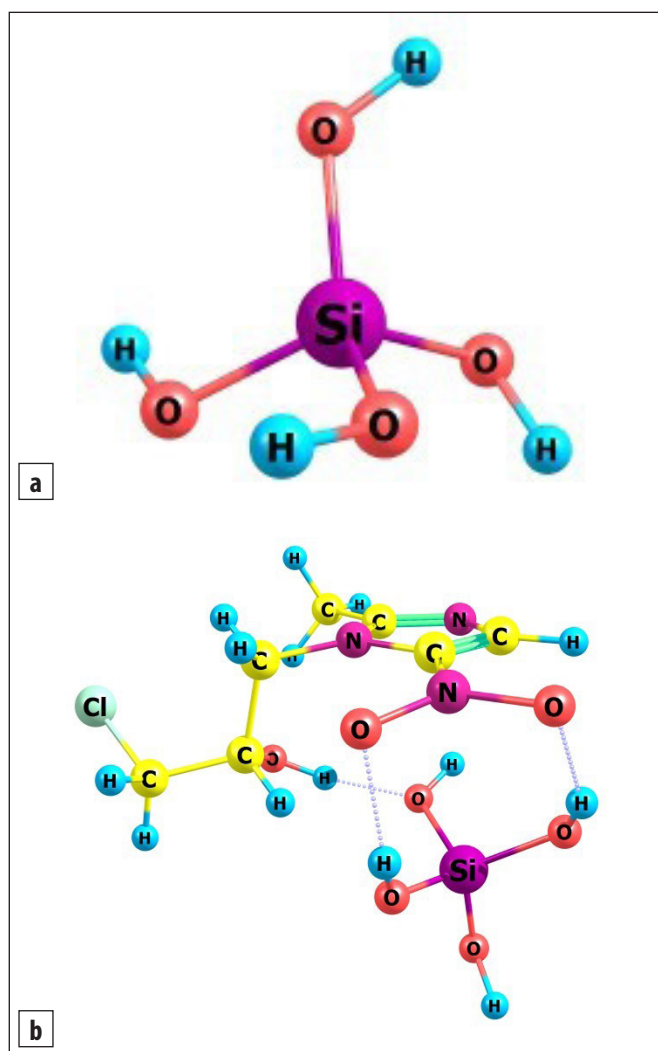


Fig. 6. Used for hydroxylated silica surface modeling orthosilicate acid (a) and most energetically efficient equilibrium structure of ornidazole and orthosilicate acid molecular complex (b).

was first established, because, according to the literature, several options are possible [25 - 27]. In view of this, the structure of the most probable conformers of the ornidazole molecule was optimized and the values of their total energies were compared, and the most thermodynamically stable of them was determined [28]. This was the structure (Fig. 3), which has the lowest value of total energy. This conformer was involved in further calculations.

Taking into account that the ornidazole molecule has several functional groups, different in their chemical nature, which may participate in the adsorption interaction with the silica surface, to establish the most active of them was simulated interaction of the ornidazole molecule with the smallest possible silica surface model - silanol molecule [24]. There is only one silanol group in this molecule, and three hydrogen atoms are attached to the silicon atom, which are weakly polarized and do not participate in the formation of hydrogen bonds

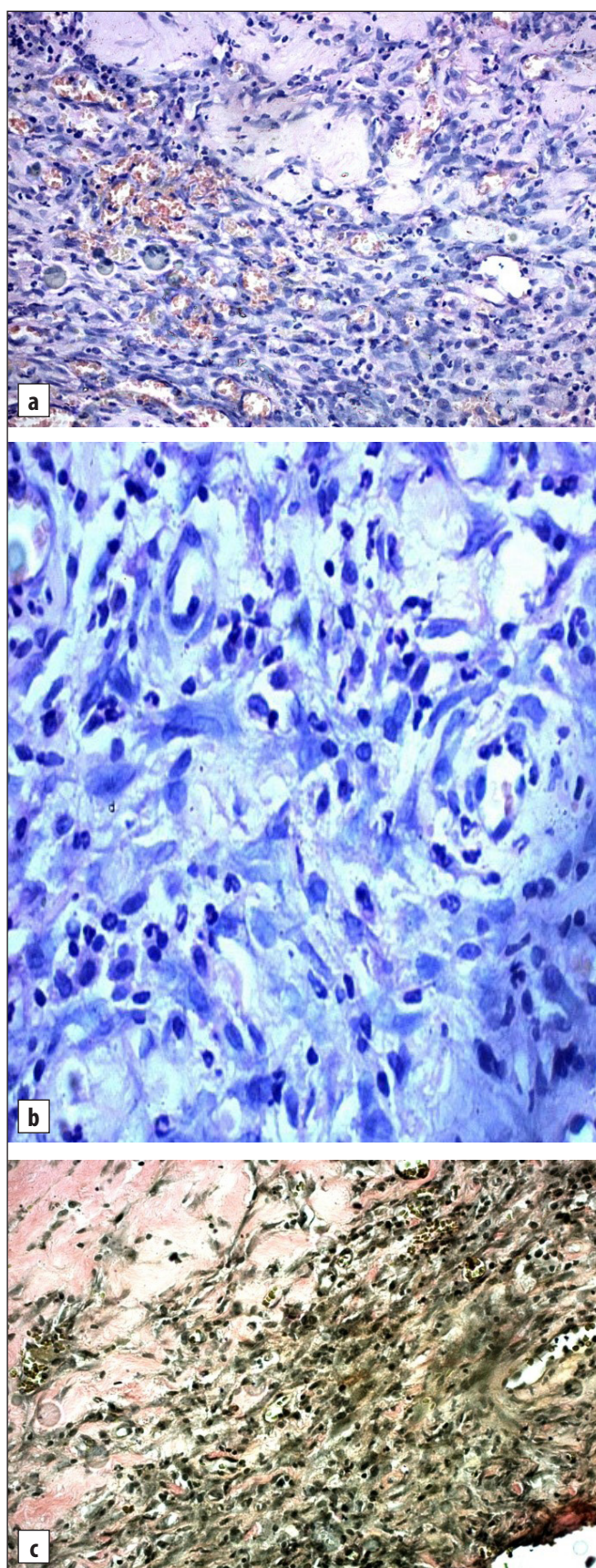


Fig. 7. Main group I, 14 days of the study. Intercellular infiltration extends to the entire depth of granulation tissue (a, b), endothelial cell proliferation (c). Staining: a, b - hematoxylin and eosin, c - van Gison. Magnification: a, c x 100, b x 400.

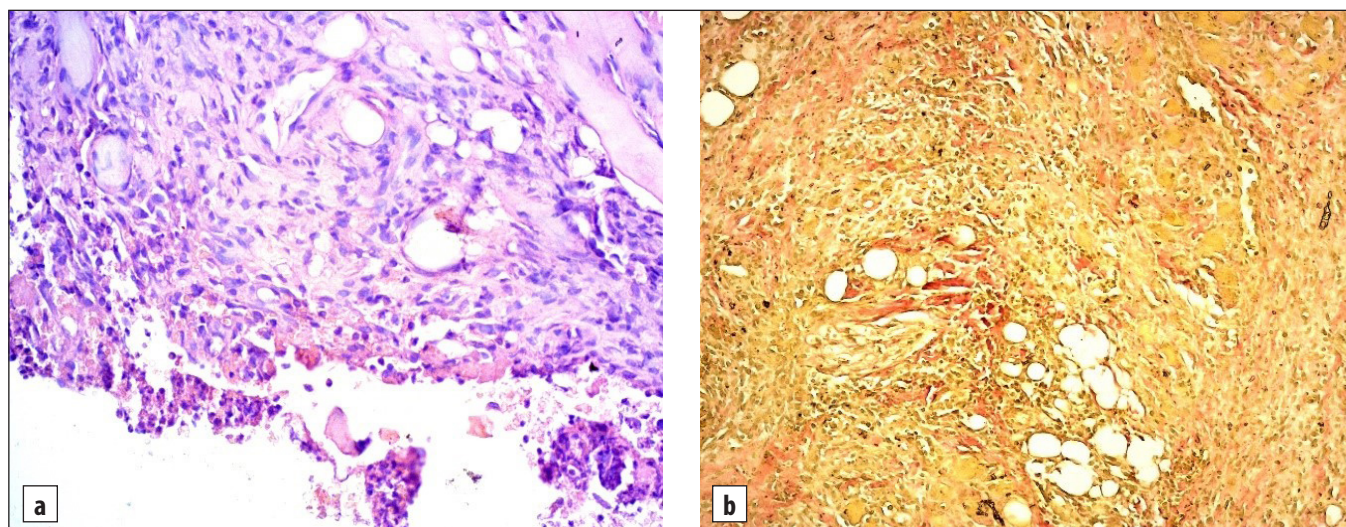


Fig. 8. Comparison group II, 14 days of the study. Fibrinous-purulent overlays (a(↑)), intercellular oedema and infiltration of granulation tissue by neutrophils and lymphocytes (b(↑)) are noted. Staining: a - hematoxylin and eosin, b - van Gizon. Magnification: x 200.

Table I. Dynamics of the wound process in clinical study groups

Group of patients	Clinical indicators				
	Cupping pain syndrome (day 24h)	Normalization of body temperature (day 24h)	Wound cleansing (day 24h)	The appearance of granulation (day 24h)	Marginal epithelialization (day 24h)
I	2,7±0,18	4,5±0,18	4,3±0,15	4,6±0,14	6,1±0,25
II	6,4±0,27	7,3±0,23	8,4±0,21	8,7±0,25	10,4±0,26
	p < 0,05	p < 0,05	p < 0,05	p < 0,05	p < 0,05

- this model is effective for preliminary estimation of adsorption energy.

When ornidazole and silanol molecules interact, the latter's silanol group may form intermolecular binding to ornidazole functional groups. In one of the adsorption complexes, the chlorine atom of the ornidazole molecule is located at a distance of 2,837 Å from the oxygen atom of the silanol group, which indicates a weak interaction, as this distance O...Cl is less than the sum of van der Waals atomic radii of oxygen and chlorine atoms ($r_w(\text{Cl}) + r_w(\text{O}) = 3.27 \text{ \AA}$). The interaction energy in this case is -10.4 kJ/mol [28]. Significantly higher complexation energy (-42.4 kJ/mol) when the nitrogen atom of the ornidazole molecule interacts with the hydrogen atom of the silanol molecule. The distance between these atoms (1,716 Å) is much smaller than the distance O...Cl in the above-mentioned complex, which indicates the possible formation of a hydrogen bond.

The hydroxyl group of the ornidazole molecule can form two types of hydrogen bonds with the silanol molecule: due to the oxygen atom of the alcohol group of the ornidazole molecule with a bond length of 1,711 Å or with the participation of its hydrogen atom with a hydrogen bond length slightly less than 1,707 Å (Fig.

4). The values of the interaction energy for these complexes are -41 and -53.0 kJ/mol, respectively.

In addition, the ornidazole molecule contains the polar group NO_2 , which can also form hydrogen bonds due to the presence of negatively polarised oxygen atoms. In this case, the energy of complexation with the participation of the oxygen atom of the nitro group, which is located closer to the «tail» of the ornidazole molecule, is slightly higher (-45.4 kJ/mol) energy of a similar bond with another oxygen atom of this group (-41,1 kJ/mol), which correlates with their lengths.

Thus, based on the analysis of the results of calculations, it was found that the lowest energy obtained for intermolecular interaction of the silanol group of the silanol molecule with the chlorine atom of the ornidazole molecule, and the highest - with the OH group, whose hydrogen atom forms a hydrogen bond with the oxygen atom of the silanol group. In addition, the nominal nitrogen atom and the oxygen atoms of the nitro group may also be involved in the intermolecular interaction.

Due to the fact that the adsorption of ornidazole occurs from aqueous solution, it is desirable to consider the interaction of the water molecule with the OH group of the ornidazole molecule. It was found that the length

of the hydrogen bond between the oxygen atom of the water molecule and the hydrogen atom of the OH group of the ornidazole molecule is smaller (Fig. 5, a) and is 1.67 Å, compared with that formed by the interaction of the silanol group with the same group (Fig. 4, d) and is 1.707 Å, respectively. This means that the energy of this bond is higher and is 56 kJ/mol, which is 3 kJ/mol more than the absolute value of the energy of interaction with silanol (-53 kJ/mol). Comparing these values with the energy effect of hydrogen bonding between two water molecules (Fig. 5, b) (-31 kJ/mol), it can be argued that ornidazole will be washed away by water, passing into the contact solution, because the absolute value of the interaction energy between water molecules and ornidazole are higher compared to the binding energy between water molecules in the dimer (Fig. 5, b) and in the complex of water and silanol molecules, which is -28.4 kJ/mol (Fig. 5, c).

To determine the influence of the chemical nature of the functional groups of the silica surface on its adsorption capacity relative to the ornidazole molecule, adsorption complexes were considered, in which the orthosilicic acid molecule ruled over the silica surface (Fig. 6).

The equilibrium structure of the adsorption complex of the ornidazole molecule with orthosilicic acid is presented in Fig. 6, b. It is obvious that the largest number of hydrogen bonds (namely - three) is formed by interaction with the original silica (Fig. 6, b), which is confirmed by the values of adsorption energy calculated by formula (1), which is -87.5 kJ/mol.

Therefore, complex studies using quantum chemical calculations and IR spectroscopy have shown that the interaction of ornidazole with hydroxylated silica is slightly different. The formation of active substance complexes with hydroxylated matrices is due to hydrogen bonds between the oxygen atom of the silanol group of the silica surface and the hydrogen atom of the alcohol group of the ornidazole molecule. This promotes the gradual release of ornidazole from the surface of such a matrix into the wound exudate.

The results of the study of the therapeutic effect of "Ornidasil" *in vivo* show that in the main group I already on the seventh day in comparison with group II was granulation tissue with a large number of newly formed vessels of the microcirculatory tract and pronounced proliferation of fibroblasts, indicating acceleration. In the comparison group, the regeneration process was slower (Fig. 8). Thus, on the 7th day of the study, the best results of healing purulent wounds are observed in the first group (main) of experimental animals.

Thus, on day 13, 9 experimental rats of group I healed completely, 11 rats had a small wound surface, complete healing occurred on day 15. In the group comparing rats

on day 21 of the experiment, complete wound healing was not observed. On the 14th day of the experiment in 11 animals of the basic group from data of histological research, there was the formed granulation fabric that consists of young collagen fibers and plenty of vascular loops. There were areas where a wide strip of granulation tissue with the formation of thin multidirectional collagen fibres, between which many cells were seen: macrophages, lymphocytes, fibroblasts cells of varying maturity and large poorly differentiated cells (Fig. 7).

We also investigated the effectiveness of the application sorbent Ornidasil in the clinic. The main group of IA included 15 patients who received NO-therapy in combination with the application of sorbent Ornidasil in the complex treatment of DFS (Diabetic foot syndrome). The IB group included 23 patients who received the application sorbent Ornidasil for local treatment of DFS. The comparison group IIA included 27 patients who received the application sorbent Gentaxan in complex treatment. The IIB comparison group included 19 patients who received 10% NaCl solution for local treatment of DFS with subsequent transition to Levomecol ointment (Table I). The method of the application sorbent in patients with DFS of the main group was as follows: after treatment of the wound with 0.9% NaCl solution on the wound surface for 24 hours applied application sorbent «Ornidasil» layer 1-3 mm with subsequent overlay by a sterile gauze bandage. Bandages are applied daily with this symptom until the wound is completely healed.

One of the important manifestations of diabetic foot syndrome (DFS) is the presence of pain. Cupping pain syndrome occurred in the IA group (main) compared to the IIA group (comparison) 2.1 times faster, with the IIB group (comparison) - respectively 2.4 times faster. In the IB group (main) compared with the IIA group (comparison) cupping pain syndrome occurred 1.2 times faster, with the IIB group (comparison) - respectively 1.4 times faster.

To determine the effectiveness of treatment, an important indicator is the purification of the wound from necrotic tissue, which in the IA group in comparison with the IIA group was 1.8 times faster, and with the IIB group - respectively 1.95 times faster. In the IB group, compared with the IIA group, wound cleansing was 1.4 times faster, and in the IIB group - respectively 1.5 times faster.

Wound cleansing begins with the appearance of granulation tissue, which is an objective criterion for the effectiveness of treatment. In the IA group, the appearance of granulation tissue occurred on 4.6 ± 0.14 days, while in the comparison groups (IIA, IIB) the appearance of granulation was observed 1.8 and 1.9

times later, respectively. In the IV group, the appearance of granulation tissue occurred at 5.3 ± 0.15 days, while in the comparison groups (IIA, IIB) the appearance of granulation was observed 1.6 times later.

Also, an important indicator of the wound process is the appearance of marginal epithelialization, which indicates the beginning of wound cleansing. In the IA group, the appearance of epithelialization was observed at 6.1 ± 0.25 days, which is 1.6 times faster than in the IIA group, and 1.7 times faster in the IIB group. In the IV group, the appearance of epithelialization was observed at 7.3 ± 0.15 days, which is 1.4 times faster than in the IIA group, and 1.7 times faster in the IIB group.

The wounding process in all patients ran with all the signs of each phase, but with their different duration. The most significant was the phase of hydration, which lasted much longer in patients with massive purulent processes.

One of the serious problems of abdominal surgery is the problem of peritonitis. Frequent complications of peritonitis are wound complications - seromas, hematomas and suppuration of wounds. The most dangerous complication is suppuration of postoperative wounds, which in diffuse and general peritonitis, according to various authors, occurs in 11 - 72% [29]. These complications prolong the length of stay of patients in the hospital, increase the duration of disability, the cost of treatment and worsen its results.

The critical number of microorganisms for the occurrence of suppuration is 105 microbial bodies per 1 g of tissue and in hypoxia enough 100 microbial bodies per 1 g of tissue. Therefore, in order to study the pathogenesis of suppuration of postoperative wounds and to develop mechanisms for its prevention, we studied the pollution by microorganisms of the surgical wound at the end of the operation. The study was performed in 43 patients with diffuse and general purulent peritonitis in the toxic and terminal stages. At the end of the operation, pollution of wounds with microorganisms above the critical level of suppuration was observed in 35 patients, which amounted to 81.4%.

We have proven the effectiveness of the application of sorbent «Ornidasil» for the prevention of suppuration of postoperative wounds in patients with purulent peritonitis in the toxic and terminal stages. The comparison group consisted of 19 patients who for the prevention of suppuration of postoperative wounds used a polyurethane wound expander (wound protector) with variable height. The main group included 24 patients in whom polyurethane wound protector was used in combination with the application sorbent «Ornidasil». The groups were comparable in age, sex, prevalence and nature of peritonitis. The method of protecting the wound from infection in patients of the main group

was as follows: when performing surgical access to the abdominal organs (middle laparotomy) cut the skin, subcutaneous fat and aponeurosis to the parietal peritoneum; at the edge of the aponeurosis, clamps were applied and traction was performed upwards, after which the parietal peritoneum was dissected; a suction cup was introduced into the abdominal cavity with the help of which the exudate was evacuated; then the lower ring of the polyurethane wound protector was wound into the abdominal cavity and the clamps were removed from the aponeurosis, then the upward traction was performed behind the upper ring of the wound protector; between the wall of the wound protector and the surgical wound was applied a thin layer of application sorbent «Ornidasil», and then wound on the upper ring wall of the wound protector, carrying out its final installation and fixation in the surgical wound; at the end of the surgery, the wound protector was removed, and the remnants of the sorbent on the surgical wound were washed away with 0.9% NaCl solution. In the comparison group, postoperative wound suppuration occurred in 6 patients (31.6%), and in the main group - in 3 patients (12.5%).

DISCUSSION

On the basis of studies of the biological activity of the nanocomposition "Ornidasil" in *in vivo* and in clinical studies it's obvious advantages over traditional methods of treatment have been established. As shown by IR spectral data and data on the study of adsorption and desorption of ornidazole, as well as the results of quantum chemical calculations, the molecule of the active substance binds to the surface of the carrier with the formation of adsorption complexes.

The material thus obtained is a composite consisting of silica nanoparticles [10], the surface of which is covered with ornidazole adsorbed due to hydrogen bonds, mainly connected to the active silanol groups by the hydroxyl of adsorbate molecule. Moreover, the interaction of other polar groups of ornidazole with the active centers of the silica surface is not excluded. In particular, judging by the calculated interaction energies, a hydrogen bond with the oxygens of the nitro group is very likely [19].

The energy of interaction of ornidazole with water molecules, that is, the energy of solvation, is relatively large and close to the energy of interaction of the adsorbate with the surface due to one hydrogen bond. The solvation energy determines the ability of the adsorbate to be hydrated and dissolve in water.

Therefore, after the nanocomposite enters the wound solution, ornidazole, bound by one hydrogen bond,

begins to desorb and pass into the solution due to a shift in the equilibrium because of the predominance of concentrations of water molecules and destroys bacterial microflora [25]. The surface of silica freed in this way begins to adsorb pus and other contamination of the wound, primarily of oligo- and polypeptide nature [7]. Those ornidazole molecules that are tightly bound to the silica surface by multiple hydrogen bonds are retained by the surface and gradually releasing from the surface over longer periods of time [11]. Thanks to this multifunctional ability, the wound is cleaned of microorganisms, their waste products and debris [8].

At the same time, there is a synergism of the action of the adsorbent and the antimicrobial agent. Our studies of the effects of ornidazole and nanosilica separately on the most common microorganisms of wound infection, such as *S. aureus* and *Pseudomonas aeruginosa* [24], showed either their weak inhibitory effect or even the absence of activity (silica). While together they showed a high inhibitory capacity for all tested bacterial strains, and the main thing is the prolongation of the action of the composite. Such a prolonged effect can be explained precisely by the easy release of the active substance into the solution, as well as the presence of residual adsorbed molecules of ornidazole. Apparently, such molecules are tightly bound to the surface due to the simultaneous binding by several hydrogen bonds of different polar groups of ornidazole, which slows down the desorption of the active substance and determines the prolongation of the drug's effect [25].

The synergism or enhancement of the antimicrobial activity of ornidazole in the presence of silica can be explained by the adsorption of silica nanoparticles to the surface of bacteria due to the active centers of the surface of silica and the phospholipid membrane [4] of bacterial cells and the weakening of bacteria for their effective destruction by the antibacterial agent ornidazole.

Thus, the mechanism of action of the drug Ornidasil consists in the joint action of nanosilica and ornidazole, which is released in portions into the wound solution at first quickly and then slowly, creating a prolonged antimicrobial and simultaneously cleansing effect.

CONCLUSIONS

Nanocomposites obtained by immobilization of ornidazole on the surface of the hydroxylated silica matrix were studied using quantum chemical calculations and IR spectroscopy.

Comparing the IR spectra of nanocomposites, before and after the release of the active substance (ornidazole) after 24 h, it was found that this process occurs gradually and even after 24 h the active ingredient still remains in the sorbent.

Quantum chemical modelling of the interaction of ornidazole with surface functional groups showed that the lowest energy is inherent in the intermolecular interaction of the silanol group of the silanol molecule with the chlorine atom of the ornidazole molecule, and the highest with the OH group whose hydrogen atom forms a hydrogen bond. The nominal Nitrogen atom and the Oxygen atoms of the nitro group may also be involved in the intermolecular interaction. Also, quantum chemistry methods have shown that regardless of the size of the silica model, the highest adsorption energy of ornidazole is inherent in hydroxylated silica.

The results of the study in rats show that in the main group, which was treated with nanocomposite "Ornidasil" on the seventh day compared with the comparison group was granulation tissue with a large number of newly formed vessels of the microcirculatory tract and pronounced proliferation of fibroblasts, indicating acceleration. In the comparison group, which was treated with Gentaxan sorbent, the regeneration process was slower. In the main group of experimental animals, wound healing was observed in 9 rats on day 13, in 11 rats on day 15, while in the comparison group, even on day 21, complete wound healing did not occur.

A study of the effectiveness of allocating sorbet based on nanosilicon and ornidazole (Ornidasil) in the complex treatment of Diabetic foot syndrome showed that in the experimental groups, wound healing occurred 1.6 -1.9 times faster than in the control group.

The use of polyurethane wound protector in combination with the application of sorbent Ornidasil to prevent suppuration of postoperative wounds in patients with diffuse and general peritonitis in toxic and terminal stages reduced the suppuration of postoperative wounds in patients of the main group by 2.5 times relative to patients in the comparison group.

REFERENCES

1. Feldman D. Polymer Nanocomposites in medicine. *Journal of Macromolecular Science, Part A*. 2016; 53(1):55-62. doi: 10.1080/10601325.2016.1110459.
2. Siddiqui B, Rehman A, Haq I et al. Exploiting recent trends for the synthesis and surface functionalization of mesoporous silica nanoparticles towards biomedical applications. *Int J Pharm X*. 2022;4:100116. doi: 10.1016/j.ijpx.2022.100116.
3. Zhang R, Hua M, Liu H et al. How to design nanoporous silica nanoparticles in regulating drug delivery: Surface modification and porous control. *Mater. Sci. Eng. B*. 2021;263:114835. doi: 10.1016/j.mseb.2020.114835.

4. McCarthy CA, Ahern RJ, Dontireddy R et al. Mesoporous silica formulation strategies for drug dissolution enhancement: a review. *Expert Opin Drug Deliv.* 2016;13(1):93-108. doi: 10.1517/17425247.2016.1100165.
5. Fatullayeva S, Tagiyev D, Zeynalov N. A review on enterosorbents and their application in clinical practice: Removal of toxic metals. *Colloid and Interface Science Communications.* 2021;45:100545. doi: 10.1016/j.colcom.2021.100545.
6. Budnyak T, Vlasova N, Golovkova L et al. Bile acids adsorption by chitoan-fumed silica enterosorbent. *Colloid and Interface Science Communications.* 2019;32:100194. doi: 10.1016/j.colcom.2019.100194.
7. Meissner J, Prause A, Bharti B et al. Characterization of protein adsorption onto silica nanoparticles: influence of pH and ionic strength. *Colloid Polym Sci.* 2015;293(11):3381-3391. doi:10.1007/s00396-015-3754-x.
8. Natan M, Banin E. From Nano to Micro: using nanotechnology to combat microorganisms and their multidrug resistance. *FEMS Microbiology Reviews.* 2017;41(3):302-322. doi: 10.1093/femsre/fux003.
9. Saleh TA. Nanomaterials: classification, properties, and environmental toxicities, *Environ Technol Innov.* 2020;20:101067. doi: 10.1016/j.eti.2020.101067.
10. Perni S, Martini-Gilching K, Prokopovich P. Controlling release kinetics of gentamicin from silica nano-carriers. *Colloids and Surfaces A: Physicochemical and Engineering Aspects.* 2018;541:212-221. doi: 10.1016/j.colsurfa.2017.04.063.
11. Croissant JG, Butler KS, Zink JI et al. Synthetic amorphous silica nanoparticles: toxicity, biomedical and environmental implications. *Nature Reviews Materials.* 2020;5:886-909. doi: 10.1038/s41578-020-0230-0.
12. Becke AD. Density functional thermochemistry. III. The role of exact exchange. *J. Chem. Phys.* 1993;98(7):5648. doi: 10.1063/1.464913.
13. Araghi S, Entezari M, Googheri M. Configurational study of amino-functionalized silica surfaces: A density functional theory modeling. *Journal of Molecular Graphics and Modelling.* 2015;59:21-30. doi: 10.1016/j.jmgm.2015.03.006.
14. Schmidt MW, Baldrige KK, Boatz JA et al. General atomic and molecular electronic structure system. *J. Comput. Chem.* 1993;14(11):1347-1363. doi: 10.1002/jcc.540141112.
15. Grimme S, Ehrlich S, Goerigk L. Effect of the damping function in dispersion corrected density functional theory. *J. Comput Chem.* 2011;32(7):1456-65. doi: 10.1002/jcc.21759.
16. Grimme S. Density functional theory with London dispersion corrections. *WIREs Comput. Mol. Sci.* 2011;1:211-228. doi: 10.1002/wcms.30.
17. Montiel-Centeno K, Barrera D, García-Villén F et al. Cephalixin loading and controlled release studies on mesoporous silica functionalized with amino groups. *Journal of Drug Delivery Science and Technology.* 2022;72:103348. doi: 10.1016/j.jddst.2022.103348.
18. Gueddida S, Badawi M, Reynel-Ávila HE et al. Selective adsorption of glucose towards itaconic acid on amorphous silica surfaces: Insights from density functional theory calculations. *Journal of Molecular Liquids.* 2021;343:117586. doi: 10.1016/j.molliq.2021.117586.
19. Gaidai AR, Vakuliuk PV, Furtat IM et al. Stvorennia ta vlastyvoli nanokompozytiv na osnovi kremnezemnykh matryts, modyfikovanykh antymikrobnymi preparatamy [Preparation and properties of nanocomposites based on silica matrix modified with antimicrobial preparations]. *Voprosy khimii i khimicheskoi tekhnologii.* 2019;3:6-16. (In Ukrainian).
20. Biliaieva OO, Karol IV, Kryzhevskiy YeYe, vynakhidnyky. Sposib modeliuvannia ranovoi infektsii. Patent Ukrainy na KM № 121047. 2017 Lyst. 27. (In Ukrainian).
21. Biliaieva OO, Holub OA, Karol IV et al, vynakhidnyky. Kompleksnyi antymikrobnyi sorbtsiinyi preparat ornidasyl dlia profilaktyky aerobnoi i anaerobnoi infektsii ta likuvannia hniinykh ran, trofichnykh vyrazok, opikiv. Patent Ukrainy na KM № 112523. 2016 Hrud.26. (In Ukrainian).
22. Biliaieva OO, Holub OA, Karol IV et al, vynakhidnyky. Sposib oderzhannia kompleksnoho antymikrobnoho sorbtsiinoho preparatu ornidasyl dlia profilaktyky aerobnoi i anaerobnoi infektsii ta likuvannia hniinykh ran, trofichnykh vyrazok, opikiv. Patent Ukrainy na KM № 115228. 2017 Kvit.10. (In Ukrainian).
23. Pavlovich KV. Mistseve likuvannia hniinykh ran i trofichnykh vyrazok sorbentom «Hentaksan» na foni obtiazhenoho zahalnoho stanu khvorykh [Local treatment of purulent wounds and trophic ulcers with sorbent «Gentaxan» on the background of the aggravated general condition of patients]. *Kharkiv Surgical School.* 2010;4:31-35. (In Ukrainian).
24. Furtat I, Lupatsii M, Murlanova T et al. Nanocomposites with ornidazole – antibacterial and antiadhesive agents against Gram-positive and Gram-negative bacteria. *Appl Nanosci.* 2020;10:3193-3203. doi: 10.1007/s13204-020-01260-x.
25. Rajesh P, Gunasekaran S, Gnanasambandan T et al. Experimental and theoretical study of ornidazole. *Spectrochim Acta A Mol Biomol Spectrosc.* 2016;153:496-504. doi: 10.1016/j.saa.2015.08.032.
26. Chandrasekara K, Kumarb RT. Molecular properties prediction, docking studies and antimicrobial screening of ornidazole and its derivatives. *Journal of Chemical and Pharmaceutical Research.* 2016;8(3):849-861.
27. Thompson KC, Margey P. Hydrogen bonded complexes between nitrogen dioxide, nitric acid, nitrous acid and water with SiH₃OH and Si(OH)₄. *Phys. Chem. Chem. Phys.* 2003;5:2970-2975. doi: 10.1039/B303507G.
28. Gaidai AR, Vakuliuk PV, Demianenko EM et al. Interaction of ornidazole with initial and functionalized silicas. *Applied Surface Science.* 2022;580:152218. doi: 10.1016/j.apsusc.2021.152218.
29. Beljaeva OA. Kompleksnoe lechenie peritonita i profilaktika ego oslozhenij (jeksperimental'no-klinicheskoe issledovanie) [dissertacija]. Kiev. 1999, p.375. (in Russian).

ORCID and contributionship:

Olga Bilyayeva: 0000-0003-2862-0423^F

Ivan Karol: 0000-0003-3684-0127^{C,D}

Eugeniy Demianenko: 0000-0001-6068-9151^B

Alina Gaidai: 0000-0002-5833-0868^D

Yevhenii Kryzhevskiy: 0000-0003-1403-1476^D

Polina Vakuliuk: 0000-0001-7828-1349^A

Alexander Golub: 0000-0003-1823-2523^E

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Ivan Karol

Shupyk National Healthcare University of Ukraine

9 Dorohozhitska St., 04112 Kyiv, Ukraine

e-mail: drkarol@ukr.net

Received: 13.05.2022

Accepted: 14.04.2023

A - Work concept and design, **B** - Data collection and analysis, **C** - Responsibility for statistical analysis, **D** - Writing the article, **E** - Critical review, **F** - Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

CYTOLOGIC CHARACTERISTIC OF THE CELLULAR COMPOSITION OF THE GUM MUCOUS MEMBRANE IN SCHOOL-AGE CHILDREN

DOI: 10.36740/WLek202306105

Sofia S. Bauman, Olga V. Sheshukova, Valentyna P. Trufanova, Iryna O. Kuz, Tetiana V. Polishchuk, Anna S. Mosiienko, Kateryna S. Kazakova
POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To establish the characteristics of the gingival mucosa cellular composition in school-age children.

Materials and methods: We made a dental and cytological examination on 150 Ukrainian (Poltava city) children aged 6, 12, and 15 years. Smears were got by scraping from the gum mucosa and stained with a May-Grunwald solution. Cytograms were made by using a Biorex-3 BM-500T microscope with a DCM-900 digital microphotographic attachment. The programs were adapted for these types of studies. We used a magnification of 1000. The t-test for paired samples was used to compare values. The difference was considered statistically significant at $P < 0.05$.

Results: The number of superficial epitheliocytes in children aged 12 and 15 was significantly higher than in 6-year-olds but did not differ from each other.

Conclusions: The process of physiological keratinization of the cells of the gingival mucosa in schoolchildren is diverse and keratinization occurs both due to the phenomenon of physiological necrosis, namely, apoptosis of surface cells and due to orthokeratosis. From the age of 6, the average number of surface cells in cytograms decreases, while the number of intermediate and dead keratinized cells increases up to 12 years and remains on the previous level in children of 15 years.

KEY WORDS: cytograms, gum, children, epitheliocytes, diagnostic method

Wiad Lek. 2023;76(6):1359-1362

INTRODUCTION

The diseases of periodontium have a leading place in the structure of dental morbidity in both adults and children of various ages [1-4]. It has been proven that chronic inflammation of the periodontium affects the development of tissues of the oral cavity and the body negatively [5-8].

The morphological method is the most adequate and effective method of treatment and preventing complications at an early stage of the development of periodontal diseases [9-11]. Due to the minimally invasive intervention, high informativeness, and accessibility, the cytological method is one of the most appropriate for use in children [12-15]. To diagnose a pathological condition, it is necessary to determine the stages of physiological maturation of gum tissues in children of key age groups - 6, 12, and 15 years. The choice of age groups depends on the stages of development of the maxillofacial system.

THE AIM

The aim of the research work was to establish the special characteristics of the gingival mucosa cellular composition in school-age children.

MATERIALS AND METHODS

We made a dental and cytological examination on 150 Ukrainian (Poltava city) children aged 6, 12, and 15 years. All the children we examined had no clinical signs of infection or any diseases of the oral cavity. Smears were got by scraping with a sickle-shaped spatula from the gum mucosa. Subsequently, then this material was applied to a sterile glass slide. The smears were dried according to the method of dry fixation, namely, at room temperature with open access to air. The smears were placed into a special container for glass slides and put into a May-Grunwald's fixative solution.

The procedure was done as follows: the smears were fixed for 5 minutes, after that, they were washed with water, and stained with a May-Grunwald solution (10 ml of dye per 100 ml of distilled water). The next step was washing the slides with water and laying them out in a special support stand for drying.

We analyzed cytograms by using a Biorex-3 BM-500T microscope with a DCM-900 digital microphotographic attachment. The programs were adapted for these types of studies. We used a magnification of 1000.

Quantitative indicators were traditionally determined by counting cellular elements in five fields of view. And

Table I. Average values of the percentage of different classes of the stratified squamous epithelium of the gums in examined children

The age	Cellular composition of cytograms		
	Intermediate cells	Superficial cells	Dead keratinized cells
6 years	5,54±0,71	93,85±0,77	0,61±0,18
12 years	10,42±1,06 *	87,17±1,39 *	2,41±0,46 *
15 years	11,6±0,76	86,51±0,85	1,89±0,31

Note: * - the difference is significant if $P < 0.05$ (compared with 6-year-old children).

the fixing in absolute numbers and counting of the average values were done using the Excel program. The latter data were used to determine the percentage of different classes of epithelial cells to establish standard values.

The materials of our research work comply with the Council of Europe Convention on Human Rights and Biomedicine, the Helsinki Declaration of Human Rights, the rules of the Tokyo Declaration of the World Medical Association, the legislation of Ukraine, orders of the Ministry of Health of Ukraine, and the requirements of the Doctor's Ethical Code of Ukraine.

Ethical committee clearance reference (Commission on Ethical Issues and Biomedical Ethics of Poltava State Medical University, Ukraine) № 210 dated November 23, 2022.

The findings obtained were statistically processed using Microsoft Office Excel 2016 software pack. The distribution was checked by the Shapiro-Wilk test. The arithmetic mean (M), the representativeness error of the mean (m), and the significance level of the differences in the mean values (P) were calculated. The t-test for paired samples was used to compare values. The difference was considered statistically significant at $P < 0.05$.

RESULTS

It is known that there are 4 classes of cells in the epithelium of the human gingival mucosa, namely, superficial, intermediate, parabasal, and basal [15]. Cytograms from the gingival mucosa of children lack basal and parabasal epithelial cells normally. It is associated with the functional characteristics of the gums as chewing mucosa.

It was found that intermediate gingival epitheliocytes had a hexagonal shape. The nucleus had a rounded shape, and clear contours, and was localized mainly in the centre of the cells. Also, the class affiliation of epitheliocytes was indicated by the active contamination of microorganisms, mainly by representatives of the rod flora.

The cytoplasm stained basophilically, and glycogen granules appeared as azure-positive (Fig. 1).

The surface epithelial cells had clear contours of the plasmolemma, a centrally or eccentrically localized nucleus, and thin filaments of tonofilaments in the cytoplasm after using May-Grunwald stain (Fig. 2).

We visualized surface eosinophilic epitheliocytes in cytograms along with basophilic azure-positive surface epitheliocytes, in school-age children with clinically healthy gums. Their characteristic feature, in contrast to basophilic cells, was the presence of different sizes of eosinophilic granules in the cytoplasm, which were stained in different shades of pink after May-Grunwald solution. The volume of the cytoplasm of these cells significantly exceeded the size of the nucleus. Most of the granules were located diffusely around the nucleus, and they were located centrally relative to the cytoplasm, thus shifting the nucleus to an eccentric position. Homogeneous eosinophilic masses were detected in the cytoplasm (Fig. 3).

The above-mentioned information indicates that the process of gum keratinization is characterized by stages, starting from basophilic and eosinophilic superficial cells to horny scales (Fig. 4).

It was found that superficial cells predominate in cytograms, according to the results of cytological studies of the cellular composition of gum cytograms in school-age children. The largest number was determined in children of 6 years of age (Table I).

The number of superficial epitheliocytes in children aged 12 and 15 was significantly higher than in 6-year-olds but did not differ from each other. Among the three age groups, the average number of intermediate cells in 6-year-old children was half that of others, and the average number of dead keratinized cells was three times less (Table I).

DISCUSSION

In our opinion, the different content of eosinophilic granules and homogeneous eosinophilic structures causes the process of keratinization of epitheliocytes in the form of keratinization of the gums, characterized by the appearance in the surface cells of the gums of horny substance, namely, keratohyalin and a layer of horny scales. Previous studies show that keratohyalin has the property of staining with eosin [1, 6, 13]. The eccentric arrangement of keratohyalin granules is a morphological manifestation of the gradual process of physiological keratinization of the gums.

The process of physiological keratinization of the epithelial cells of the gingival mucosa in schoolchild-

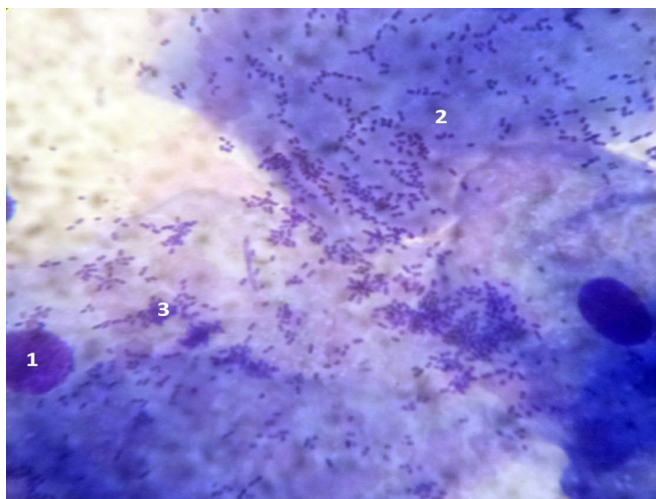


Fig. 1. Intermediate epitheliocytes in the cytogram of the gingival mucosa. May-Grunwald's stain. Magn: obj. x 100, eyepiece x 10.
1 - the nucleus of the intermediate epitheliocyte; 2 - cytoplasm; 3 - contamination of microorganisms.

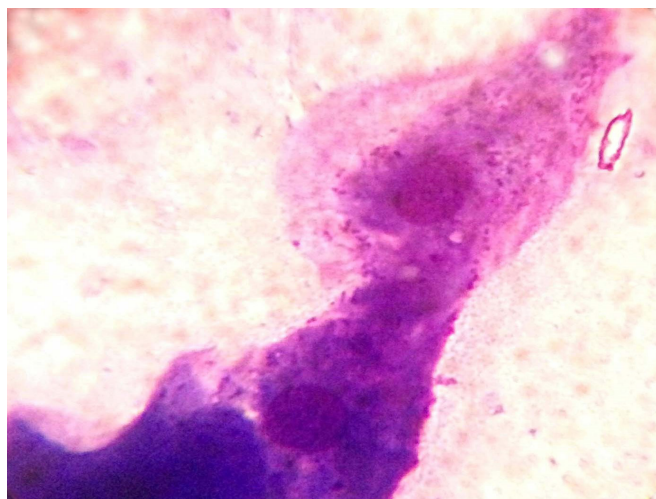


Fig. 3. Superficial eosinophilic epitheliocyte. Cytogram of the gingival mucosa. May-Grunwald's stain. Magn: obj. x 100, eyepiece x 10.
1 - eosinophilic granules; 2 - nucleus; 3 - homogeneous eosinophilic masses.



Fig. 2. Superficial basophilic (azure-positive) epitheliocyte. Cytogram of the gingival mucosa. May-Grunwald's stain. Magn: obj. x 100, eyepiece x 10.
1 - tonofilaments; 2 - nucleus; 3 - cytoplasm.

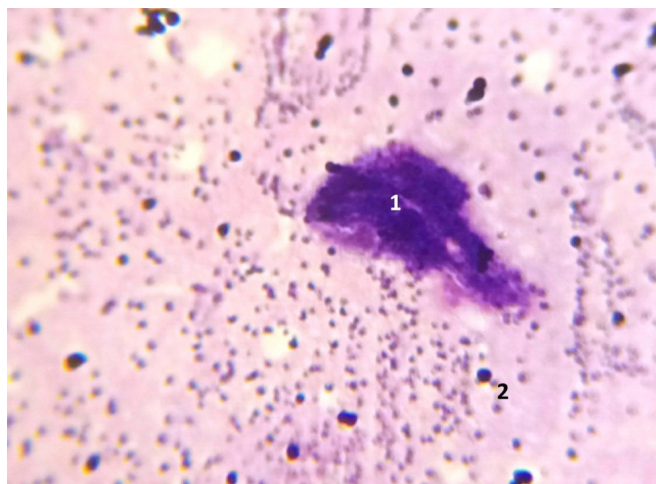


Fig. 4. Horny scales in the cytogram of the gingival mucosa. May-Grunwald's stain. Magn: obj. x 100, eyepiece x 10.
1 - dead keratinized cell; 2 - microorganisms.

dren is diverse and keratinization occurs both due to the phenomenon of physiological necrosis, namely, apoptosis of surface cells and due to orthokeratosis, namely, in the form of eosinophils in the cytoplasm of epithelial cells. This type of keratinization is the main one, along with the destruction of mitochondria and a decrease in the number of enzymes in dead keratinized cells.

REFERENCES

1. Groeger S, Meyle J. Oral Mucosal Epithelial Cells. *Front Immunol.* 2019;10:208.
2. Sheshukova OV, Kuz IO, Kostenko VO et al. Functioning of NO-cycle in the oral fluid in children of primary school age with type 1 diabetes mellitus in the treatment of chronic catarrhal gingivitis. *Wiad Lek.* 2022;75(3):654-658.
3. Jiang L, Fang M, Tao R et al. Recombinant human interleukin 17A enhances the anti-Candida effect of human oral mucosal epithelial cells by inhibiting *Candida albicans* growth and inducing antimicrobial peptides secretion. *J Oral Pathol Med.* 2020;49(4):320-327.

CONCLUSIONS

As a result of the conducted research, we established the peculiarities of the cellular composition of the mucous membrane of the gums in school-aged children. From the age of 6, the average number of surface cells in cytograms decreases, while the number of intermediate and dead keratinized cells increases up to 12 years and remains on the previous level in children of 15 years.

4. Maksymenko AI, Sheshukova OV, Kuz IO et al. The level of interleukin-18 in the oral fluid in primary school children with chronic catarrhal gingivitis and type I diabetes mellitus. *Wiad Lek.* 2021;74(6):1336-1340.
5. Pelaez-Prestel HF, Sanchez-Trincado JL, Lafuente EM, Reche PA. Immune Tolerance in the Oral Mucosa. *Int J Mol Sci.* 2021;22(22):12149.
6. Petrushanko TA, Tchereda VV, Loban GA. The screening diagnostic of micro ecological disorders of oral cavity. *Klin Lab Diagn.* 2014;(6):48-50.
7. Hyun DW, Kim YH, Koh AY et al. Characterization of biomaterial-free cell sheets cultured from human oral mucosal epithelial cells. *J Tissue Eng Regen Med.* 2017;11(3):743-750.
8. Groeger SE, Meyle J. Epithelial barrier and oral bacterial infection. *Periodontol 2000.* 2015;69(1):46-67.
9. Yazdani M, Shahdadfar A, Reppe S et al. Response of human oral mucosal epithelial cells to different storage temperatures: A structural and transcriptional study. *PLoS One.* 2020;15(12):e0243914.
10. Shynkevych VI, Kolomiets SV, Kaidashev IP. Effects of L-arginine and L-ornithine supplementations on the treatment of chronic periodontitis: A preliminary randomized short-term clinical trial. *Heliyon.* 2021;7(11):e08353.
11. Williams DW, Greenwell-Wild T, Brenchley L et al. NIDCD/NIDCR Genomics and Computational Biology Core, Hajishengallis G, Divaris K, Morasso M, Haniffa M, Moutsopoulos NM. Human oral mucosa cell atlas reveals a stromal-neutrophil axis regulating tissue immunity. *Cell.* 2021;184(15):4090-4104.e15.
12. Hasiuk P, Hasiuk N, Kindiy D et al. Characteristics of cellular composition of periodontal pockets. *Interv Med Appl Sci.* 2016;8(4):172-177.
13. Oliva J, Bardag-Gorce F, Niihara Y. Clinical Trials of Limbal Stem Cell Deficiency Treated with Oral Mucosal Epithelial Cells. *Int J Mol Sci.* 2020;21(2):411.
14. Wang SS, Tang YL, Pang X et al. The maintenance of an oral epithelial barrier. *Life Sci.* 2019 Jun 15;227:129-136.
15. Onyschenko AV, Sheshukova OV, Yeroshenko HA. Clinical and cytological characteristics of the gums in children of primary school age with normal body weight and overweight. *Wiad Lek.* 2021;74(3 cz 1):423-428.

Improvement of forecasting, diagnostics, treatment and prevention of dental and periodontal diseases in children with taking into account exogenous and endogenous risk factors. State number registration: 0122U000204. Implementation years: 2022-2026.

ORCID and contributionship:

Sofia S. Bauman: 0000-0002-9029-8968^{B,D}

Olga V. Sheshukova: 0000-0002-4739-4890^{A,E,F}

Valentyna P. Trufanova: 0000-0002-7819-0188^{B,C}

Iryna O. Kuz: 0000-0003-0287-4783^{A,B,D}

Tetiana V. Polishchuk: 0000-0003-1114-5830^{B,C}

Anna S. Mosiienko: 0000-0003-2129-8304^{B,C}

Kateryna S. Kazakova: 0000-0003-2645-5778^{B,C}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Sofia S. Bauman

Poltava State Medical University

23 Shevchenko st., 36000 Poltava, Ukraine

tel: +380663632104

e-mail: sofibauman92@gmail.com

Received: 12.12.2022

Accepted: 27.05.2023

A - Work concept and design, **B** - Data collection and analysis, **C** - Responsibility for statistical analysis, **D** - Writing the article, **E** - Critical review, **F** - Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

ORIGINAL ARTICLE

ACCEPTANCE OF THE COVID-19 VACCINE AND ITS RELATED FACTORS AMONG IRAQI ADOLESCENTS: A CROSS-SECTIONAL STUDY

DOI: 10.36740/WLek202306106

Hayder Ch. Assad¹, Fadhil A. Rizij¹, Ayad A. Hussien¹, Zainab Hadi²¹KUFA UNIVERSITY, KUFA, IRAQ²NAJAF HEALTH DIRECTORATE, NAJAF, IRAQ**ABSTRACT****The aim:** To evaluate the acceptance rate of COVID-19 vaccine among adolescents and exploring the association factors that affect the acceptability of the vaccine.**Materials and methods:** The study is descriptive cross-sectional study based on online survey conducted on 541 adolescents in Iraqi middle Euphrates provinces. Survey data was collected from November 28, 2021 to April 20, 2022.**Results:** The study showed that about 53% (288 adolescents out of total 541) had not been vaccinated yet and approximately 55% of the not vaccinated adolescents refused to take the vaccine. The mean reasons of this hesitancy were falsified information, insufficient information, concerned about safety and effectiveness of the vaccine. The parents whether infected with COVID-19 or vaccinated considered as strong independent factors that will increase acceptance of vaccination among the adolescents while afraid from the vaccine was considerable independent factor that decrease the acceptance rate.**Conclusions:** High hesitancy rate toward COVID-19 vaccination among adolescents and their parents play significant role model in increasing the acceptability while concerning of the vaccine safety decreasing acceptability.**KEY WORDS:** Vaccine, COVID-19, Adolescents, Hesitancy

Wiad Lek. 2023;76(6):1363-1370

INTRODUCTION

Vaccination toward COVID-19 is a mandatory preventive measure to limit the spread of this devastating viral infection and to help in ending of COVID-19 pandemic [1]. The U.S. FDA has approved Pfizer-BioNTech COVID-19 vaccine since December 2020 in people above 16 years old. On May 2021, FDA extended its Emergency Use Authorization for the mRNA vaccine to include adolescents (12–15 years old) [2] because COVID-19 infection is counted as seventh cause of mortality in these age group and the vaccine proven to be safe and effective in preventing the infection or minimizing the symptoms [3].

In Iraq, Ministry of Health mentioned that first shipment of COVID-19 vaccine had arrived in March 2021 [4]. By the end of July 2022, about 19% of the Iraq population (about 8 million Iraqis) had been fully vaccinated while 28% had received at least one dose of COVID-19 [5]. This percentage of vaccinated people is significantly lower than that reported vaccination status worldwide as the percentage of fully vaccinated people exceeded 60% of global population as per

July 2022 WHO report [6]. According to WHO's global vision, vaccination coverage in each country must reached to at least 40% to ensure herd immunity, therefore the concern of WHO and health authorities in Iraq have raised and imposed many actions to increase vaccination campaign and activities. The Iraqi Ministry of Health (MOH) announced the opening of more vaccination outlets across the country and that those over 12 years of age were to be vaccinated in order to increase vaccination coverage [7]. For many decades, vaccines have been considered a very successful measure in preventing the spreading of highly contagious disease [8]. However, vaccination hesitancy and rejection are considerable worries globally therefore WHO announced this vaccination hesitancy one of the top 10 health warnings in 2019 [9].

Vaccination hesitancy defined as refusal or delayed in acceptance to take the vaccine nurtured by many reasons such as confusing and incorrect information about safety and efficacy, personal belief and rumors including that vaccine might cause infertility or brain damage, etc. [10, 11].

In Iraq, the compliance rate toward vaccination is low because there are some myths about COVID-19 vaccines, some think that these vaccines are a part of conspiracy operations, possible side effects and not trust the manufacturer companies [12]. Along with the issues of efficacy and the delivery of the vaccine, it is important to monitor public confidence in immunization programs. Vaccination hesitancy is a major barrier to vaccine uptake and achievement of herd immunity, which is critical to protect the most vulnerable populations and contain the pandemic [13]. The level of acceptability to COVID-19 vaccine might be a tentative block in global efforts to contain this viral pandemic and its associated health and socioeconomic consequences. Therefore, several studies are considered necessary across the world to get better understanding of the influencing factors on vaccine acceptance. In Iraq, there is no previous study have been carried out to explore the acceptance and belief as well as the barriers toward COVID-19 vaccine among adolescent therefore we conducted this cross-sectional study.

THE AIM

To evaluate the acceptability of COVID-19 vaccination among the adolescents aged 12-18 years old and to investigate the associated independent factors that might increase or decrease the likelihood of vaccinations.

MATERIALS AND METHODS

STUDY DESIGN

Cross-section observational study based on online survey conducted on adolescent student with age of 12 to less than 18 years old in middle Euphrates provinces of Iraq. Respondents were chosen using nonprobability convenience sampling from adolescent students. Survey data was collected from November 28, 2021 to April 20, 2022. The study questionnaire was created by using Google Form and distributed through invitation link on WhatsApp for the closed school group after coordination and taken agreement of the student school administration. Upon opening of the survey link, there was statements highlighting the purpose of the survey and requesting the consent of the student to participate in the research survey.

STUDY QUESTIONNAIRE

The survey questionnaire was adapted from previously validated questionnaires in the previous studies and most of the questions were slightly modified based

on expert opinion to ensure clarity and understanding from Iraqi students. Also, we performed pilot study on small groups to optimize validity and reliability of the questionnaire. This study questionnaire was consisting of three parts. First part included sociodemographic character of the participants such age, gender, place of residence and their education level. The second part was designed to collect information about participants' clinical information such having chronic disease or comorbidities, previous COVID-19 infections, severity of the symptoms and vaccination status. The last part of the study questionnaire was focused on their acceptance and belief about COVID-19 vaccine as well as the reasons if they not willing to having the vaccine. The measures of student response to these questions were based on Yes and No. We included "May be" in the third part of the questionnaire about COVID-19 vaccine to further explore the uncertainty among the study participant about their willingness to take the vaccine as well as their attitude.

ETHICAL CONSIDERATION

The ethical standards of Helsinki Declaration was considered in conducting this study. The study proposal and questionnaire were reviewed and approved the scientific committee of clinical pharmacy in college of Pharmacy university of Kufa. Permission forms were incorporated at the opening of the questionnaires.

SAMPLE SIZE

To calculate the required sample size of participants in this descriptive cross-sectional study, we used 95% confidence interval and 5% precision percent [14]. The required sample size was minimum of 385 participants. We aimed for higher sample size than calculated one considering some incomplete or missing data. Then we considered the rule of events for each variable to verify the sample required to carry out a logistic regression in which a minimum of 10 sample for each variable included univariate analysis therefore a total sample size of 541 was so enough to run all required analysis accurately.

STATISTICAL ANALYSIS

Statistical analyses were conducted using the SPSS version 26. Categorical variables were presented as count and frequency (%). If the cross-table is bigger than a 2x2 contingency table we used (Chi-squared test), while for 2x2 contingency table either Fisher's exact test used to determine the association between categorical

Table I. Baseline characteristics of adolescents aged 12-18.

Variables	Adolescents aged 12-18 (n=541)	
Gender, N (%)	Male	186 (34.38)
	Female	355 (65.62)
Age, N (%)	12-15	152 (28.10)
	15-18	389 (71.90)
Residency, N (%)	Urban	437 (80.78)
	Rural	104 (19.22)
Education level, N (%)	Middle school	183 (33.83)
	Secondary school	358 (66.17)
Smoker, N (%)	No	476 (87.99)
	Yes	26 (4.80)
	Sometimes	39 (7.21)
Do you have chronic disease? N (%)	No	437 (80.78)
	Allergies and immune disease	20 (3.70)
	Cardiovascular disease	8 (1.48)
	Chronic kidney disease	5 (0.92)
	Diabetes	8 (1.48)
	Obesity	33 (6.10)
	Respiratory diseases and asthma	30 (5.54)
COVID-19 infection, N (%)	No	344 (68.58)
	Yes	197 (31.42)
How strong are the symptoms? N (%)	No	344 (53.59)
	Mild	59 (10.90)
	Moderate	144 (26.62)
	Severe	24 (4.44)
Parents COVID-19 N (%)	No	215 (39.74)
	Yes	326 (60.26)
Parents COVID-19 Vaccination, N (%)	No	140 (25.88)
	Yes	401 (74.12)
Did you get the corona vaccine? (%)	No	288 (53.23)
	Yes	253 (46.76)
Source of medical information, N (%)	Audio or TV media	71 (13.12)
	Government institutions	72 (13.31)
	Relatives and friends	122 (22.55)
	Social Media	276 (51.02)

variables and the acceptance of COVID-19 vaccine (if expected values more than 5), or Yate's Chi-squared test when at least one of the groups with expected value less than 5, with unadjusted odds ratio and p-value. Backward multivariate logistic regression including all significant variables, with adjusted odds ratio and 95% confidence interval, determined the association between independent variables and the acceptance of COVID-19 vaccine for all other significant variables [15]. A p-value less than 0.05 was treated as significant.

RESULTS

BASELINE CHARACTERS OF THE PARTICIPATED ADOLESCENTS

Total of 541 student adolescents participated in this cross-sectional survey. Most of them were female aged 15-18years old. More than 80% of them were from urban area. Most of the participants did not have documented COVID-19 infection. More than half of them (288 adolescents) did not get the vaccine yet

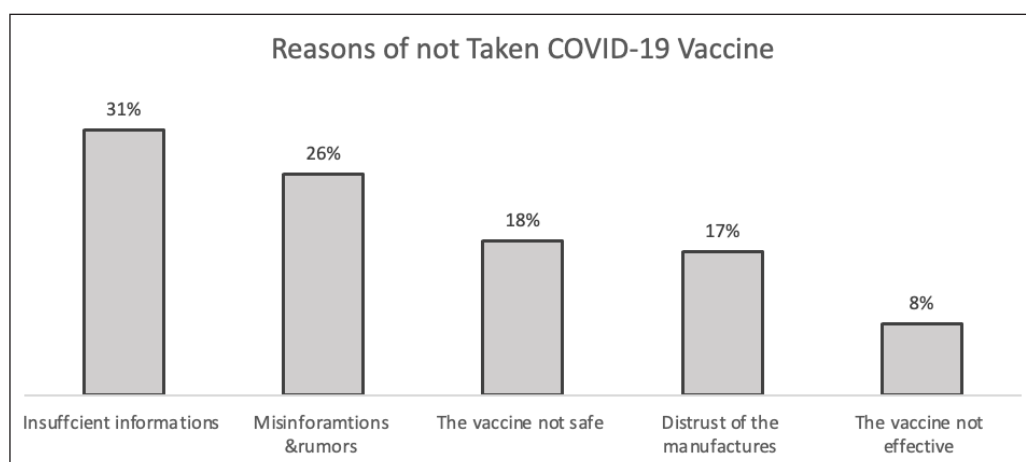


Fig. 1. Reasons of not taken COVID-19 Vaccine

Table II. Acceptability and attitude of non-vaccinated adolescents toward COVID-19 vaccine.

Questions	Non vaccinated adolescent aged 12-18 (N=288)	
Will you take the corona vaccine?	No	157 (54.51)
	Yes	131 (45.49)
Are you afraid of getting the Corona vaccine?	No	197 (68.40)
	Yes	91 (31.60)
Do you think that the Corona vaccine will prevent infection or reduce its severity?	No	196 (68.06)
	Yes	92 (31.94)
Do you think that the vaccine is important to eliminate the Corona virus in Iraq?	No	180 (62.50)
	Yes	108 (37.50)
Will you recommend and encourage others to take the vaccine?	No	164 (56.94)
	Yes	124 (43.06)
Do you intend to take the vaccine in the future?	No	141 (89.8)
	Yes	16 (10.2)

while their parents` vaccination status was higher as it exceeded 60% of the parents. The source of information was mainly through non-official channel such as social media (51%) followed by relatives and friends (22.55%) as shown in table I.

ACCEPTABILITY OF COVID-19 VACCINE AMONG NOT VACCINATED ADOLESCENTS

About 55% of not vaccinated adolescents showed refusal to take the vaccine and almost most of them (89.8%) showed resistance to take it in the future. About third of them (31.6%) showed fear from the vaccination while about 68% of them believed that the vaccine might not prevent the infection nor reduced its severity as well as they have doubt about vaccine importance in eliminating the pandemic of Corona virus (Table II). The main reasons of not taken corona vaccine by the participants primarily attributed to unavailability of sufficient information as stated by 31% of the participants and 26% of the adolescent mentioned false information or rumors about the vaccine. Only 17% of

participants showed distrust of vaccine suppliers while the remaining 18% and 8% showed doubtful belief about vaccine safety and effectiveness respectively (Figure 1).

THE ASSOCIATIONS OF PARTICIPANTS VARIABLES WITH ACCEPTANCE OF COVID-19 VACCINE BY UNIVARIATE AND MULTIVARIATE ANALYSIS

Univariate analysis of the adolescent variables with acceptance rate of COVID-19 vaccine showed that five variables including parents with COVID-19, vaccinated parents, belief that vaccine will prevent infection and belief vaccine will eliminate pandemic corona virus as well as positive attitude by recommending vaccine were significantly ($p < 0.05$) associated increased vaccine acceptability (Table III). After adjustment of the analysis by multiple regression, only three variable revealed statistically significant ($p < 0.05$) association and considered as independent cofactors that will increase the level of acceptance for COVID-19 vaccine. These

Table III. The association between adolescents' variables and the acceptance of COVID-19 vaccine by univariate analysis unadjusted odd ratio and p-value.

Variables	Overall (N=288)	Acceptance level		Odds ratio (95%CI)	p-value	
		Accepted (N=131)	Non accepted (N=157)			
Gender, N (%)	Male	106 (36.81)	49 (37.40)	57 (36.31)	1.0	0.90
	Female	182 (63.19)	82 (62.60)	100 (63.69)	0.95 (0.59 to 1.55)	
Age, N (%)	12-15	100 (34.72)	50 (38.17)	50 (31.85)	1.0	0.27
	15-18	188 (65.28)	81 (61.83)	107 (68.15)	0.76 (0.46 to 1.24)	
Residency, N (%)	Urban	215 (74.65)	94 (71.76)	121 (77.07)	1.0	0.34
	Rural	73 (25.35)	37 (28.24)	36 (22.93)	1.32 (0.79 to 2.23)	
Education level, N (%)	Middle school	122 (42.36)	56 (42.75)	66 (42.04)	1.0	0.90
	Secondary school	166 (57.64)	75 (57.25)	91 (57.96)	0.97 (0.61 to 1.54)	
Smoker, N (%)	No	265 (92.01)	121 (92.37)	144 (91.72)	1.0	>0.99
	Yes	23 (7.99)	10 (7.63)	13 (8.28)	0.92 (0.39 to 2.19)	
Do you have chronic disease? N (%)	No	231 (80.21)	104 (79.39)	127 (80.89)	1.0	0.97
	Allergies and immune disease	12 (4.17)	6 (4.58)	6 (3.82)	1.22 (0.37 to 4.01)	
	Cardiovascular disease	6 (2.08)	1 (0.76)	5 (3.18)	0.24 (0.02 to 1.82)	
	Diabetes	6 (2.08)	3 (2.29)	3 (1.91)	0.22 (0.28 to 5.31)	
	Obesity	18 (6.25)	9 (6.87)	9 (5.73)	1.22 (0.50 to 2.95)	
	Respiratory diseases	15 (5.21)	8 (6.11)	7 (4.46)	1.39 (0.48 to 3.69)	
COVID-19 infection, N (%)	No	218 (75.69)	99 (75.57)	119 (75.80)	1.0	>0.99
	Yes	70 (24.31)	32 (24.43)	38 (24.20)	1.01 (0.59 to 1.72)	
How strong are the symptoms? N (%)	No	209 (72.57)	98 (74.81)	111 (70.70)	1.0	0.92
	Mild	26 (9.02)	10 (7.633)	12 (7.64)	0.94 (0.39 to 2.16)	
	Moderate	44 (15.28)	22 (16.79)	22 (14.01)	1.133 (0.59 to 2.15)	
Parent COVID-19 N (%)	No	9 (3.13)	1 (0.76)	8 (5.10)	0.14 (0.02 to 1.15)	0.08
	Severe	9 (3.13)	1 (0.76)	8 (5.10)	0.14 (0.02 to 1.15)	0.08
	Severe	9 (3.13)	1 (0.76)	8 (5.10)	0.14 (0.02 to 1.15)	0.08
Parent COVID-19 N (%)	No	117 (40.63)	44 (33.59)	73 (46.50)	1.0	0.03
	Yes	171 (59.37)	87 (66.41)	84 (53.50)	1.72 (1.07 to 2.81)	
Parents COVID-19 Vaccination N (%)	No	109 (37.86)	28 (21.37)	81 (51.59)	1.0	<0.001
	Yes	179 (62.15)	103 (78.63)	76 (48.41)	3.92 (2.29 to 6.66)	
Are you afraid of getting the Corona vaccine? N (%)	No	197 (68.40)	118 (90.08)	79 (50.32)	1.0	<0.001
	Yes	91 (31.60)	13 (9.92)	78 (49.68)	0.11 (0.06 to 0.21)	
The vaccine will prevent infection or reduce its severity, N (%)	No	196 (68.06)	71 (54.20)	125 (79.62)	1.0	<0.001
	Yes	92 (31.941)	60 (45.80)	32 (20.38)	3.30 (1.99 to 5.51)	
The vaccine is important to eliminate the Corona virus in Iraq. N (%)	No	180 (62.50)	63 (48.09)	117 (74.52)	1.0	<0.001
	Yes	108 (37.50)	68 (51.91)	40 (25.48)	3.16 (1.92 to 5.19)	
Will you recommend and encourage others to take the vaccine? N (%)	No	164 (56.94)	39 (29.77)	125 (79.62)	1.0	<0.001
	Yes	124 (43.06)	92 (70.23)	32 (20.38)	9.21 (5.38 to 15.5)	

independent variables are the parents with COVID-19 infection with odd ratio - 2.66 (95%CI 1.40 to 5.05), parents COVID-19 vaccination with odd ratio 2.87 (95%CI 1.51 to 5.44) and will you recommend and encourage

others to take the vaccine with its odd ratio 8.62 (95%CI 4.60 to 16.17) as shown in table IV. From other side, being afraid from corona vaccine is negatively associated with acceptability of COVID-19 vaccine and consider as

Table IV. Multivariate analysis for the association between participants variables and the acceptance of COVID-19 with adjusted odds ratio and p-value.

Variables	B	S.E.	Wald	Adjusted Odds ratio (95% CI)	Adjusted p-value
Parents COVID-19	0.977	0.33	8.89	2.66 (1.40 to 5.05)	0.003
Parents COVID-19 Vaccination	1.052	0.33	10.38	2.87 (1.51 to 5.44)	0.001
Are you afraid of getting the Corona vaccine?	-1.999	0.38	27.38	0.14 (0.06 to 0.29)	<.001
Will you recommend and encourage others to take the vaccine?	2.154	0.32	45.03	8.62 (4.60 to 16.17)	<.001

independent variables that decrease the likelihood of vaccine acceptance as shown by negative coefficient and adjusted odd ratio less than one 0.14 (95%CI 0.06 to 0.29) in table IV. Other cofactors considered dependent variables and non-significantly ($p > 0.05$) associated with acceptance for COVID-19 vaccine.

DISCUSSION

It is very well proven that vaccination has an essential role in diminishing the burden of infectious diseases, for example on vaccines importance, 33,000 deaths was avoided, and 14 million diseases were prevented in 2001 [16]. COVID-19 vaccine has been approved to the adolescent age group however the hesitancy and barriers toward vaccination could be a major barrier that counteracting the immunization process and accordingly not achieving the aim herd immunity. The findings from this online based study showed that more than 50% of the adolescents had not taken the vaccine yet and more than half of the not vaccinated adolescents (about 54%) would not accept to take the vaccine as well as almost most (about 90%) revealed negative intention toward future vaccination. These findings are reflecting low rate of vaccination and high level of hesitancy toward future vaccination among adolescents. We could not find a previous study on adolescents in Iraq however recent study conducting on Iraqi parents showed low level of parent's willingness about 38% to vaccinate their children and 35% of them refused to vaccinate them [17]. These low levels of acceptability of vaccination were also evident in adult populations in other middle east countries such as in Kuwait acceptance rate was about 24% and about 37% in Joran [18]. In another study conducted on Chinese adolescents, the results revealed that about 32% were hesitant and about 8% were resistant toward COVID-19 vaccination [19]. From other side, Although the vaccine being available in united states for adolescents, the adolescent's vaccination rate was 53% by end of 2021 and a study showed that among adolescents, only 63% showed willingness to accept the vaccination [20]. In European countries, the hesitancy rate among adolescents was ranging from 30-40% [21, 22].

According to previous report based on 2015-2017 data from both WHO and UNICEF, the main reasons behind vaccine hesitancy were attributed to insufficient knowledge and awareness on top of lacking understanding of vaccination importance [23]. The results of the present study showed that the primary reasons were insufficient information about the vaccine and the falsified information or rumors that circulated mainly via social media. Additional reasons of vaccination hesitancy were the vaccine safety and effectiveness [24]. These reasons also reported in our studies. In other studies, concern about the safety and efficacy of the vaccine were reported as main reasons for not accepting the vaccination of COVID-19 [25]. In general, people who engaged with public media such as Facebook during COVID-19 and this social media considers as mean source of information and misinformation about the disease and /or the vaccine especially focus on negative one such as adverse effects of the vaccine and conspiracy theory as being rushed or new vaccine that led to creating fear from COVID-19 [26]. In the current study, being afraid from the vaccine was the main independent factor that negatively associated with vaccine acceptance. Also, in another cross-sectional study on Iraqi parents revealed a high hesitancy rate to vaccinate their kids mainly related to wrong perceptions about the safety and associated consequence of the vaccination [17]. The results of this study showed that both parents previous COVID-19 and parents COVID-19 vaccination were strongly associated with acceptability to the vaccine among the adolescents. COVID-19 vaccines are expected to be even better efficacy and safety than other youthful vaccines [27]. "First do not harm" is mandatory and basic character in vaccine safety and this should be clearly communicated to maintain public trust in vaccines to chip away the hesitancy from vaccination and improve acceptability rate over time [28, 29]. According to these findings, there is great importance to enrich people awareness about the necessity of COVID-19 vaccine and highlighting its safety in children via providing strong evidence-based information that will increase the adolescents and parents trust in the vaccination and improve their attitude to encourage acceptance and positive promotion toward COVID-19 vaccine.

CONCLUSIONS

Participated adolescents demonstrated hesitancy and low acceptance rate toward COVID-19 vaccine. The parents having COVID-19 or vaccinated against

COVID-19 were associated with increase the level of their adolescent's acceptance for COVID-19 vaccine while fear from Corona vaccine related to decrease the level of acceptance for the vaccination.

REFERENCES

1. Lurie N, Saville M, Hatchett R et al. Developing Covid-19 Vaccines at Pandemic Speed. *N Engl J Med.* 2020;382(21):1969-1973. doi:10.1056/NEJMp2005630.
2. Wallace M, Woodworth KR, Gargano JW et al. The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Pfizer-BioNTech COVID-19 Vaccine in Adolescents Aged 12-15 Years - United States, May 2021. *MMWR Morb Mortal Wkly Rep.* 2021;70(20):749-752. doi:10.15585/mmwr.mm7020e1.
3. Gronvall GK. 10 Reasons Your Child Should Get Vaccinated For COVID-19 As Soon As Possible [Internet]. Johns Hopkins Bloomberg School of Public Health. 2021. <https://publichealth.jhu.edu/2021/10-reasons-your-child-should-get-vaccinated-for-covid-19-as-soon-as-possible> [date access 14.01.2023]
4. Iraq Receives the First Delivery of COVID-19 Vaccines through the COVAX Facility [Internet]. ReliefWeb. UN Children's Fund; WHO; 2021. <https://reliefweb.int/report/iraq/iraq-receives-first-delivery-covid-19-vaccines-through-covax-facility-enarku> [date access 14.01.2023].
5. Iraq: WHO Coronavirus Disease (COVID-19) Dashboard with Vaccination Data [Internet]. World Health Organization. World Health Organization. 2021. <https://covid19.who.int/region/emro/country/iq> [date access 14.01.2023].
6. WHO Coronavirus (COVID-19) Dashboard. World Health Organization. World Health Organization. 2021. <https://covid19.who.int/> [date access 14.01.2023]
7. Iraq Launches Nationwide Vaccination Campaign to Scale up Immunity against COVID-19 [Internet]. World Health Organization. World Health Organization. 2021. <https://www.emro.who.int/iraq/news/iraq-launches-nationwide-vaccination-campaign-to-scale-up-immunity-against-covid-19.html> [date access 14.01.2023].
8. Vaccines and Immunization. World Health Organization. World Health Organization. 2021. <https://www.who.int/health-topics/vaccines-and-immunization> [date access 14.01.2023].
9. Geoghegan S, O'Callaghan KP, Offit PA. Vaccine Safety: Myths and Misinformation. *Front Microbiol.* 2020;11:372. doi:10.3389/fmicb.2020.00372.
10. McKee C, Bohannon K. Exploring the Reasons Behind Parental Refusal of Vaccines. *J Pediatr Pharmacol Ther.* 2016;21(2):104-109. doi:10.5863/1551-6776-21.2.104.
11. Dror AA, Eisenbach N, Taiber S et al. Vaccine hesitancy: the next challenge in the fight against COVID-19. *Eur J Epidemiol.* 2020;35(8):775-779. doi:10.1007/s10654-020-00671-y.
12. Harrison EA, Wu JW. Vaccine confidence in the time of COVID-19. *Eur J Epidemiol.* 2020;35(4):325-330. doi:10.1007/s10654-020-00634-3.
13. Schaffer DeRoo S, Pudalov NJ, Fu LY. Planning for a COVID-19 Vaccination Program. *JAMA.* 2020;323(24):2458-2459. doi:10.1001/jama.2020.8711.
14. Krejcie RV, Morgan DW. Determining sample size for research activities. *Educational and Psychological Measurement.* 1970;30(3):607-610.
15. Peduzzi P, Concato J, Feinstein AR et al. Importance of events per independent variable in proportional hazards regression analysis. II. Accuracy and precision of regression estimates. *J Clin Epidemiol.* 1995;48(12):1503-1510. doi:10.1016/0895-4356(95)00048-8.
16. Zhou F, Santoli J, Messonnier ML et al. Economic evaluation of the 7-vaccine routine childhood immunization schedule in the United States, 2001. *Arch Pediatr Adolesc Med.* 2005;159(12):1136-1144. doi:10.1001/archpedi.159.12.1136.
17. Al-Qerem W, Jarab A, Hammad A et al. Iraqi Parents' Knowledge, Attitudes, and Practices towards Vaccinating Their Children: A Cross-Sectional Study. *Vaccines (Basel).* 2022;10(5):820. doi:10.3390/vaccines10050820.
18. Al-Qerem WA, Jarab AS. COVID-19 Vaccination Acceptance and Its Associated Factors Among a Middle Eastern Population. *Front Public Health.* 2021;9:632914. doi:10.3389/fpubh.2021.632914.
19. Rehati P, Amaerjiang N, Yang L et al. COVID-19 Vaccine Hesitancy among Adolescents: Cross-Sectional School Survey in Four Chinese Cities Prior to Vaccine Availability. *Vaccines (Basel).* 2022;10(3):452. doi:10.3390/vaccines10030452.
20. Hopfer S, Fields EJ, Ramirez M et al. Adolescent COVID-19 Vaccine Decision-Making among Parents in Southern California. *Int J Environ Res Public Health.* 2022;19(7):4212. doi:10.3390/ijerph19074212.
21. Fazel M, Puntis S, White SR et al. Willingness of children and adolescents to have a COVID-19 vaccination: Results of a large whole schools survey in England. *EClinicalMedicine.* 2021;40:101144. doi:10.1016/j.eclinm.2021.101144.
22. Nilsson S, Mattson J, Berghammer M et al. To be or not to be vaccinated against COVID-19 - The adolescents' perspective - A mixed-methods study in Sweden. *Vaccine X.* 2021;9:100117. doi:10.1016/j.jvax.2021.100117.
23. Lane S, MacDonald NE, Marti M et al. Vaccine hesitancy around the globe: Analysis of three years of WHO/UNICEF Joint Reporting Form data-2015-2017. *Vaccine.* 2018;36(26):3861-3867. doi:10.1016/j.vaccine.2018.03.063.
24. Gostin LO, Salmon DA. The Dual Epidemics of COVID-19 and Influenza: Vaccine Acceptance, Coverage, and Mandates. *JAMA.* 2020;324(4):335-336. doi:10.1001/jama.2020.10802.
25. Sallam M, Dababseh D, Yaseen A et al. COVID-19 misinformation: Mere harmless delusions or much more? A knowledge and attitude cross-sectional study among the general public residing in Jordan. *PLoS One.* 2020;15(12):e0243264. doi:10.1371/journal.pone.0243264.

26. Skafle I, Nordahl-Hansen A, Quintana DS et al. Misinformation About COVID-19 Vaccines on Social Media: Rapid Review. *J Med Internet Res.* 2022;24(8):e37367. doi:10.2196/37367.
27. Opel DJ, Diekema DS, Ross LF. Should We Mandate a COVID-19 Vaccine for Children?. *JAMA Pediatr.* 2021;175(2):125-126. doi:10.1001/jamapediatrics.2020.3019.
28. Kaplan RM, Milstein A. Influence of a COVID-19 vaccine's effectiveness and safety profile on vaccination acceptance. *Proc Natl Acad Sci U S A.* 2021;118(10):e2021726118. doi:10.1073/pnas.2021726118.
29. Lee H, Choe YJ, Kim S et al. Attitude and Acceptance of COVID-19 Vaccine in Parents and Adolescents: A Nationwide Survey. *J Adolesc Health.* 2022;71(2):164-171. doi:10.1016/j.jadohealth.2022.05.018.

ORCID and contributionship:

Hayder Ch. Assad: 0000-0003-3499-3007^{A-F}

Fadhil A. Rizij: 0000-0002-2791-5353^{D-F}

Ayad A. Hussien: 0000-0002-4704-5631^{C-E}

Zainab Hadi: 0000-0003-2040-0426^{B-D}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Hayder Ch. Assad

Kufa University

29CG+62H, Kufa, Iraq

tel: 009647705652560

e-mail: phhaydernajaf@gmail.com

Received: 10.11.2022

Accepted: 24.05.2023

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

MALASSEZIA COLONIZATION CORRELATES WITH THE SEVERITY OF SEBORRHEIC DERMATITIS

DOI: 10.36740/WLek202306107

Vlasta Vysochanska, Galina Koval

UZHHGOROD NATIONAL UNIVERSITY, UZHHGOROD, UKRAINE

ABSTRACT

The aim: To compare the number of fungi of the genus *Malassezia* on inflamed and healthy areas of the skin and to correlate them with the severity of seborrheic dermatitis.

Materials and methods: 168 patients with typical manifestations of seborrheic dermatitis on the scalp and face and 30 healthy individuals were recruited. SD severity was assessed by SEDASI. Samples from lesions on scalp, face and intact chest skin were cultivated and/or stained with methylene blue or cotton and inoculated onto *Malassezia* Leeming & Notman Agar Modified (MLNA).

Results: A statistical difference in colonization intensity between all body zones (Dwass-Steel-Critchlow-Flinger pairwise comparisons $p \leq 0,001$). Face zone with lesions of SD patients was two times more colonized with funguses than in the control group (38,5 vs 16,5 $p = 0,003$). The sternal area with no skin lesions was more colonized in the SD group (25,0 vs 9,0 $p = 0,013$). The SEDASI was positively correlated with the amount of CFU on the face (Spearman's rho 0,849; $p \leq 0,001$) and trunk (0,714; $p \leq 0,001$).

Conclusions: Our results demonstrate that inflamed seborrheic areas are more colonized with *Malassezia* fungi than intact areas. The intensity of *Malassezia* growth is correlated with the severity of the symptoms of seborrheic dermatitis. The level of colonization may be a potential biomarker to indicate the efficiency of new treatment approaches

KEY WORDS: seborrheic dermatitis, *Malassezia* spp, SEDASI

Wiad Lek. 2023;76(6):1371-1377

INTRODUCTION

The prevalence of clinically significant manifestations of seborrheic dermatitis (SD) in the population is approximately 3% [1], and it's even higher in immunocompromised patients [2]. Each fifth human has minor peeling of the skin described as dandruff [3]. Persistent itching, redness, and peeling of the skin, especially on the face and near the ears significantly reduces the quality of life and confidence of patients with SD [4].

Malassezia lipid-dependent commensal fungus is an important resident of the skin microbiome. Different *Malassezia* species were mentioned to cause desquamation, hypopigmented macules, and eczematous dermatitis [5]. Despite all previous studies the fact of *Malassezia* colonization of seborrheic areas requires more proof. Different studies show that the prevalence of *Malassezia* spp. in Canada is 82% [6], in Sweden 88% [7], Greece 85% [8]. The pathogenetic role remains unclear for people not colonized by *Malassezia*.

In addition, few commensalism mechanisms are described. In healthy skin, *Malassezia* interacts with keratinocytes and the immune system, as it inhabits

superficial layers of the skin and follicular infundibulum [9]. Skin fungal microbiome, mainly *Malassezia*, protects the skin through its large expansion and competition with bacteria. *Malassezia* metabolites azelaic acid, which is known to have antibacterial and anti-mycotic properties [10]. Also, *Malassezia* generates ethyl ester derivatives with in vitro show antimycotic properties [11]. *Malassezia* secreted aspartyl protease 1 may disrupt *Staphylococcus aureus* biofilms via hydrolysis [12]. In atopic dermatitis, a significant reduction of *Malassezia* was described resulting in a potentially decreased protective function against *S. aureus* [13].

Malassezia produces lipase to hydrolyze sebum triglyceride and releases unsaturated fatty acids such as oleic acid and arachidonic acid [14] These acids insult keratinocyte differentiation, which leads to stratum corneum abnormalities such as parakeratosis and corneocyte damage. These metabolites also induce keratinocyte production of pro-inflammatory cytokines such as IL-1 α , IL-1 β , IL-2, IL-4, IL-6, IL-10, IL-12, interferon-gamma, and tumor necrosis factor [15]. At the same time *M. furfur*, *M. globosa*, and *M. restricta* enhance expression

of toll-like receptor 2 IL-8, human beta-defensin 2, which benefits skin protection [16]. These cytokines recruit immune cells to skin sites with a compromised barrier, for example, follicular infundibulum where tissue-resident dendritic cells, macrophages, and myeloid cells can directly meet *Malassezia* [17]. So *Malassezia* may be a commensal and a trigger of inflammation.

THE AIM

The aim of the study was to compare the number of fungi of the genus *Malassezia* on inflamed and healthy areas of the skin and to correlate them with the severity of seborrheic dermatitis.

MATERIALS AND METHODS

168 patients with seborrheic dermatitis and 30 healthy individuals were examined. The study included patients aged 18-55 years from 2020 to 2022 who were treated at the clinical departments of the medical faculty of the State Higher Educational Institution "Uzhhorod National University"; Regional clinical skin and venereological dispensary and private dermatological clinic. Before the examination, the patients were informed about the research design, developed within the framework of the Helsinki Declaration of the World Medical Association "Ethical principles of medical research with the participation of a person as an object of research", the Convention of the Council of Europe on human rights and biomedicine, and the legislation of Ukraine, and signed the informed consent.

Patients with typical manifestations of seborrheic dermatitis on the scalp and face were included in the study after consulting a dermatologist and verifying the diagnosis. A mandatory condition was the absence of SD-associated treatment for the last month and the absence of other inflammatory skin diseases. Severity was assessed using the seborrheic dermatitis area and severity index (SEDASI) scale [18] and divided into groups: mild 1-14 points, medium severity 15-29 points, and severe 30 or more points. Medical workers with healthy skin were included in the control group.

Subjects were asked not to shower or wash in the evening and morning before sampling. Samples were taken from 3 areas: the first from the hairy part of the head, the second from the face (in places where there is inflammation, such as the mustache, nasolabial fold, and bridge of the nose), and the third from the sternum. Patients with manifestations of inflammation in the chest area were excluded from the study. First, smears were taken with a cotton swab dipped in a sterile isotonic solution, and transferred to the

transport medium. Then skin flakes were collected by the atraumatic scraping of a 1 cm² area. The scraped material was mixed with an isotonic sodium chloride solution, applied to a glass slide, and dried. 96% ethyl alcohol and direct heating were used to fix the sample. Methylene blue was applied for 1 min and washed. To count the number of yeasts, a light microscope was used at a magnification of 40 and 100 with the addition of immersion oil. The results were evaluated as follows: 1-5 yeasts per field = +; 6-10 = ++; > 10 = +++.

Swab material was inoculated directly onto *Malassezia* Leeming & Notman Agar Modified (MLNA) Kairosafe. Petri dishes were kept in a thermostat for 72 hours at a temperature of 37 °C. Gram staining was used for verification. Microscopy and lactophenol cotton blue dye were used to count the number of CFUs (colony-forming units) of fungi. The obtained results were divided into 4 groups according to the number of CFUs: no fungi, 1-sample with 1-25 CFUs, 2 - 26-50 CFUs, 3 - 51, and more CFUs.

The chi-square test was used to determine the difference in gender distribution between the SD and control groups. The Mann-Whitney t-test for independent samples was used to determine the difference in age between groups and to compare the distribution of the number of CFUs between groups. Fisher's exact test to compare the mean number of CFUs in groups. Spearman's correlation was used to determine the relationship between the severity of SD and the number of CFUs in the sample. Kruskal-Wallis test was used to compare fungi colonization in healthy and SD patients. A correlation was considered significant at $p \leq 0.05$. Dwass-Steel-Critchlow-Flinger pairwise comparisons test was used to compare CFU quantity between different skin sites.

RESULTS

According to the microscopy of skin scrapings, the prevalence of *Malassezia spp.* in patients with SD was 53% (89/168), and in healthy individuals 27% (8/30). A difference between prevalence in SD and control group is significant ($p \leq 0,05$). Both groups showed the largest number of fungi on the scalp and face, and the lowest on the trunk in the area of the sternum. A significant difference was found between the number of fungi in samples with seborrheic plaques and samples without skin inflammation (7.44; 4.51; $p \leq 0.05$) and compared with healthy individuals (2.83; $p \leq 0.05$) (Fig. 1).

Comparing the growth of colonies on modified Leming-Notman agar taken from skin swabs (Fig. 2), the prevalence of *Malassezia spp.* in patients with SD was 87% (113/168). Culture result was considered positive

Table I. Quantity of CFU *Malassezia spp.* cultivated from typical seborrheic zones in patients and healthy controls.

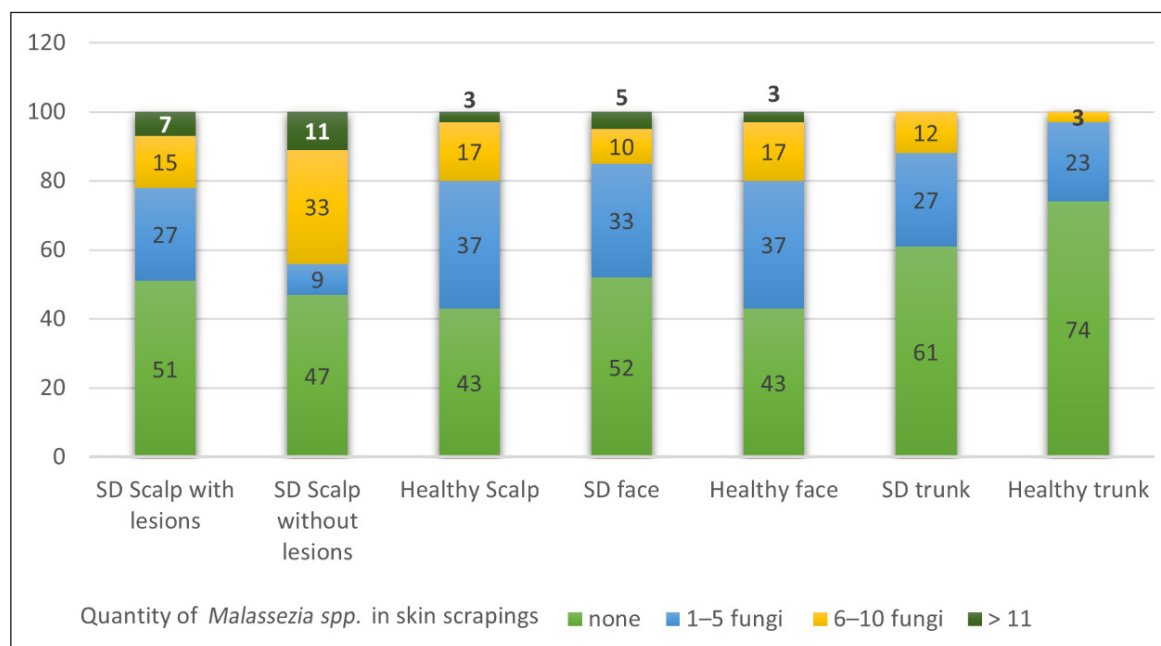
Skin zone	SD patients (total n=168)	Control (total n=30)	Statistic*	p
Scalp with seborrheic plaques	53,5 (42,8;58,5) n=36	0		
Scalp without seborrheic plaques	27,0 (16,0;42,0) n=113	16,5 (7,25;44,8) n=18	859	0,291
Face	38,5 (22,0;47,0) n=146	16,5 (8,75;40,8) n=18	744	0,003
Trunk	25,0 (19,0;36,0) n=109	9,0 (4,0;34,0) n=17	580	0,013

*Mann-Whitney U test; n=number of swab samples with *Malassezia spp.* growth on MLNA.

Table II. Quantity of CFU *Malassezia spp.* on different skin zones in patients with different SD severity.

	mild	moderate	severe	χ^2 *	df	p
Scalp with lesions (total n=36)	0	46,5(38,3;54,3) n=24	57,5(54,8;62,3) n=12	8,84	1	0,003
Scalp without lesions (total n=113)	15,0(9,0;19,0) n=55	42,0(32,0;52,3) n=58	0	79,07	1	$\leq 0,001$
Lesions on face (total n=146)	18,0(13,8;19,0) n=52	44,0(38,0;47,8) n=82	57,0(53,8;62,5) n=12	104,36	2	$\leq 0,001$
Trunk with no lesions (total n=109)	5,0(4,0;11,0) n=15	26,0(22,0;33,0) n=82	52,0(44,8;54,3) n=12	52,57	2	$\leq 0,001$

* Kruskal-Wallis test

**Fig. 1.** Distribution of patients with SD and healthy individuals according to the number of *Malassezia* fungi in the skin scrapings.

if at least one skin zone showed positive fungi growth. The minimum number of CFU was 2, the maximum was 68. In the group of healthy individuals, the prevalence of *Malassezia spp.* was 60% (18/30), the minimum number of CFUs was 2, the maximum was 65.

Similar body zones of healthy and SD people were compared to estimate the density of fungi colonization. 21% of SD patients had seborrheic plaques on the scalp.

The Mean of CFU in samples taken from inflamed skin regions was 53,5. These patients were excluded from the comparison. SD patients without scalp lesions had no statistical difference in the number of CFU compared with healthy people ($p=0,291$). In particular, the face zone with lesions of SD patients was two times more colonized with fungi than in the control group (38,5 vs 16,5 $p=0,003$). The sternal area with no skin

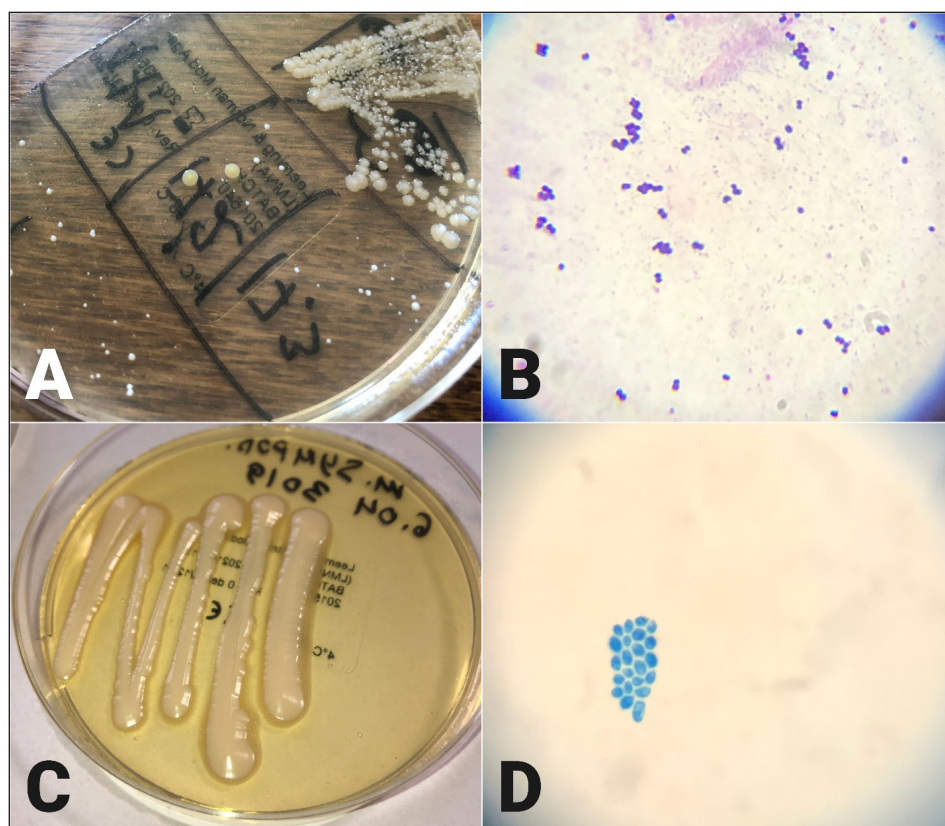


Fig. 2. (A) Representative image of direct culture on modified Leming-Notman agar from skin swab of SD patient (kept in thermostat for 3 days at 37°C). (B) Representative image of *Malassezia* spp. under a light microscope (original magnification x400) after Gram staining for species identification. (C) Representative image of purified colony of *Malassezia sympodialis* on modified Leming-Notman agar cultured at 37°C for 7 days. Clear zone around the colony indicates a lipolytic activity (D) Representative image of *Malassezia* spp. stained with lactophenol cotton blue dye under a light microscope (original magnification x400).

lesions was more colonized in the SD group (25,0 vs 9,0 $p=0,013$) (Table I). Was found a probable difference in the number of CFU depended on the skin area in patients with SD and healthy individuals (Kruskal-Wallis test χ^2 15,9; df 2; $p\leq 0,001$). The control group had no statistical difference in the number of CFU between the face and scalp and a significant difference compared with the trunk. Dwass-Steel-Critchlow-Flinger pairwise comparisons: trunk vs face (W 5.72; $p\leq 0,001$); trunk vs scalp (W 3.93; $p=0,15$); face vs scalp (W -1.32; $p=0,618$).

We have found a statistical difference in colonization intensity between all body zones (Dwass-Steel-Critchlow-Flinger pairwise comparisons $p\leq 0,001$). As shown in table II, the quantity of CFU *Malassezia* spp. has increased according to the severity of seborrheic dermatitis symptoms. Patients with a mild form of SD had a mean of 15,0 CFU on the scalp, 18 on the face, and 5 on the trunk. The mild form was associated with moderate growth of fungi, per 42 on the scalp, 44 on the face, and 26 on the trunk. Patients with severe form had the most intensive *Malassezia* spp. grows. Lesioned areas on the face and scalp were colonized more intensively than non-inflamed areas typical for SD occurrence.

Based on the severity of symptoms and percentage of inflamed skin patients were divided into having severe 7% (12/168), moderate 49 % (82/168), and mild 44% (74/168) symptoms. All patients with severe form had lesions on the scalp and face and tested positive for

Malassezia. The moderate symptom group also tested positive for *Malassezia* and the third part had scalp and face lesions. A quarter part of patients with mild symptoms tested negative for *Malassezia*. Half patients in the mild symptom group had positive cultivation results on the scalp and face but no growth on the trunk.

The correlation between the SEDASI score and quantity of CFU was counted only for the patients with positive *Malassezia* spp. grows and the absence of any lesions on the scalp. A larger inflamed area would have a logical impact on the increase in severity measured by SEDASI. To avoid false statistical evidence, we compared inflamed areas on the face with intact areas on the trunk. The severity of SD measured by SEDASI is positively correlated with the amount of CFU on the face (Spearman's rho 0,849; $p\leq 0,001$) and trunk (Spearman's rho 0,714; $p\leq 0,001$). The results suggest that the intensity of fungi growth has a strong impact on the severity of symptoms.

DISCUSSION

This study reports a difference in the prevalence of *Malassezia* spp. as a result of counting by different methods. According to the results of inoculation on modified Leming-Notman agar, the prevalence was 87%, which coincides with the results of studies in different countries [6,7,8]. When counting the number of CFU by microscopy

after staining with methylene blue, the prevalence was 60%. Only yeast forms of fungi were counted, as they are the most recognizable. Short filaments were considered accidental finds. It is described that about a third of all fungi are in the form of hyphae and predominate on seborrheic plaques. Researchers suggest using fluorescence microscopy to count CFUs, as the dye delineates the polysaccharide particles of hyphae [19].

We found a positive correlation between the number of CFUs of *Malassezia* fungi and the severity of seborrheic dermatitis. Studies that adhere to the hypothesis that *Malassezia* fungi are a main factor in pathogenesis indicate a strong correlation between the intensity of fungi colonization and SD severity [19-21]. It has been described that there is a significant difference in the intensity of fungal growth on inflamed and healthy areas of the skin in patients with SD [22]. An additional argument for this theory is the reduction of symptoms after the use of ketoconazole. Antifungal drugs inhibit the growth of *Malassezia* so they shed together with the dead epithelium particles. Inhibition of the growth of fungi leads to a decrease in redness and desquamation of the skin [23]. It was hypothesized that the triggers of inflammation are directly the hyphae and not the yeast form of the fungus. Hyphae grow into the depths of the derma, changing the immune response and metabolism of the skin [24]. Excessive colonization by fungi and the transformation of yeast into hyphae are considered novel factors of pathogenesis [25].

However, some studies consider sebum metabolism or other homeostasis changes as the main trigger factors of seborrheic dermatitis [26]. Lately described the theory of the pathogenesis of SD points to the leading role of immune and neuroendocrine factors that change the composition and amount of sebum. Such changes create favorable conditions for the growth of lipophilic *Malassezia* fungi over time inhibit the growth of other commensals and damage the integrity of the skin barrier with their waste products. Skin defects trigger a nonspecific inflammatory response that triggers

the release of inflammatory cytokines, which further destroys the skin barrier. Thus, excessive colonization by fungi starts a pathological circle of inflammatory reactions [27].

In contrast, sebum secretion, skin pH, and trans-epidermal water loss (TWEL) of SD patients were analyzed. There was no statistical difference between the normal and lesion sites on the scalp. But *Staphylococcus*, *Pseudomonas*, *Malassezia*, and *Aspergillus* were proposed as potential biomarkers for SD [28]. SD lesions were reported to have reduced *Corynebacterium spp.* amount, and were dominated by *Firmicutes*, *Pseudomonas spp.*, *Staphylococcus spp.*, and *Micrococcus spp.* at the genus level. Bacterial alterations were found to be predominating factors of SD development [29]. Another study stated that TWEL is 3 times more increased in the SD group, decreases after ketoconazole treatment but still does not reach the level of the control group. Increased *Malassezia*, *Staphylococcus*, and decreased *Cutibacterium* are treatment goals as they represent disturbed skin microbial diversity [30].

Promising results were reported in the first-ever conducted study of the identification of differentially expressed miRNAs (DEMs). Skin lesions of elderly male patients with SD had several up and downregulated miRNAs. They were predicted to be significantly associated with typical dermatological pathogenesis like immune response, cell proliferation, and apoptosis [31].

Furthermore, skin biopsy of SD patients revealed sebaceous gland atrophy that opposes the idea of greasy skin and high colonization of lipid-dependent fungi [32].

CONCLUSIONS

Our results demonstrate that inflamed seborrheic areas are more colonized with *Malassezia* fungi than intact areas. The intensity of *Malassezia* growth is correlated with the severity of the symptoms of seborrheic dermatitis. The level of colonization may be a potential biomarker to indicate the efficiency of new treatment approaches.

REFERENCES

1. Dessinioti C, Katsambas A. Seborrheic dermatitis: etiology, risk factors, and treatments: facts and controversies. *Clin Dermatol.* 2013;31(4):343-351.
2. Krzyściak P, Bakuła Z, Gniadek A et al. Prevalence of *Malassezia* species on the skin of HIV-seropositive patients. *Sci Rep.* 2020;10(1):17779.
3. Manuel F, Ranganathan S. A new postulate on two stages of dandruff: a clinical perspective. *Int J Trichology.* 2011;3(1):3-6.
4. Godbehere A, McDonald L, Baines F et al. A dissociation in judgements of confidence in people with dandruff based on self-reports compared to reports from other observers. *Int J Cosmet Sci.* 2017;39(4):457-464.
5. Saunte DML, Gaitanis G, Hay RJ. *Malassezia*-Associated Skin Diseases, the Use of Diagnostics and Treatment. *Front Cell Infect Microbiol.* 2020;10:112.
6. Gupta AK, Kohli Y, Summerbell RC, Faergemann J. Quantitative culture of *Malassezia* species from different body sites of individuals with or without dermatoses. *Med Mycol.* 2001;39(3):243-51.

7. Sandström Falk MH, Tengvall Linder M, Johansson C et al. The prevalence of *Malassezia* yeasts in patients with atopic dermatitis, seborrhoeic dermatitis and healthy controls. *Acta Derm Venereol.* 2005;85(1):17-23.
8. Gaitanis G, Velegaki A, Alexopoulos EC et al. Distribution of *Malassezia* species in pityriasis versicolor and seborrhoeic dermatitis in Greece. Typing of the major pityriasis versicolor isolate *M. globosa*. *Br J Dermatol.* 2006;154(5):854-9.
9. SanMiguel A, Grice EA. Interactions between host factors and the skin microbiome. *Cell Mol Life Sci.* 2015;72(8):1499-515.
10. Del Rosso JQ. Azelaic Acid Topical Formulations: Differentiation of 15% Gel and 15% Foam. *J Clin Aesthet Dermatol.* 2017;10(3):37-40.
11. Mayser P. Medium chain fatty acid ethyl esters - activation of antimicrobial effects by *Malassezia* enzymes. *Mycoses.* 2015;58(4):215-9.
12. Li H, Goh BN, Teh WK et al. Skin Commensal *Malassezia globosa* Secreted Protease Attenuates *Staphylococcus aureus* Biofilm Formation. *J Invest Dermatol.* 2018;138(5):1137-1145.
13. Chng KR, Tay AS, Li C et al. Whole metagenome profiling reveals skin microbiome-dependent susceptibility to atopic dermatitis flare. *Nat Microbiol.* 2016;1(9):16106.
14. Stehr F, Kretschmar M, Kröger C et al. Microbial lipases as virulence factors. *J. Mol. Catal. B Enzym.* 2003;22:347–355.
15. Park M, Park S, Jung WH. Skin Commensal Fungus *Malassezia* and Its Lipases. *J Microbiol Biotechnol.* 2021;31(5):637-644.
16. Georgountzou A, Papadopoulos NG. Postnatal Innate Immune Development: From Birth to Adulthood. *Front Immunol.* 2017;8:957.
17. Sparber F, LeibundGut-Landmann S. Host Responses to *Malassezia* spp. in the Mammalian Skin. *Front Immunol.* 2017;8:1614.
18. A new proposed severity score for seborrheic dermatitis of the face: SEborrheic Dermatitis Area and Severity Index (SEDASI) *Journal of the American academy of dermatology.* 2017;76(6).
19. Li J, Feng Y, Liu C et al. Presence of *Malassezia* Hyphae Is Correlated with Pathogenesis of Seborrheic Dermatitis. *Microbiol Spectr.* 2022;10(1):e0116921.
20. Ghodsi SZ, Abbas Z, Abedeni R. Efficacy of Oral Itraconazole in the Treatment and Relapse Prevention of Moderate to Severe Seborrheic Dermatitis: A Randomized, Placebo-Controlled Trial. *Am J Clin Dermatol.* 2015;16(5):431-7.
21. Alizadeh N, Monadi Nori H, Golchi J et al. Comparison the efficacy of fluconazole and terbinafine in patients with moderate to severe seborrheic dermatitis. *Dermatol Res Pract.* 2014;2014:705402.
22. Barac A, Pekmezovic M, Milobratovic D et al. Presence, species distribution, and density of *Malassezia* yeast in patients with seborrhoeic dermatitis - a community-based case-control study and review of literature. *Mycoses.* 2015;58(2):69-75.
23. Massiot P, Clavaud C, Thomas M et al. Continuous clinical improvement of mild-to-moderate seborrheic dermatitis and rebalancing of the scalp microbiome using a selenium disulfide-based shampoo after an initial treatment with ketoconazole. *J Cosmet Dermatol.* 2022;21(5):2215-2225.
24. Torres M, Pinzón EN, Rey FM et al. *Galleria mellonella* as a Novelty in vivo Model of Host-Pathogen Interaction for *Malassezia furfur* CBS 1878 and *Malassezia pachydermatis* CBS 1879. *Front Cell Infect Microbiol.* 2020;10:199.
25. Cho O, Unno M, Aoki K et al. *Malassezia* Display a Hyphae-like “Spaghetti-and-Meatballs” Configuration in Keratotic Plugs. *Med Mycol J.* 2022;63(3):81-84.
26. Shi VY, Leo M, Hassoun L et al. Role of sebaceous glands in inflammatory dermatoses. *J Am Acad Dermatol.* 2015;73(5):856-63.
27. Wikramanayake TC, Borda LJ, Miteva M, Paus R. Seborrheic dermatitis-Looking beyond *Malassezia*. *Exp Dermatol.* 2019;28(9):991-1001.
28. Lin Q, Panchamukhi A, Li P et al. *Malassezia* and *Staphylococcus* dominate scalp microbiome for seborrheic dermatitis. *Bioprocess Biosyst Eng.* 2021;44(5):965-975.
29. Dityen K, Soonthornchai W, Kueanjinda P et al. Analysis of cutaneous bacterial microbiota of Thai patients with seborrheic dermatitis. *Exp Dermatol.* 2022;31(12):1949-1955.
30. Tao R, Wang R, Wan Z et al. Ketoconazole 2% cream alters the skin fungal microbiome in seborrhoeic dermatitis: a cohort study. *Clin Exp Dermatol.* 2022;47(6):1088-1096.
31. Kim H, Yun JW, Baek G et al. Differential microRNA profiles in elderly males with seborrheic dermatitis. *Sci Rep.* 2022;12(1):21241.
32. Nagrani NS, Goldberg LJ. Sebaceous gland atrophy in seborrheic dermatitis of the scalp; a pilot study. *J Cutan Pathol.* 2022;49(11):988-992.

ORCID and contributionship:

Vlasta Vysochanska: 0000-0003-0998-554X^{A-D}

Galina Koval: 0000-0002-0623-2326^{E,F}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Vlasta Vysochanska

Uzhhorod National University

1 Narodna sq., 88000 Uzhhorod, Ukraine

e-mail: lachupakabramail@gmail.com

Received: 28.12.2022

Accepted: 24.05.2023

A - Work concept and design, **B** - Data collection and analysis, **C** - Responsibility for statistical analysis, **D** - Writing the article, **E** - Critical review, **F** - Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

ORIGINAL ARTICLE

ASSESSMENT OF THE ASSOCIATION OF SEROTONIN TRANSPORTER GENE (5-HTTVNTR & 5-HTTLPR) POLYMORPHISM IN PATIENTS WITH FIBROMYALGIA SYNDROME

DOI: 10.36740/WLek202306108

Sidrah Parvez¹, Ghizal Fatima¹, Farzana Mahdi¹, Najah R. Hadi², Jan Fedacko³¹ERA UNIVERSITY, LUCKNOW, INDIA²UNIVERSITY OF KUFA, NAJAF, IRAQ³PAVOL JOZEF SAFARIK UNIVERSITY, KOSICE, SLOVAKIA

ABSTRACT

The aim: To study the clinical and the genetic association of 5-HTTVNTR and the 5-HTTLPR polymorphisms in women with FMS.**Materials and methods:** 105 FMS patients and 105 controls were enrolled in the study. Polymerase chain method was used to analyse the 5-HTTLPR & 5-HTTVNTR gene polymorphism. The psychopathology status of the 105 FMS patients and 105 healthy controls was assessed using the Beck Depression Inventory (BDI) and the Symptom Checklist-90-Revised (SCL-90-R) questionnaires.**Results:** In FMS patients and controls, the 10/10, 10/12, and 12/12 genotypes of the 5-HTTVNTR polymorphism were found in 3.8% and 2.9%, 20% and 15.2%, and 76.28% and 81.90%, respectively. Additionally, the L/L, S/L, and S/S genotypes of the 5-HTTLPR polymorphism were found in 4.8% and 2.9%, 36.2% and 40%, 59% and 57.1%, in FMS patients and healthy controls, respectively. There were no significant differences in the frequency of genotypes between FMS patients and controls. There were no significant differences in the BDI and the SCL-90-R scores according to the serotonin transporter genotypes.**Conclusions:** We found no significant difference between 5-HTT gene polymorphism (5-HTTVNTR and 5-HTTLPR) and the psychiatric test results ($P > 0.05$) in FMS patients. Hence, we conclude that serotonin gene polymorphism (5-HTTLPR & 5-HTTVNTR) is not associated with FMS in north Indian women. Our results suggests that the serotonin transporter polymorphism does not seem to be a susceptibility factor for FMS.**KEY WORDS:** Fibromyalgia syndrome, Serotonin transporter gene Polymorphism, 5-HTTLPR, 5-HTTVNTR, PCR

Wiad Lek. 2023;76(6):1378-1384

INTRODUCTION

Fibromyalgia (FMS) is a syndrome characterized by persistent widespread pain, extreme sensitivity on palp, and other problems such as insomnia, stiffness, tiredness, and psychosocial problems [1]. Disturbances in serotonin metabolism and transmission are hypothesized to be pathophysiologic mechanisms that cause FMS [2]. This hypothesis is supported by numerous studies. According to Das et al., patients with FMS have a lower level of 5-HT in their blood plasma, which can be associated with sleep disorders and pain [3]. In the cerebrospinal fluid of FMS patients, similar alterations in 5-HT metabolism have been reported [4].

The sodium-dependent serotonin transporter gene (5-HTT), encoded by SLC6A4 which transports serotonin from synaptic space into presynaptic neurons for recycling, therefore playing a crucial role in serotonergic transmission termination [5]. The location of the 5-HTT

gene on the chromosome is 17q11.1-q12, which has been reported for two polymorphisms. first, in the second intronic region, that contains 17 variable number tandem repeats (VNTR) with 9, 10, and 12 number repeats [6]. Several studies have associated 5-HTTVNTR to various mental diseases, including schizophrenia and bipolar disorder [7,8]. But several researches have concluded that this polymorphism is not significantly associated with psychiatric disorders [9, 10].

Second, another polymorphic region is the 5-HTTLPR promoter region, a 44-base pair polymorphism that results in two different alleles, including deletion(S/short) alleles and insertion(L/long) alleles [7]. The presence of the S allele reduced the transcription activity of the 5-HTT promoter gene as compared to the L allele, resulting in lower serotonin transporter binding and uptake [11]. As a result, this genetic variation may raise the risk of developing psychiatric diseases; indeed,

studies have related the 5-HTTLPR polymorphism to significant psychiatric problems [12]. Only a few studies have found that the 5-HTT gene polymorphism is related to depression and anxiety in patients with FMS [13]. These studies provide evidence supporting that the 5-HTTVNTR and the 5-HTTLPR could be candidate gene polymorphism for psychiatric disorders.

Currently, there is insufficient data supporting the role of 5-HTT gene polymorphism in FMS. However, the use of 5-hydroxytryptamine type-3 receptor antagonist and re-uptake blockers in the treatment of FMS suggests that genes influencing the serotonergic pathway may be involved in the pathogenesis of FMS [14]. Depression, anxiety, and fatigue are common in FMS patients, and the serotonergic pathway indirectly influences these symptoms [15]. Therefore, it is possible that 5-HTT gene polymorphism may contribute to the clinical symptoms in FMS. To our knowledge, no study has reported the association of the 5-HTTVNTR and the 5-HTTLPR gene polymorphism with clinical phenotypes or symptoms in North Indian women with FMS. Therefore, the present study investigates the association of the 5-HTTVNTR and the 5-HTTLPR gene polymorphisms in North Indian women with FMS.

THE AIM

The aim of the study was to determine the clinical and the genetic association of 5-HTTVNTR and the 5-HTTLPR polymorphisms in women with FMS.

MATERIALS AND METHODS

PATIENTS AND CONTROLS SELECTION

All procedures performed in this study involving human participants were done according to the ethical standards of Era's Lucknow Medical College and Hospital (ELMCH), Era University, Lucknow, India. This study was approved by the ethics committee of the ELMCH. 105 FMS patients and 105 healthy control participants from ELMCH were recruited in this case control study. The study includes only those FMS patients who satisfied the American College of Rheumatology 2016 inclusion criteria for FMS [16]. All the patients diagnosed as having FMS between 2019 and 2022 at the Department of Rheumatology, ELMCH, Era University, Lucknow, India. The patients with multiple comorbidities like diabetes, rheumatoid arthritis, systematic lupus erythematosus and multiple myeloma were excluded from the study. The patients suffering from any other endocrine disorder were also excluded. The FMS patients and controls were all female belonging from the same ethnicity

and geography. The controls were participants of the ELMCH, Lucknow who are visiting for routine check-up. The controls were defined as those without FMS and no past history of rheumatic disease and none of them receiving any medicine at the time of enrolment in the study will be included. The mean age of the FMS patients was 36.1 ± 11.1 years and controls were 34.6 ± 10.3 years. The duration of illness for the patients suffering from FMS was 19.5 ± 2.5 weeks. The blood samples were collected from all patients and controls after signing an informed consent form. The psychiatric test was evaluated using Beck Depression Inventory (BDI) and symptom Checklist-90-revised (SCL-90-R). Therefore, BDI and SCL-90-R were used to identify the psychological distress in all patients and controls. The patients with psychiatric disorders were excluded from the study.

GENOTYPING OF 5-HTTVNTR AND 5-HTTLPR

The peripheral blood was taken in a blood collection tube from the subjects after taking written consent. Salting out method was used for isolating DNA from the blood samples. Extracted DNA was used for the amplification of the 5-HTTVNTR and 5-HTTLPR gene polymorphism by Polymerase chain reaction (PCR) method. The primer details for the 5-HTTVNTR are given in Table I.

PCR was performed in a final volume of 25 μ l consisting of 150-200ng genomic DNA, 10pmol of each primer and 2x master mix (Takara) per tube using a gradient Master-Cycler (BIO-RAD). PCR amplification consisted of an initial denaturation at 94 °C for 5 min, followed by 30 cycles of denaturation were carried out at 94 °C for 40 sec, annealing was carried out at 61.1 °C for 40 sec, extension was carried out at 72 °C for 40 sec, followed by final extension at 72 °C for 5 min. PCR products were run on agarose gel (3%) containing ethidium bromide and visualized by gel documentation apparatus (EZ BIO-RAD, California), which allow the identification of 267 bp product (10 repeats) and 300 bp product (12 repeats), constituting three types of genotypes, 10/10, 10/12, and 12/12 (Fig.1)

Primer details for 5-HTTLPR are given in Table I. PCR was performed in a final volume of 25 μ l consisting of 150-200ng genomic DNA, 10pmol of each primer and 2x master mix (Takara) per tube using a gradient Master-Cycler (BIO-RAD). PCR amplification consisted of an initial denaturation at 94 °C for 5 min, followed by 30 cycles of denaturation were carried out at 94 °C for 40 sec, annealing was carried out at 61.1 °C for 40 sec, extension was carried out at 72 °C for 40 sec, followed

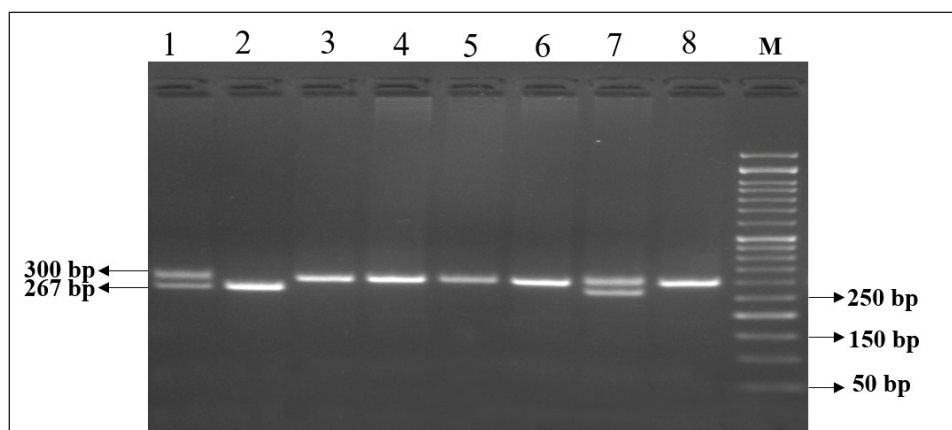


Fig. 1. Representative agarose gel showing three types of genotypes of 5-HTTVNTR. Lane 2- 267 bp (10/10); Lane 1 & 7- 300 bp, 267 bp (10/12); Lane 3, 4, 5, 6 & 8- 300 bp (12/12); M- DNA Ladder (50 bp).

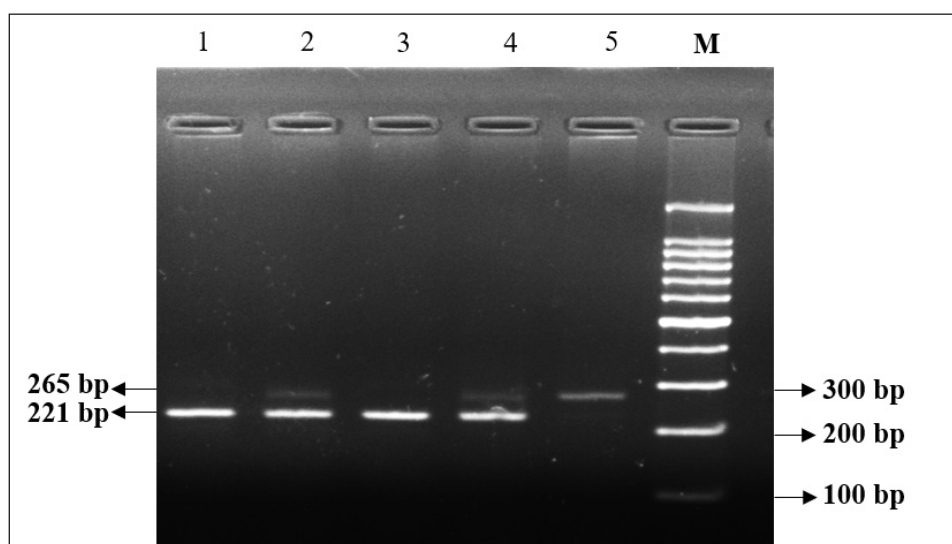


Fig. 2. Representative agarose gel showing three types of genotypes of 5-HTTLPR. Lane 1 & 3- 221 bp (S/S); Lane 2 & 4- 221 bp, 265bp (S/L); Lane 5- 265 bp (L/L); M-DNA Ladder (100 bp).

Table I. Primer sequences used for 5-HTTVNTR and 5-HTTLPR PCR.

Primer		Sequence
5-HTTVNTR	Forward	5'-GTCAGTATCACAGGCTGCGAG-3'
	Reverse	5'-TGTTCCCTA GTCTTACGCCAGTG-3'
5-HTTLPR	Forward	5'-GGCGTTGCCGCTCTGAATGCC-3'
	Reverse	5'-CAGGGGAGATCCTGGGAGAGGT-3'

by final extension at 72 °C for 5 min. PCR products were run on agarose gel (3%) containing ethidium bromide and visualized by gel documentation apparatus (EZ BIO-RAD, California), which allows for the identification of long (265 bp) and short (221 bp) alleles, resulting in three genotypes: S/S, S/L, and L/L (Fig.2).

STATISTICAL ANALYSIS

FMS patients and controls were compared using statistical analysis performed with sufficient post hoc analysis using SPSS statics 28.0 software (IBM). The chi-square (χ^2) test or Fisher's exact test were used to compare the genotyping data between FMS patients and controls. χ^2 test was used to evaluate the Hardy-Weinberg Equilibrium (HWE) for the genotype distribution of the patients

and controls. Logistic regression was used to calculate Odds Ratio (OR), 95% Confidence Interval (CI), and Risk Ratio (RR) of genotype. To evaluate the relationship between genotype and the occurrence of FMS, we used three different models, including co-dominant, dominant, and recessive models. The value was considered to be significant when $P < 0.05$.

RESULTS

Table II shows the clinical characteristics of FMS patients according to both serotonin transporter polymorphisms. However, no significant association was observed with the clinical symptoms such as BDI and SCL-90-R score include Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety,

Table II. Clinical characteristics (data on depression and psychological problems as measured by the BDI and the SCL-90-R) of FMS patients according to the serotonin transporter genotypes.

Variable	5-HTTVNTR			P-value	5-HTTLPR			P-value
	10/10 (n=4)	10/12 (n=21)	12/12 (n=80)		L/L (n=5)	S/L (n=38)	S/S (n=62)	
BDI score	23.7±9.1	21.2±11.4	21.1±11.3	0.90	18.2±7.3	21.8±11.4	21.1±11.3	0.78
SCL-90-R score Somatization	1.2±0.3	1.1±0.3	1.2±0.6	0.72	1.1±0.4	1.0±0.4	1.2±0.6	0.44
Obsessive-Compulsive	0.8±0.1	1.0±0.3	1.1±0.4	0.46	1.0±0.3	0.9±0.2	1.1±0.4	0.05
Interpersonal Sensitivity	1.2±0.4	1.1±0.3	1.0±0.3	0.79	0.9±0.1	1.0±0.3	1.1±0.3	0.29
Depression	1.1±0.4	1.1±0.3	1.1±0.4	0.82	1.1±0.3	1.0±0.2	1.2±0.4	0.10
Anxiety	1.3±0.4	1.3±0.6	1.2±0.4	0.39	1.1±0.4	1.1±0.3	1.3±0.5	0.07
Hostility	0.9±0.1	1.0±0.4	1.0±0.4	0.94	1.0±0.2	0.9±0.4	1.0±0.3	0.76
Phobic Anxiety	0.7±0.5	0.8±0.5	0.9±0.4	0.49	0.6±0.5	0.8±0.4	0.9±0.5	0.25
Paranoid Ideation	0.4±0.4	0.5±0.4	0.7±0.5	0.06	0.3±0.4	0.6±0.4	0.7±0.5	0.05
Psychoticism	0.6±0.4	0.5±0.4	0.7±0.5	0.45	0.4±0.4	0.5±0.3	0.7±0.5	0.14
GSI (Global Severity Index)	0.9±0.1	1.0±0.3	1.0±0.4	0.84	0.8±0.1	0.9±0.1	1.0±0.4	0.70

Table III. Genotype frequency of the 5-HTTVNTR gene polymorphism in the FMS patients and control groups.

Subjects	5-HTTVNTR			χ^2	df	P-value
	10/10	10/12	12/12			
Patients (105)	4(3.8%)	21(20%)	80 (76.2%)	1.035	2	0.596
Controls (105)	3(2.9%)	16(15.2%)	86(81.90%)			

Hardy–Weinberg equilibrium test for 5-HTTVNTR: ($\chi^2 = 2.68$, $df = 1$, $p = 0.10$ in FMS patients), ($\chi^2 = 3.69$, $df = 1$, $p = 0.05$ in control groups).

Table IV. Genotype frequency of 5-HTTLPR gene polymorphism in the FMS patients and controls.

Subjects	5-HTTLPR			χ^2	df	P-value
	L/L	S/L	S/S			
Patients (105)	5(4.8%)	38(36.2%)	62(59%)	0.641	2	0.732
Controls (105)	3(2.8%)	42(40.3%)	60(57%)			

Hardy–Weinberg equilibrium test for 5-HTTLPR: ($\chi^2 = 0.07$, $df = 1$, $p = 0.79$ in FMS patients), ($\chi^2 = 1.89$, $df = 1$, $p = 0.16$ in controls).

Hostility, Phobic Anxiety, Paranoid Ideation, Psychoticism, and GSI (Global Severity Index) ($p > 0.05$) according to the serotonin transporter polymorphisms. Despite not reaching statistical significance, FMS patients with S/S genotype had higher the BDI and the SCL-90-R mean scores as compared to the L/L and S/L.

Table III shows the genotype frequency of the 5-HTTVNTR gene polymorphism in the FMS patients ($n = 105$) and control groups ($n = 105$). In both FMS patients and healthy controls, the 10/10, 10/12 and 12/12 genotypes were represented in 3.8% and 2.9%, 20% and 15.2%, and 76.2% and 81.90%, respectively. The genotype distributions of the two groups were in Hardy-Weinberg equilibrium. Despite not reaching statistical significance ($p = 0.59$), the incidence of 10/10 and 10/12 genotypes was higher in FMS patients than in the control.

Table IV shows the genotype frequency of the 5-HTTLPR gene polymorphism in the FMS patients

and control groups ($n = 105$). In both FMS patients and healthy controls, the L/L, S/L and S/S genotypes were represented in 4.8% and 2.8%, 36.2% and 40.3%, 59% and 57%, respectively. The genotype distributions of the two groups were in Hardy-Weinberg equilibrium. There was no significant difference in the 5-HTTLPR genotypes distribution between FMS patients and controls ($P > 0.05$).

Comparison of frequency distribution of genotype of 5-HTTVNTR and 5-HTTLPR polymorphism among FMS patients and controls were performed by logistic regression analysis in Table V and VI. In 5-HTTVNTR and 5-HTTLPR polymorphism, none of the models show any significant differences between FMS patients and controls by logistic regression analysis. Therefore, 5-HTTVNTR and 5-HTTLPR polymorphism is not associated with the increased risk of FMS in North Indian women, according to our findings. As a result, the 5-HTTVNTR

Table V. Comparison of 5-HTTVNTR genotype in FMS patients by logistic regression analysis.

Genotype	Patients (n=105)	Controls (n=105)	OR (95% CI)	Risk Ratio (RR)	P-value
Co-dominant Model					
12/12	80 (76.2%)	86 (81.9%)	1 (ref.)	1 (ref.)	
10/12	21 (20%)	16 (15.2%)	1.41 (0.68-2.89)	1.17 (0.85-1.62)	0.44
10/10	4 (3.8%)	3 (2.9%)	1.43 (0.31-6.60)	1.18 (0.61-2.29)	0.93
Dominant Model					
12/12	80 (76.2%)	86 (81.9%)	1 (ref.)	1 (ref.)	
10/12 + 10/10	25 (23.8%)	19 (18.1%)	1.41 (0.72-2.76)	1.17 (0.87-1.59)	0.39
Recessive Model					
12/12 + 10/12	25 (23.8%)	19 (18.1%)	1 (ref.)	1 (ref.)	
10/10	4 (3.8%)	3 (2.9%)	0.98 (0.19-4.94)	0.99 (0.49-1.98)	0.98

Table VI. Comparison of 5-HTTLPR genotype in FMS patients by logistic regression analysis.

Genotype	Patients (n=105)	Controls (n=105)	OR (95% CI)	Risk Ratio (RR)	P-value
Co-dominant Model					
L/L	5 (4.8%)	3 (2.9%)	1 (ref.)	1 (ref.)	
S/L	38 (36.2%)	42 (40%)	0.54 (0.12-2.42)	0.76 (0.42-1.36)	0.66
S/S	62 (59%)	60 (57.1%)	0.62 (0.14-2.71)	0.81 (0.46-1.43)	0.78
Dominant Model					
L/L	5 (4.8%)	3 (2.9%)	1 (ref.)	1 (ref.)	
S/L + S/S	100 (95.2%)	102 (97.1%)	0.58 (0.13-2.52)	0.79 (0.45-1.37)	0.71
Recessive Model					
L/L + S/L	43 (41%)	45 (42.9%)	1 (ref.)	1 (ref.)	
S/S	62 (59%)	60 (57.11%)	1.08 (0.62-1.87)	1.04 (0.78-1.37)	0.88

and 5-HTTLPR gene polymorphism is not associated with FMS susceptibility in the North Indian population.

DISCUSSION

This study was designed to investigate the association of 5-HTTVNTR and 5-HTTLPR gene polymorphisms in North Indian women with FMS. 5-HTT gene polymorphisms have been most extensively investigated in various populations. To our knowledge, this is the first study to investigate the correlation between 5-HTTVNTR

and 5-HTTLPR polymorphism with clinical symptoms in North Indian women with FMS. According to our findings, there is no significant difference between the psychiatric test results and 5-HTT gene polymorphism (5-HTTVNTR and 5-HTTLPR) in North Indian women with FMS. Similar result was also reported by Gursory (2002), who showed that neither 5-HTTVNTR nor 5-HTTLPR gene polymorphism were associated with FMS susceptibility in patients with normal psychiatric status [10]. Likewise, a meta-analysis found no correlation between the variations in the 5-HTT gene and FMS [17].

In contrast to our results, Cohen et al. (2002), investigated polymorphism in 5-HTTLPR (5-HTT promoter region) in FMS patients. Female patients with FMS selected from two different ethnic groups of Israeli like Arab and Jewish were genotyped. Tridimensional Personality Questionnaire (TPQ) was used to assess each patient with a self-reported assessment consisting of one hundred Yes/No questions. The result showed that FMS and 5-HTTLPR polymorphism were associated in both Israeli groups. Moreover, TPQ scores of FMS patients were associated with the 5-HTTLPR polymorphism [18]. Leschi et al. (1996), found that the S allele of 5-HTTLPR polymorphism was associated with anxiety [19].

These results are consistence with our finding that Offenbaecher et al. (1999), studied the genotypes in the 5-HTT gene in FM patients. The genotype S/S was high, comprising 31% in FM patients compared to 16% in controls. Moreover, the patients with S/S genotype had more severe depressive symptoms and psychological problems, as demonstrated by the high scores in SCL-90-R and BDI compared with the group of L/L and L/S genotype patients. However, they did not analyse

significant association with 5-HTTVNTR gene polymorphism in FMS patients [20].

We examined both 5-HTTLPR and 5-HTTVNTR gene polymorphism in North Indian women with FMS. There was no statistical difference between FMS patients and controls. The following explanations may account for the above findings. First, the sample size of this study is small; second, the genetic variations depend on the region or the population being studied; third, genetic diversity could have also affected the outcome. Also, not enough information on the influence of 5-HTT gene polymorphism on FMS susceptibility is available. Consequently, the role of 5-HTT gene variants in the pathogenesis of FMS patients remained inconclusive till date. Further research with a large sample size is needed to confirm our observation in FMS patients.

CONCLUSIONS

No association of 5-HTTVNTR ($p=0.59$) and 5-HTTLPR ($p=0.73$) gene polymorphism was observed in FMS patients. Thus, we could say that 5-HTTVNTR and 5-HTTLPR gene polymorphism is not important contributor in FMS patients.

REFERENCES

1. Parvez S, Fatima G, Das SK et al. Serotonin role in fibromyalgia. *EJMR*. 2021;8(1):55-58.
2. Wolfe F, Russell IJ, Vipraio G et al. Serotonin levels, pain threshold, and fibromyalgia symptoms in the general population. *J Rheumatol*. 1997;24:555-559.
3. Fatima G, Das SK, Khan FH et al. Circadian variations of 5-hydroxytryptamine in female with fibromyalgia syndrome: A case control study. *Sleep Biol Rhythms*. 2013;11:261-267. doi:10.1111/sbr.12038.
4. Russell IJ, Vaeroy H, Javors M et al. Cerebrospinal fluid biogenic amine metabolites in fibromyalgia/fibrositis syndrome and rheumatoid arthritis. *Arthritis Rheum*. 1992;35:550-556. doi:10.1002/art.1780350509.
5. Chen FX, Chen XS, Guo JC et al. Serotonin transporter-linked polymorphic region genotypes in relation to stress conditions among patients with papillary thyroid carcinoma. *Int J Clin Exp Pathol*. 2019;12:968-977.
6. Hranilovic D, Stefulj J, Schwab S et al. Serotonin transporter promoter and intron 2 polymorphisms: relationship between allelic variants and gene expression. *Biol Psychiatry*. 2004a;55:1090-1094. doi:10.1016/j.biopsych.2004.01.029.
7. Battersby S, Ogilvie AD, Smith CA et al. Structure of a variable number tandem repeat of the serotonin transporter gene and association with affective disorder. *Psychiatr Genet*. 1996;6:177-181. doi:10.1097/00041444-199624000-00001.
8. Ogilvie AD, Battersby S, Bubb VJ et al. Polymorphism in serotonin transporter gene associated with susceptibility to major depression. *Lancet*. 1996;347:731-733. doi:10.1016/s0140-6736(96)90079-3.
9. Stober G, Jatzke S, Heils A et al. Susceptibility for schizophrenia is not influenced by a functional insertion/deletion variant in the promoter of the serotonin transporter gene. *Eur Arch Psychiatry Clin Neurosci*. 1998;248:82-86. doi:10.1007/s004060050022.
10. Gursoy S. Absence of association of the serotonin transporter gene polymorphism with the mentally healthy subset of fibromyalgia patients. *Clin Rheumatol*. 2002;21:194-197. doi:10.1007/s10067-002-8284-5.
11. Ming Q, Zhang Y, Yi J et al. Serotonin transporter gene polymorphism (5-HTTLPR) L allele interacts with stress to increase anxiety symptoms in Chinese adolescents: A multiwave longitudinal study. *BMC Psychiatry*. 2015;15:1-8. doi:10.1186/s12888-015-0639-y.
12. Basu A, Chadda R, Sood M et al. A preliminary association study between serotonin transporter (5-HTTLPR), receptor polymorphisms (5-HTR1A, 5-HTR2A) and depression symptom-clusters in a north Indian population suffering from Major Depressive Disorder (MDD). *Asian J Psychiatry*. 2019;43:184-188. doi:10.1016/j.ajp.2019.05.028.
13. Tour J, Lofgren M, Mannerkorpi K et al. Gene-to-gene interactions regulate endogenous pain modulation in fibromyalgia patients and healthy controls-antagonistic effects between opioid and serotonin-related genes. *Pain*. 2017;158:1194-1203. doi:10.1097/j.pain.0000000000000896.

14. Hrycaj P, Stratz T, Mennet P et al. Pathogenetic aspects of responsiveness to ondansetron (5-hydroxytryptamine type 3 receptor antagonist) in patients with primary fibromyalgia syndrome: a preliminary study. *J Rheumatol*. 1996;23:1418-1423.
15. Murphy DL, Andrews AM, Wichems CH et al. Brain serotonin neurotransmission: an overview and update with an emphasis on serotonin subsystem heterogeneity, multiple receptors, interactions with other neurotransmitter systems, and consequent implications for understanding the actions of serotonergic drugs. *J Clin Psychiatry*. 1998;59(15):4-12.
16. Wolfe F, Clauw DJ, Fitzcharles MA et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. *Semin Arthritis Rheum*. 2016;46(3):319-329. doi:10.1016/j.semarthrit.2016.08.012.
17. Lee YH, Choi SJ, Ji JD et al. Candidate gene studies of fibromyalgia: a systematic review and meta-analysis. *Rheumatol Int*. 2012;32:417-426. doi:10.1007/s00296-010-1678-9.
18. Cohen H, Buskila D, Neumann L et al. Confirmation of an association between fibromyalgia and serotonin transporter promoter region (5-HTTLPR) polymorphism, and relationship to anxiety-related personality traits. *Arthritis Rheum*. 2002;46:845–847. doi:10.1002/art.10103.
19. Lesch KP, Bengel D, Heils A et al. Association of anxiety-related traits with a polymorphism in the serotonin transporter gene regulatory region. *N Y Sci J*. 1996;274:1527–1531. doi:10.1126/science.274.5292.1527.
20. Offenbaecher M, Bondy B, de Jonge S et al. Possible association of fibromyalgia with a polymorphism in the serotonin transporter gene regulatory region. *Arthritis Rheum*. 1999;42:2482–2488. doi:10.1002/1529-0131(199911)42:11%3C2482::aid-anr27%3E3.0.co;2-b.

We greatly acknowledge the Indian Council of Medical Research vide Award letter no. 3/1/2(11)/CD/2021-NCD-II for providing grant for this work.

ORCID and contributionship:

Sidrah Parvez: 0000-0002-7779-7308^{A-F}

Ghizal Fatima: 0000-0001-8516-655X^{C,E,F}

Farzana Mahdi: 0000-0002-2188-2992^F

Najah R. Hadi: 0000-0002-8415-5311^F

Jan Fedacko: 0000-0002-4940-0393^F

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Ghizal Fatima

Era University

VVHF+726, Lucknow, India

e-mail: ghizalfatima8@gmail.com

Received: 22.12.2022

Accepted: 24.05.2023

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

THE ASSESSMENT OF COMPENSATION OF CARBOHYDRATE METABOLISM IN PATIENTS WITH TYPE 2 DIABETES MELLITUS WITH METABOLIC SYNDROME BEYOND THE LIMITS OF GLYCATED HEMOGLOBIN

DOI: 10.36740/WLek202306109

Taras V. Romaniv¹, Nadiya V. Skrypnyk¹, Ulyana V. Synko¹, Nataliia M. Voronych-Semchenko¹, Oleh V. Melnyk², Anna O. Hryb¹, Igor B. Boruchok¹

¹IVANO-FRANKIVSK NATIONAL MEDICAL UNIVERSITY, IVANO-FRANKIVSK, UKRAINE

²DAUGHTER ENTERPRISE «SANATORIUM “MORSHYNRESORT” PRIVATE JOINT STOCK COMPANY «UKRPROFOZDOROVNYTSIA», MORSHYN, UKRAINE

ABSTRACT

The aim: To investigate glycemic variability in type 2 diabetes patients with metabolic syndrome (MS) and to assess its effect on diabetes compensation.

Materials and methods: We used traditional indicators of glycemia variability according to the recommendations of the American Diabetes Association Professional Practice Committee. We proved that patients with type 2 diabetes mellitus with MS reliably have worse CGM indicators: Time in range TIR: (3.9–10.0 mmol/l) – 53.30±5.90%; Time above range (TAR): (time above range) (>10.1 mmol/l) – 43.33±5.96%; Time above TAR range (>13.9 mmol/l) – 22.1±3.91%; Glucose Variability CV – 44.10±4.89% compared to patients with type 2 diabetes without MS, which proves the negative effect of insulin resistance on compensation of diabetes.

Results: Determination of the level of EI in the blood, calculation of the Caro index, HOMA-IR are informative for verifying the presence of IR in patients with type 2 diabetes with MS. For optimal diabetes control, in addition to HbA1c, we must consider CGM data and % Time in range (TIR).

Conclusions: TIR should be used as a target point and an indicator of glycemic control in routine clinical practice. TIR provides accurate data on a patient's glycemic status and helps better control diabetes.

KEY WORDS: type 2 diabetes mellitus, metabolic syndrome, continuous glucose monitoring

Wiad Lek. 2023;76(6):1385-1390

INTRODUCTION

Diabetes mellitus (DM) is a complex chronic disease that requires constant medical care with multifactorial risk reduction strategies and extraglycemic control [1]. The prevalence of diabetes in 2019 was estimated at 9.3% (463 million people), rising to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045. [2]. Compensation – a state in which, under the influence of antidiabetic treatment, normalization of glycemia, as well as indicators of lipid metabolism, blood pressure, and body weight has been achieved [1]. The criteria for compensation of carbohydrate metabolism of type 2 diabetes mellitus according to the American Diabetes Association are: glycated hemoglobin (HbA1c) - less than 7%; fasting plasma glucose - 4.4-7.2 mmol/l (80-130 mg/dL); postprandial glycemia in capillary plasma - <10.0 mmol/l (<180 mg/dL). These glycemic goals are relevant for the majority of patients with type 2 diabetes, but

one should not forget about the individual characteristics of each patient, which depend on the presence of concomitant pathology, the presence of hypoglycemic states, the duration of the disease, expected length of life, vascular complications, patient compliance, and material resources. HbA1c is a hemoglobin in which a glucose molecule is non-enzymatically linked to the β-terminal valine of the β-chains of globin hemoglobin A1. The content of HbA1c has a direct correlation with the level of blood glucose, and thus it is used as the gold standard for assessing glycemic control and predicting chronic complications of diabetes [3-5]. An increase in the level of HbA1c determines the development and progression of chronic diabetic micro- and macroangiopathies [6,7]. According to scientists, until today there was an era of HbA1c, because it was considered to be the main glycemic marker for the intensification of therapy, the main glycemic marker of the quality

of diabetes control and the effectiveness of drugs, a diagnostic criterion for diabetes and various metabolic disorders, a standard marker of the risk of developing chronic complications, a target index of the algorithm intensification of therapy in clinical practice and research [8]. The average level of glycemia does not reflect the real situation, does not indicate experienced hypoglycemia or high variability of glycemia, the accuracy of determining the level of HbA1c may be impaired in the case of: hemoglobinopathies, iron deficiency anemia, CKD, liver diseases, individual lifespan of erythrocytes, unknown genetic factors that lead to glycation disorders, it does not provide complete information on diabetes control compared to Continuous glucose monitoring (CGM) [9]. CGM measures glucose levels in the interstitial fluid. Thanks to new trends in glucose measurement, we can more accurately determine the variability of glycemia, namely the amplitude of fluctuations. According to the latest recommendations, achieving diabetes compensation and low glycemic variability will allow achieving strategic goals and criteria for the effectiveness of diabetes treatment [10]. Measurement of the level of HbA1c, CGM and self-monitoring of the level of glucose in the blood are used for the purpose of evaluating treatment and, if necessary, adjusting therapy. CGM plays an important role in evaluating the effectiveness and safety of treatment, including the prevention of hypoglycemia [1, 11].

THE AIM

The aim of our study was to investigate glycemic variability in type 2 diabetes patients with metabolic syndrome (MS) and to evaluate its effect on diabetes compensation.

MATERIALS AND METHODS

In accordance with the aim and objectives of the study, the examined group consisted of 52 patients with type 2 diabetes mellitus with MS and without MS who were undergoing inpatient treatment at the endocrinology department of the Communal non-profit enterprise "Regional Clinical Hospital" of the Ivano-Frankivsk Regional Council and the daughter enterprise "Sanatorium "Morshynresort" Private Joint Stock Company "Ukrprofzodorovnytsia". Patients with type 2 diabetes were on oral glucose-lowering therapy (metformin monotherapy and in combination with sulfonylurea derivatives, DPP inhibitors, inhibitors of sodium-dependent glucose cotransporter type 2, thiazolidinediones, etc.). Patients were recommended with moderate physical activity and an appropriate diet. Each patient signed an informed

consent. IDF criteria, 2005 were used to detect signs of MS in the examined persons. According to the structure of the work, elements of typological sampling (stratification randomization) were used in the controlled clinical study of MS patients with type 2 diabetes. Depending on the applied treatment methods, all examined patients with type 2 diabetes were divided into 2 groups, representative by age, gender, and degree of compensation of diabetes: group of patients with type 2 diabetes with MS – 28, group of patients with type 2 diabetes without MS – 24. The degree of IR was determined by waist circumference (WC), IR indices: HOMA-IR index (Homeostasis Model Assessment Insulin Resistance) and Caro index. The HOMA IR indicator was calculated according to the formula: $\text{HOMA IR} = \frac{\text{fasting blood glucose (mmol/l)} \times \text{fasting blood insulin } (\mu\text{U/l})}{22.5}$ [Matthew D. R., 1985]; the Caro index was calculated according to the formula: $\text{Caro index} = \frac{\text{ratio: glucose (mmol/l)}}{\text{insulin } (\mu\text{U/l})}$ [Caro A. A., 2004]. Using BMI indicators, the degree of general obesity was assessed according to the recommendations of the WHO (1997) and the International Diabetes Federation (2005). BMI was considered normal - less than 24 kg/m²; OT - less than 80 cm in women, less than 94 cm in men, HOMA IR indicator, which does not normally exceed 2.77, Caro index, which normally exceeds 0.33. Mandatory scope of laboratory tests included: general clinical analysis of blood and urine, fasting blood glucose and postprandial glycemia, blood glycemic profile by the glucose oxidase method using the Exan apparatus. The concentration of endogenous insulin (EI) was determined by a set of reagents DRG (USA), by the enzyme immunoassay method using the "StatFax - 303" analyzer. Glycated hemoglobin (HbA1c) was determined by the chromatographic method using a test system (fully automated analyzer) for determining the content of hemoglobin D-10TM of the company "Bio-Rad" (USA).

CGM was performed using the Guardian Connect system of the Metronic company in 28 patients with type 2 diabetes and MS and 24 patients with diabetes without MS for an average of 14 days, who were treated in the endocrinology department of the Communal non-profit enterprise "Regional Clinical Hospital" of the Ivano-Frankivsk Regional Council and the daughter enterprise "Sanatorium "Morshynresort" Private Joint Stock Company "Ukrprofzodorovnytsia". We used traditional indicators of glycemia variability according to the recommendations of the American Diabetes Association Professional Practice Committee [1]: Time below range (TBR): <54 mg/dl (<3 mmol/l) - <1% was considered the norm; Time below range (TBR): <69 mg/dl (3.8 mmol/L) - <4%; Time in range TIR: 70 - 180 mg/dl (3.9-10.0 mmol/l) - >70%; Time above range (TAR): >181 mg/dl (10.1 mmol/l) - <25%; Time above

Table I. Indicators of carbohydrate metabolism and variability of glycemia in patients with type 2 diabetes with MS

Indicators	Type 2 diabetes with MS n=28	Type 2 diabetes without MS n=24
Age of diabetes, years	9,8±6,10	8,6±8,63
Age, years	54,8±10,03	52,8±6,11
Gender, M/F	16/12	10/14
Diabetes severity, mild/moderate/severe	3/15/10	3/14/7
Circumference Waist, cm (M)	114,8±11,54*	91,06±0,59
Circumference Waist, cm (F)	109,94±2,32 *	77,64±0,46
BMI	31,85±4,72164*	24,57±0,34
EI, micro IU/ml	28,45±2,49 *	12,85±0,40
HOMA IR index	10,32±0,80 *	2,37±0,07
Caro index	0,34±0,01*	0,29±0,03
Fasting blood glucose, mmol/l	9,53±0,24	9,47±0,21
Postprandial glycemia, mmol/l	11,54±0,28	11,67±0,21
HbA1c%	9,32±0,13	8,57±0,86
Glucose Management Indicator (GMI) % no CGM	8,26±1,05	7,26±1,05
Time below range (TBR): (<3 mmol/l), %	0,19±0,07	0,13±0,06
Time below range TBR (<3,8 mmol/l), %	0,91±0,54*	1,4±0,62
Time in range TIR: (3,9–10,0 mmol/l), %	53,30±5,90*	74,42±7,83
Time above range (TAR): (>10,1 mmol/l), %	43,33±5,96*	25,41 ±7,86
Time above range TAR (>13,9 mmol/l), %	22,1±3,91*	12,34±2,39
Glucose Variability CV,%	44,10±4,89*	28.32 ±6,27
Average Glucose, mmol/l	10,1±0,52*	8,41±0,56
Glucose Management Indicator (GMI), %	9,6 ±1,19	8,6 ±1,12

Notes: 1.* – the difference is reliable in relation to the indicators of the comparison group ($p < 0.05$).

range TAR: >250 mg/dl (13.9 mmol/l) – <5%; Glucose Variability CV (coefficient of variation) – ≤36%; Average Glucose - goal <154 mg/dl (8.6 mmol/l); Glucose Management Indicator (GMI) - HbA1% level according to CGM - goal < 7%; < 8%.

Statistical processing of the obtained results was carried out using the "STATISTICA" statistical data analysis package on a Pentium-IV personal computer and the use of parametric and non-parametric methods of evaluating the obtained results.

RESULTS

According to our data, the average age of 28 patients with type 2 diabetes with MS was 54.8±10.03, of which 16 were men and 12 were women. All patients with type 2 diabetes and MS had signs of abdominal obesity, which was evidenced by an increase not only in BMI, but also in OT compared to patients with type 2 diabetes without MS ($p < 0.05$) (Table I). Their waist circumference was 114.8±15.54 in men and 109.94±2.32 in women. The analysis of the obtained results indicates an increase in the fasting blood glucose level of 9.53±0.24

mmol/l and 9.47±0.21 mmol/l, the relative content of HbA1c in the range of 9.32±0.13% and 8.57±0.86%, postprandial glycemia within 11.54±0.28 mmol/l and 11.67±0.21 mmol/l in two comparison groups ($p > 0.05$). Thus, all examined patients of the two groups were equally representative in terms of age, gender, and degree of DM compensation.

Determination of the level of EI in the blood, calculation of the Caro index, HOMA-IR are informative for the verification of the presence of IR in patients with MS. We found a probable difference in the EI indicator in the group of patients with type 2 diabetes with MS compared to patients without signs of MS by almost 2.3 times ($p < 0.05$). The HOMA IR score was inconsistent in different groups. In particular, in patients with type 2 diabetes without MS, this indicator fluctuated within the normal range. In patients with type 2 diabetes with MS, the HOMA IR indicator was elevated - 10.32±0.80 ($p < 0.05$), which indicated insulin resistance. Analyzing the indicators of the Caro index, it was established that in patients with type 2 diabetes with MS it was significantly different from the index of patients with type 2 diabetes without MS ($p < 0.05$). CGM was performed using the

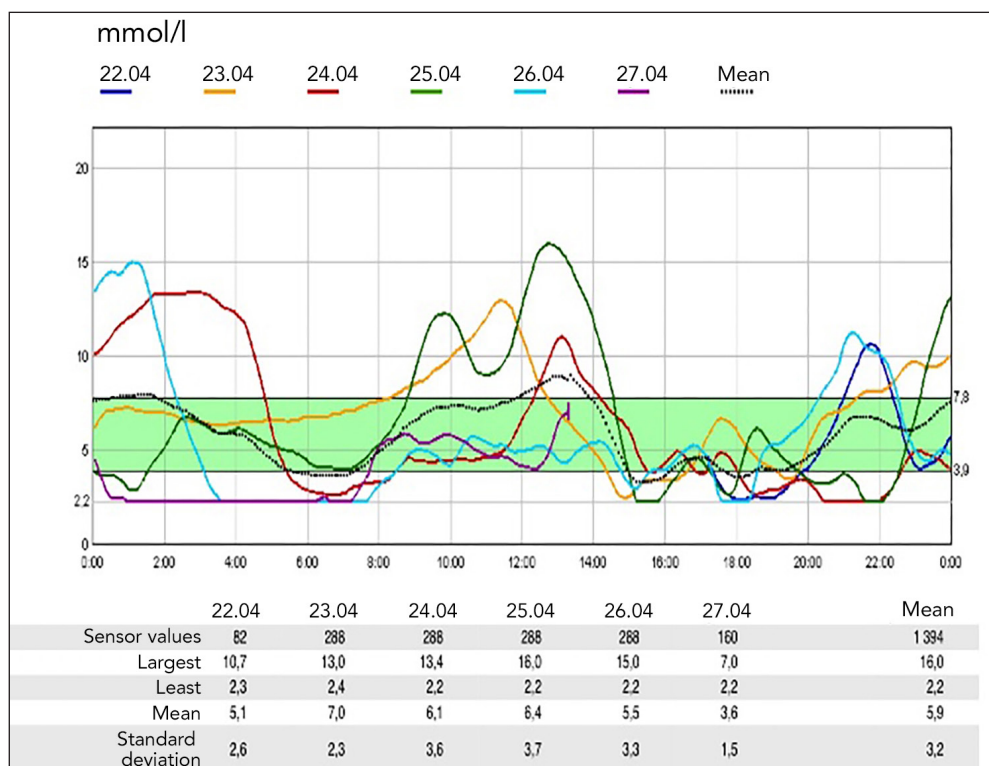


Fig. 1. Variability of glycemia at HbA1c = 6,4% CV = 54%

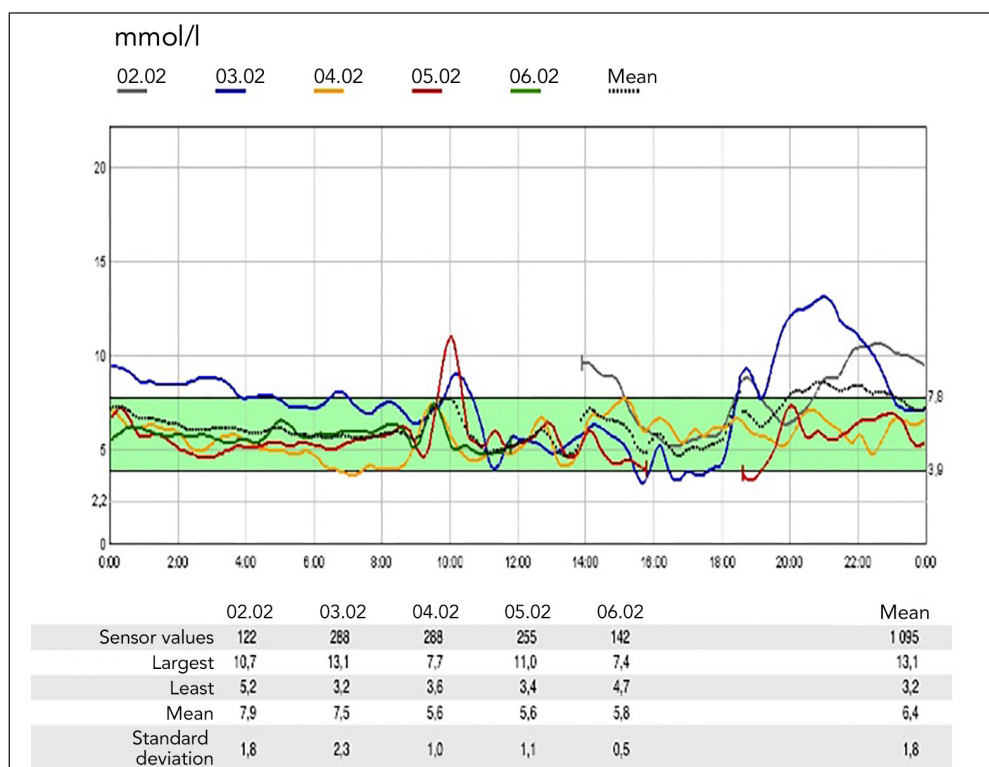


Fig. 2. Variability of glycemia at HbA1c = 6,8% CV = 28%

Guardian Connect system of the Metronic company in 28 patients with type 2 diabetes and MS and 24 patients with diabetes without MS for an average of 14 days, who were treated in the endocrinology department of the Communal non-profit enterprise "Regional Clinical Hospital" of the Ivano-Frankivsk Regional Council and Daughter enterprise "Sanatorium"Morshynresort"Private

Joint Stock Company "Ukrprofozdorovnytsia" (see Table I). The absence of hypoglycemia is an essential condition for the successful and safe treatment of patients with blood sugar levels less than 3.8 mmol/l and 3.0 mmol/l. Time below range (TBR): (<3 mmol/l) in patients with diabetes with MS was 0.19±0.07% and probably did not differ in patients with diabetes in the type without

MS (<1% was considered the norm); Time below range (TBR): (<3.8 mmol/l) in patients with diabetes mellitus with MS was $0.91 \pm 0.54\%$ (<4% was considered the norm); Time in range TIR: (3.9–10.0 mmol/l) in patients with diabetes mellitus with MS - $53.30 \pm 5.90\%$ probably differed from patients with diabetes mellitus without MS - $74.42 \pm 7.83\%$ ($p < 0.05$) (with a norm of >70%); Time above range (TAR): (>10.1 mmol/l) in patients with diabetes with MS was $43.33 \pm 5.96\%$ and was significantly different from patients in the other group ($p < 0.05$) (norm <25%); Time above range TAR: >13.9 mmol/l in patients with DM with MS - $22.1 \pm 3.91\%$, in patients with DM without MS - $12.34 \pm 2.39\%$ (norm <5%); Glucose Variability CV in patients with diabetes mellitus with MS was $44.10 \pm 4.89\%$, which probably differed in patients with diabetes mellitus without MS - $28.32 \pm 6.27\%$ ($p < 0.05$), (norm $\leq 36\%$); Average Glucose in patients with diabetes with MS was 10.1 ± 0.52 mmol/l (target < 8.6 mmol/l); Glucose Management Indicator (GMI) – the level of HbA1c by CGM in patients with diabetes mellitus with MS was $9.6 \pm 1.19\%$ (target < 7%; < 8%).

HbA1c is the gold standard for diabetes control, but it has its limitations. HbA1c does not indicate previous hypoglycemia or high variability of glycemia, does not provide complete information about diabetes control. We give an example of patients with the same level of HbA1c and a difference in the variability of glycemia (Fig. 1, Fig. 2).

DISCUSSION

In view of the updated international guidelines for diabetes care and the standardized CGM report [1], CGM plays an important role in evaluating the effectiveness and safety of treatment, including the prevention of hypoglycemia in patients with diabetes. The results of our study prove that patients with type 2 diabetes and MS tend to have marked glycemic variability. None of the examinees had a mild degree of glycemia variability. Similar conclusions coincide with the results of P. Pozzilli's study that in patients with type 2 diabetes who had good glycemic control, the HbA1c level did not correlate with the parameters of glycemia variability calculated from CGM data [13]. HbA1c is the gold standard for diabetes control, but it has its limitations: it only assesses HbA1c every 3 months, does not record glycemic/hypo-/hyperglycemic

variability, does not allow assessment of the patient's condition immediately after a change in therapy, does not correspond very well to patient-reported condition, has insufficient accuracy (different laboratories, anemia, age, other), correlates well with clinical outcomes, has a large number of long-term studies [13]. We have obtained indisputable data that coincide with the studies of Cappon G, Curt Rohlfing et al., which prove that TIR provides accurate data on the patient's glycemic status and helps better control diabetes: the blood glucose level is continuously assessed; any time periods are evaluated; reflects glucose fluctuations more informatively than HbA1c and determines the time of stay within safe limits; allows to assess the patient's condition immediately after the change of therapy; correlates well with patient-reported condition; has sufficient accuracy; the correlation with clinical consequences has not yet been clarified; there are no long-term studies [9, 12].

CONCLUSIONS

1. HbA1c is the gold standard for diabetes control, but it has its limitations. HbA1c does not indicate previous hypoglycemia or high variability of glycemia, does not provide complete information about diabetes control.
2. For optimal diabetes control, in addition to HbA1c, we must consider CGM data and % Time in range (TIR). TIR should be used as a target point as an indicator of glycemic control in routine clinical practice.
3. TIR provides accurate data on a patient's glycemic status and helps better control diabetes.
4. Determination of the level of EI in the blood, calculation of the Sago index, HOMA-IR are informative for the verification of the presence of IR in patients with type 2 diabetes with MS.
5. We proved that patients with type 2 diabetes mellitus with MS reliably have worse CGM indicators: Time in range TIR: (3.9–10.0 mmol/l) - $53.30 \pm 5.90\%$; Time above range (TAR): (time above range) (>10.1 mmol/l) - $43.33 \pm 5.96\%$; Time above TAR range (>13.9 mmol/l) - $22.1 \pm 3.91\%$; Glucose Variability CV - $44.10 \pm 4.89\%$ compared to patients with type 2 diabetes without MS, which proves the negative effect of insulin resistance on compensation of diabetes.

REFERENCES

1. American Diabetes Association Professional Practice Committee; 17. Diabetes Advocacy: Standards of Medical Care in Diabetes—2022. *Diabetes Care* 1 January 2022; 45: S254–S255.
2. Saedi P, Petersohn I, Salpea P et al. IDF Diabetes Atlas Committee. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract.* 2019; 157:107843. doi: 10.1016/j.diabres.2019.107843.

3. DCCT. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus/N. Engl. J. Med. 1993; 329:977-986.
4. International Expert Committee Report on the Role of the A1c Assay in the Diagnosis of Diabetes. Diabetes Care. 2009; 32(7):1327-1334.
5. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet. 1998; 352:837-853.
6. Daryabor G, Atashzar MR, Kabelitz D et al. The Effects of Type 2 Diabetes Mellitus on Organ Metabolism and the Immune System. Front Immunol. 2020; 11:1582. doi: 10.3389/fimmu.2020.01582.
7. Gaborit B, Julla JB, Besbes S et al. Glucagon-like Peptide 1 Receptor Agonists, Diabetic Retinopathy and Angiogenesis: The AngioSafe Type 2 Diabetes Study. J Clin Endocrinol Metab. 2020; 105(4):dgz069. doi: 10.1210/clinem/dgz069.
8. Rohlfing C, Hanson S, Estey M et al. Evaluation of interference from hemoglobin C, D, E and S traits on measurements of hemoglobin A1c by fifteen methods. Clinica Chimica Acta. 2021; 522:31-5.
9. Cappon G, Vettoretti M, Sparacino G, Facchinetti A. Continuous Glucose Monitoring Sensors for Diabetes Management: A Review of Technologies and Applications. Diabetes Metab J. 2019; 43(4):383-397. doi: 10.4093/dmj.2019.0121.
10. Kovatchev BP. Metrics for glycaemic control from HbA1c to continuous glucose monitoring. Nat Rev Endocrinol. 2017; 13:425-436.
11. Bergenstal RM, Gal RL, Connor CG et al. T1D Exchange Racial Differences Study Group. Racial differences in the relationship of glucose concentrations and hemoglobin A1C levels. Ann. Intern. Med. 2017; 167: 95–102.
12. Danne T et al. "International consensus on use of continuous glucose monitoring". Diabetes care. 2017; 40 (12):1631-1640.
13. Pozzilli P. CSII and other technologies for preventing beta cell failure in type 2 diabetes. Diabetes Technol Ther 2016; 18:A1.

ORCID and contributionship:

Taras V. Romaniv: 0000-0003-0702-3291 ^{A,C-F}

Nadiya V. Skrypnyk: 0000-0003-1294-7042 ^{A,C-E}

Ulyana V. Synko: 0000-0002-9647-0327 ^{B-D}

Nataliia M. Voronych-Semchenko: 0000-0001-9872-6640 ^{A,D}

Oleh V. Melnyk: 0000-0002-9681-8215 ^{B,E}

Anna O. Hryb: 0000-0003-3175-7025 ^{B,C}

Igor B. Boruchok: 0000-0002-1257-0401 ^B

Conflict of interest:

The Authors declare no conflict of interest

CORRESPONDING AUTHOR

Taras V. Romaniv

Ivano-Frankivsk National Medical University
2 Halytska St., 76018 Ivano-Frankivsk, Ukraine
tel: +380673448577
e-mail: taras_gresko@ukr.net

Received: 07.09.2022

Accepted: 14.04.2023

A - Work concept and design, **B** - Data collection and analysis, **C** - Responsibility for statistical analysis, **D** - Writing the article, **E** - Critical review, **F** - Final approval of the article



Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

PECULIARITIES OF STRUCTURAL CHANGES IN THE BRAIN SUBSTANCE IN PATIENTS WITH ARRHYTHMIAS DEPENDING ON THE SEVERITY OF COGNITIVE DISORDERS

DOI: 10.36740/WLek202306110

Sergiy Stadnik, Olena Radchenko, Orest Komarytsia, Iryna Zhakun, Angelica Filipyuk, Nataliya Bek

DANYLO HALYTSKY LVIV NATIONAL MEDICAL UNIVERSITY, LVIV, UKRAINE

ABSTRACT

The aim: To evaluate the structural changes of the brain in relation to the formation of cognitive disorders (CD) in patients with arrhythmias

Materials and methods: 147 patients with different clinical forms arrhythmias against the background of ischemic heart disease were examined. At the first stage, all patients with arrhythmias assessed cognitive functions. At the second stage, patients were distributed into two groups: the main group patients with CD, control – patients without CD. These groups underwent computed tomography examination of the brain.

Results: CD were established in 83% patients with arrhythmias. Mild CD were more often diagnosed in patients with persistent form of atrial fibrillation (AF), severe CD – in patients with permanent form of AF and atrioventricular blockade II-III degrees. Neuroimaging changes were found in 73.8% patients with CD and in 36% patients without CD. They were manifested by atrophic changes of the cortex, internal hydrocephalus, a decrease in the density of the brain substance of the periventricular area. In patients with CD, compared to patients without CD, showed lacunar foci with predominant localization in the parietal and frontal lobes of the brain, periventricular and subcortical leukoariosis. Multiple correlations were established between CD and structural changes of the brain.

Conclusions: The increase in the severity of CD in patients with arrhythmias is associated with atrophic changes at the cortical-subcortical level, accompanied by the phenomena of internal hydrocephalus, periventricular and subcortical LA, lacunar foci, with a predominant localization in the frontal-temporal-occipital lobes, in the visual hump and basal ganglia of both cerebral hemispheres.

KEY WORDS: computed tomography, arrhythmias, cognitive disorders, leukoariosis

Wiad Lek. 2023;76(6):1391-1399

INTRODUCTION

Violations of higher brain functions are one of the most urgent medical and social problems, as they lead to a decrease in the quality of life, disorders of social and professional activity of a person, and with a long course – to the development of dementia and complete social disadaptation [1-3]. Early diagnosis of cognitive disorders (CD) makes it possible to prescribe timely treatment and postpone the onset of disability. Predemented CD have important clinical significance, as they are more amenable to therapeutic correction [4]. Detection of early, potentially reversible CD against the background of cardiovascular pathology makes it possible to timely identify groups of patients with an increased risk of developing cognitive dysfunction, especially among people of working age.

In most works devoted to the study of CD, their role in the occurrence of arterial hypertension and cerebral atherosclerosis was investigated [5, 6], however, the impact of arrhythmias on the development of cognitive deficits

has not been sufficiently studied. In the literature, the question of changes on the part of the nervous system in various forms of arrhythmias has been reflected [7-9], but most of the data on this issue have been obtained in elderly patients, including patients with a history of stroke. The possibilities of the development of CD in young and middle-aged patients with arrhythmias and the absence of obvious morphological cerebrovascular disorders have not been fully explored. The importance of the problem is evidenced by the fact that in March 2018 the joint consensus of the «European Heart Rhythm Association (EHRA), Heart Rhythm Society (HRS), Latin American Heart Rhythm Society (LAHRS), Asia-Pacific Heart Rhythm Society (APHRS) was published on the problem arrhythmias and cognitive functions: what is the best strategy?» [10]. The document deals with approaches to the diagnosis and tactics of treating CD in patients with various arrhythmias.

Possible mechanisms of CD in arrhythmias are: decrease in brain perfusion due to low cardiac output;

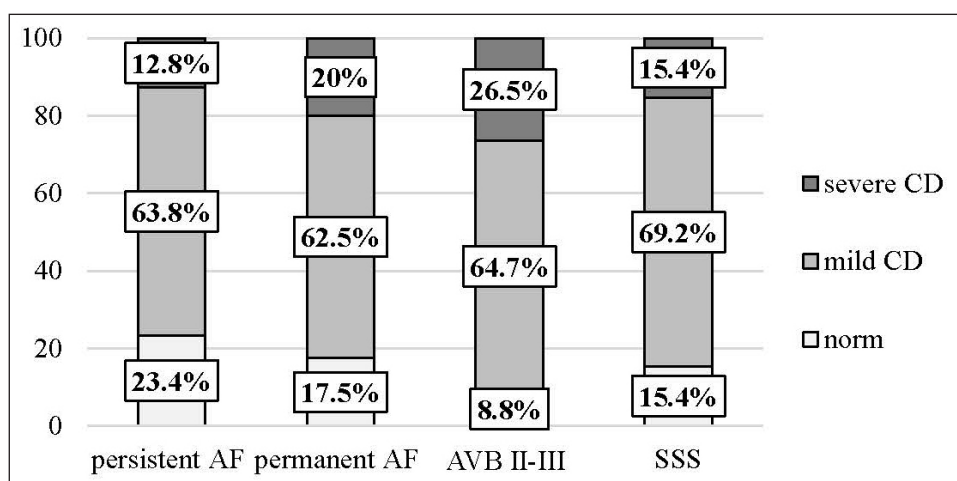


Fig. 1. The structure of cognitive disorders in patients of the studied groups

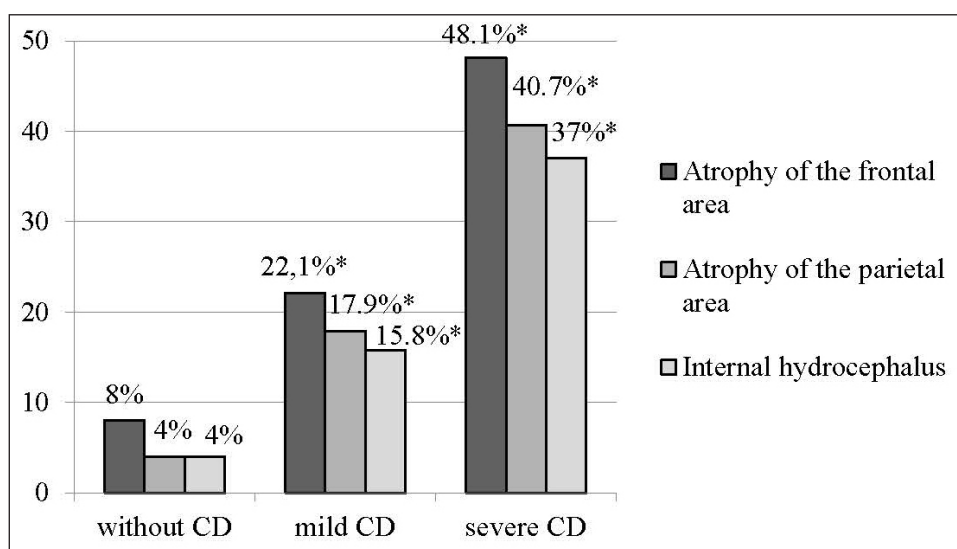


Fig. 2. Frequency of neuroimaging changes in patients depending on the severity of CD

* – statistically significant differences when compared with patients without CD ($p < 0.05$)

occurrence of leukoaraiosis, «silent» brain infarctions; transient ischemic attacks; hypercoagulation; neurodegenerative cerebral changes [11]. Structural lesions of the brain of a focal or diffuse nature due to ischemia are considered as one of the factors of vascular dementia, and arrhythmias are considered a predictor of CD [12].

An integrated complex approach to the study of the mechanisms of development of CD in patients with arrhythmias, their early diagnosis, the choice of the correct strategy for the treatment of arrhythmias can slow down the progression of cognitive deficits, which will make it possible to improve not only the clinical status of patients, but also their prognosis. The above positions determined the relevance of the chosen direction of research and determined its purpose.

THE AIM

The aim of our work was to evaluate the structural changes of the brain in relation to the formation of CD in patients with arrhythmias.

MATERIALS AND METHODS

To solve the set goal of followed 147 patients aged from 30 to 75 years (mean age 62.7 ± 4.6 years) with different clinical forms arrhythmias against the background of ischemic heart disease. Persistent form of atrial fibrillation (AF) diagnostic staged in 47 (32%) patients, permanent form of AF – in 40 (27.2%) patients, atrioventricular blockade (AVB) II-III degrees – in 34 (23.1%) patients, sick sinus syndrome (SSS) – in 26 (17.7%) patients. The group of patients with SSS included patients with persistent sinus bradycardia (42.3%), recurrent sinus auricular block (23.1%), sudden periodic disappearance of the sinus node (sinus node arrest) (15.4%), persistent bradysystolic form of atrial fibrillation (11.5%), the syndrome of «tachycardia-bradycardia» (7.7%).

The criterion for inclusion in the study is arrhythmias was associated with ischemic heart disease. In research not included patients who had acute forms of acute forms of coronary heart disease, expressed female extracardiac pathology, diabetes mellitus, acute history of cerebral circulation. Besides, the study did not include patients with contraindications to proconducting computed tomography (CT) of the brain.

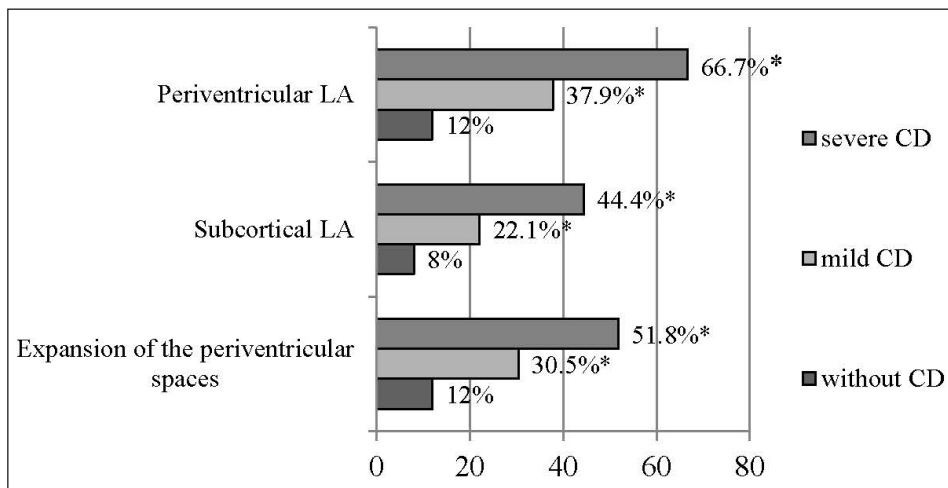


Fig. 3. Frequency of diffuse brain changes in patients depending on the severity of CD, * – statistically significant differences when compared with patients without CD ($p < 0.05$)

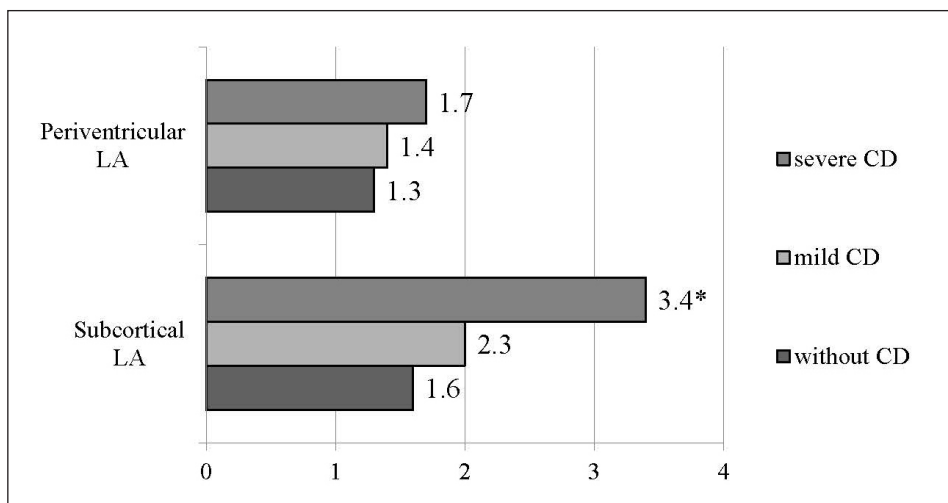


Fig. 4. Diffuse changes in the brain (in points) in patients depending on the severity of CD (* $p < 0.05$)

Table I. Localization of lacunar foci in patients with arrhythmias depending on the severity of CD

Localization of lacunar foci	without CD	mild CD	severe CD
Subcortical white matter	1 (50.0%)	6 (54.5%)	8 (44.4%)
Basal ganglia and thalamus	1 (50.0%)	3 (27.3%)	5 (27.8%)
Pons and cerebellum	0	2 (18.2%)	5 (27.8%)
In total	2	11	18

Table II. Relationship between CD risk and neuroimaging changes in patients

Indicator	OR	95% CI	p
CD and external hydrocephalus	1.61	1.14–2.2	0.008
CD and internal hydrocephalus	1.84	1.16–2.64	0.007
CD and periventricular LA	3.57	1.54–5.82	0.006
CD and subcortical LA	5.68	2.21–9.62	<0.001
CD and lacunar foci	4.68	1.92–7.54	0.003

The choice of inclusion and exclusion criteria is determined by the following considerations. Thus, ischemic heart disease is considered the most common cause of arrhythmias. Patients with myocarditis, congenital and acquired heart disease and other diseases associated with arrhythmias in many relationships are not compa-

rable with patients suffering from ischemic heart disease, are relatively rare and, obviously, need a separate research. Selection of exclusion criteria is also explained by the need to exclude as much as possible all possible diseases and states capable of being independent cause of brain damage.

The research was carried out in two stages. At the first stage, all patients with arrhythmias assessed cognitive functions using a set of neuropsychological tests. Neuropsychological examination included: Mini-Mental State Examination (MMSE) (Folstein M. et al., 1975), Frontal Assessment Battery (FAB) (Dubois B. et al., 2000), dementia scale of Mattis (DSM) (Mattis S., 1976), test "10 words" (Luria AR, 1969), test "5 words" (Grober E. et al., 1988), verbal association test (Kazdin A., 1982), lines orientation test (Benton A., 1975), test "unpainted objects" (Luria AR, 1969), clock drawing test (Sunderland T. et al., 1989), test of connection of numbers and letters (Trail making test) (Reitan RM, 1958), Boston naming test (Kaplan J. et al., 1978), Spilberger-Khanin anxiety self-assessment scale (Spilberger C.D. et al, 1976), Beck depression scale (Beck A.T. et al, 1975) [13].

At the second stage, patients were distributed divided into two groups: the main group consisted of patients who, in the course of neuropsychological testing, had the presence of cognitive dysfunction; control – patients without CD. These groups underwent computed tomography (CT) examination of the brain on a multi-system spiral computed tomograph «Asteion-4 mod. TSX-021B» (Japan). The severity of internal and external atrophy, periventricular and subcortical leukoaraiosis (LA), lacunar foci (LV) were evaluated.

When analyzing the obtained data, we solved such tasks as describing the studied parameters in groups, evaluating the significance of differences in quantitative and qualitative indicators, checking the empirical distribution of variables for compliance with the law of normal distribution, and identifying the factor structure in the multidimensional space of features. Depending on the type of distribution of the investigated quantitative variables, the results of their statistical processing are represented by the average value and standard deviation $M \pm \sigma$. Frequencies – n (%) were determined for qualitative data.

During the study, the following methods of statistical analysis were used:

- determination of numerical characteristics of variables;
- comparison of parametric data (after checking the number of data for normal distribution using the Kolmogorov-Smirnov and Shapiro-Wilk tests) using the Student's test (for 2 independent elections) and the ANOVA method – for several groups;
- assessment of the significance of differences in quantitative indicators in independent samples: according to the Mann-Whitney U Test – for 2 independent samples and the Kruskal-Wallis test – for several groups. Comparison of paired samples was performed using the Wilcoxon test (for 2 groups);
- to find differences in frequencies, the odds ratio was

determined – Odds Ratio (OR), which was calculated as a fraction of the division of the frequency of occurrence of cases in the examined groups. A 95% confidence interval (CI) was calculated for the indicators of OR. An indicator was considered reliable if the CI did not contain an odds ratio value equal to 1;

- assessment of the strength and direction of the relationship between quantitative indicators using the Pearson correlation coefficient (r); the strength of the relationship was assessed by the following values of the correlation coefficient: a value < 0.3 was considered as the absence of a relationship, $0.3-0.7$ – a moderate relationship, and > 0.7 – the presence of a strong correlation.

The study used application packages Statistica for Windows v. 8.0 (StatSoft Inc, USA, 2012) in accordance with the recommendations for processing the results of biomedical research.

RESULTS

Cognitive disorders were established in 36 (76.6%) patients with persistent form of AF, in 33 (82.5%) patients with permanent form of AF, in 31 (91.2%) patients with AVB II-III degrees, in 22 (84.6%) patients with SSS. Mild CD were more often diagnosed in patients with persistent form of AF (OR 1.47, CI 1.13–1.88, $p=0.036$), severe CD – in patients with permanent form of AF (OR 2.15, CI 1.45–3.32, $p<0.001$) and patients with AVB II-III degrees (OR 2.62, CI 1.51–4.13, $p<0.001$) (Fig. 1).

Heart rhythm and conduction disorders are an independent risk factor for cognitive disorders and are characterized by a diffuse deterioration of all cognitive functions. In most cases, these disorders were of moderate and mild degrees.

In patients with a persistent form of AF, a violation of the neurodynamic component of cognitive activity has been established, which do not reach clinically significant CD and do not affect professional and social activity. In patients with a permanent form of AF, violations of regulatory functions come to the fore, forming a polymodal cognitive deficit with a relatively uniform violation of all cognitive functions. In patients with bradyarrhythmias, the leading neuropsychological mechanism of cognitive disorders is the lack of voluntary regulation of activity against the background of a decrease in general mental activity, which is manifested by a significant decrease in cognitive functions and emotional maladaptation, most pronounced in AVB.

Neuroimaging changes were found in 90 (73.8%) patients with CD and in 9 (36%) patients without CD ($p=0.037$). They were manifested by atrophic changes of the cortex, internal hydrocephalus, a decrease in the

density of the brain substance of the periventricular area, which depended on the duration of the arrhythmia ($r=0.42$, $p=0.026$), its severity ($r=0.31$, $p=0.032$), the variability of the daily BP rhythm ($r=0.36$, $p=0.035$), BP increase episodes ($r=0.32$, $p=0.032$). Atrophic changes and internal hydrocephalus occurred more often in patients with severe CD ($p=0.04$) (Fig. 2).

On the basis of the evaluation of densitometric data, in 45 (36.8%) patients with CD and in 6 (24%) patients without CD, expansion of the ventricular system was established in the absence of changes or with slight expansion of subarachnoid spaces. In 40 (32.8%) patients with CD and in 6 (24%) patients without CD, predominant expansion of the subarachnoid spaces was noted, while expansion of the cerebellar space, frontal and parietal lobes was more common. Combined expansion of the ventricles and subarachnoid spaces was noted in 37 (30.3%) patients with CD and in 5 (20%) patients without CD. At the same time, the frequency of expansion of the ventricular system of the brain among patients with CD significantly exceeded that of patients with severe CD ($p=0.033$).

Compared to patients without CD, the absolute transverse dimensions of the anterior and posterior horns of the lateral ventricles significantly increased in patients with CD – by $8.7\pm 0,3\%$ and $8.1\pm 0,2\%$, respectively ($p=0.048$); indices of the front horns increased by $9.4\pm 1,7\%$ ($p=0.036$), rear – by $6.5\pm 1,3\%$ ($p=0.18$). The absolute transverse dimensions of the central parts of the lateral ventricles increased by $8.1\pm 0,4\%$ ($p=0.04$), the index of the III ventricle – by $25\pm 3,5\%$ ($p=0.027$), the width of the III ventricle – by $13.1\pm 2,2\%$ ($p=0.027$), the width IV ventricle – by $8.1\pm 0,7\%$ ($p=0.047$). The maximum width of the sylvian fissure increased by $23.8\pm 2,9\%$ ($p=0.047$ and $p=0.021$), the front sections – by $16.4\pm 2,5\%$ ($p=0.047$). Expansion of the subarachnoid spaces of the large hemispheres of the brain and cerebellum is more pronounced in patients with severe CD. In patients with CD, a moderate expansion of all sections of the ventricular system and subarachnoid spaces was observed, more pronounced in patients with severe CD ($p=0.025$).

An increase in the average values of linear indices was found in patients with CD compared to patients without CD. They were uneven: the highest rates were observed in the projection of the parietal lobes (by 1.38 times) and less pronounced – in the projection of the frontal lobes (by 1.2 times). The parameters of the ventriculo-lobular indices, indicating predominantly central atrophy of the brain substance, increased approximately equally in the projection of the parietal and frontal lobes (respectively by 2.3 and 2.4 times) and to a lesser extent in the projection of the temporal lobes (in

1.6 times). The volume of subarachnoid spaces, determined by the value of the subarachnoid-partial indices and which reflects the degree of cortical atrophy of the brain substance, increased with the progression of chronic brain ischemia in the parietal area (by 1.4 times) and to a lesser extent (by 1.3 times) in the projection of the mediobasal divisions of the temporal lobes. The results in the projection of the parietal lobes were reliable ($p=0.034$).

Lacunar foci of reduced density with a diameter of up to 2 cm, localized mainly in the deep parts of the white matter of the parietal and frontal lobes of the brain, were found in 29 (23.7%) patients with CD, of them – in 11 (9%) of patients with mild CD ($p=0.053$) and in 18 (14.8%) patients with severe CD ($p=0.027$). Lacunar foci occurred in 2 (8%) patients without CD.

In patients with severe CD, multiple hypodense foci were found, localized in almost all departments with a preference in the cerebellar hemispheres, temporal and occipital lobes (Table I). Foci of 1–3 mm indicate the expansion of perivascular spaces as a result of chronic brain ischemia. Their localization is characteristic of damage mainly to the vessels of the vertebro-basilar basin.

Diffuse changes in the white matter of the brain are presented in 57 (46.7%) patients with CD and in 5 (20%) patients without CD by periventricular and/or subcortical leukoaraiosis (LA) and expansion of the periventricular spaces. Subcortical LA was visualized to a greater extent in the occipital and parietal lobes, periventricular LA – in the white matter in the area of the posterior horns of the lateral ventricles (occipital «caps»). In 54 (44.3%) patients with CD, there were signs of periventricular LA, in 33 (27%) patients – subcortical LA, in 43 (35.2%) patients – expansion of the periventricular spaces (Fig. 3).

Intergroup differences related not only to the frequency of detection of LA, but also to the severity of changes in the white matter of the brain. The degree of severity of periventricular LA in 20 (37%) patients with CD reached 1 point, which corresponded to single foci with a diameter of less than 5 mm, limited to the front or back areas. Such changes were considered as a variant of the age norm [14]. Foci with a diameter of 6–10 mm were found in 34 (63%) patients. The expressiveness of periventricular LA in them was estimated at 2 points. In patients without CD, changes in the periventricular substance amounted 1 point in 3 (100%) patients.

In 20 (60.6%) patients with CD, less than 5 small, up to 5 mm in diameter, local subcortical LA foci or less than 2 large, 6–10 mm in diameter, foci were found, which corresponded to 1–3 points. In 10 (30.3%) patients, multiple foci (more than 6, size of 6–10 mm) of subcortical LA were found, which corresponded to 4

points. In 3 (9.1%) patients, a focus with a diameter of more than 10 mm was found, which corresponded to 5 points. In all patients without CD, less than 5 small, up to 5 mm in diameter, local foci or less than 2 large, 6–10 mm in diameter, subcortical LA foci were found, which corresponded to 1–3 points. Differences in the severity of subcortical LA between patients with severe CD and those without CD were significant ($p=0.034$) (Fig. 4).

We determined the influence of heart rate level (according to the results of daily blood pressure monitoring) on the severity of periventricular LA ($r=0.34$, $p=0.041$) and subcortical LA ($r=0.37$, $p=0.038$) in the frontal lobes of the brain. The influence of blood pressure on the degree of severity of white matter damage was established in middle-aged and elderly patients: the level of systolic blood pressure was correlated with the severity of subcortical LA in the frontal lobes of the brain ($r=0.42$, $p=0.007$), and the level of diastolic blood pressure was correlated with the severity of widespread subcortical LA ($r=0.34$, $p=0.046$) and subcortical LA in the occipital lobes of the brain ($r=0.41$, $p=0.008$).

The presence of small vascular foci in the white matter of the large hemispheres of the brain was associated with the daily BP rhythm of the «non-dipper» type ($r=0.35$, $p<0.05$). At the same time, the frequency of small foci in «non-dipper» was 2.1 times higher (OR 2.14, CI 1.43–3.00, $p=0.012$). The presence of small vascular foci was associated with the average night time index of systolic blood pressure ($r=0.38$, $p=0.04$). With increased systolic blood pressure load at night, the frequency of small vascular foci in the white matter of the brain was 1.8 times higher (OR 1.81, CI 1.46–2.24, $p=0.002$). Thus, the systolic blood pressure load at night reliably influenced the risk of structural damage to the brain.

Thus, in patients with CD on the background of arrhythmias, compared to patients without CD, brain spiral computed tomography showed lacunar foci with predominant localization in the parietal and frontal lobes of the brain, periventricular and subcortical LA, signs of an atrophic process.

Correlations were established between the expansion of the lateral ventricles and the results of FAB ($r=-0.33$, $p=0.036$), DSM ($r=-0.4$, $p=0.024$), tests of «10 words» ($r=-0.37$, $p=0.028$), drawing a clock ($r=-0.39$, $p=0.017$), undrawn objects ($r=-0.35$, $p=0.025$); between the expansion of the periventricular spaces and the «concentration» subtest of DSM ($r=-0.36$, $p=0.041$); between the index of the III ventricle and the total score according to the screening scales (MMSE – $r=-0.38$, $p=0.007$; FAB – $r=-0.32$, $p=0.032$; DSM – $r=-0.32$, $p=0.027$); between the index of the III ventricle and the «10 and 5 words» tests ($r=-0.35$, $p=0.038$ and $r=-0.33$, $p=0.026$, respectively); between the dimensions

of the anterior horn of the lateral ventricle on the left / right and the «orientation» subtest of MMSE ($r=-0.36$, $p=0.008$ and $r=-0.24$, $p=0.046$, respectively); between the sizes of the anterior horns of the lateral ventricle and the tests of «literal associations» ($r=-0.43$, $p=0.004$), «categorical associations» ($r=-0.38$, $p=0.008$), «undrawn objects» ($r=-0.4$, $p=0.01$), «line orientations» ($r=-0.43$, $p=0.006$); between the total temporal index and MMSE ($r=-0.34$, $p=0.037$), FAB ($r=-0.32$, $p=0.041$); between the ventriculo-partial temporal index and the tests «10 words» ($r=-0.33$, $p=0.036$), «connection of numbers and letters» ($r=0.35$, $p=0.028$); between the central linear index and the tests «10 words» ($r=-0.31$, $p=0.034$), «line orientations» ($r=-0.4$, $p=0.007$); between the posterior linear index and the «underdrawn objects» test ($r=-0.33$, $p=0.035$).

A correlation was observed between the presence of the LA phenomenon and the degree of cognitive decline ($r=-0.41$, $p=0.006$). LA is a sufficiently specific pattern for CD vascular genesis.

We established correlations between the severity of LA and the tests: MMSE ($r=-0.41$, $p=0.032$), FAB ($r=-0.38$, $p=0.034$), DSM ($r=-0.38$, $p=0.027$), «10 words» ($r=-0.36$, $p=0.035$), «5 words» ($r=-0.35$, $p=0.028$), literal associations ($r=-0.31$, $p=0.041$), categorical associations ($r=-0.39$, $p=0.035$), undrawn objects ($r=-0.35$, $p=0.04$), clock drawing ($r=-0.36$, $p=0.028$), both blocks of the number and letter association test ($r=0.37$, $p=0.027$ and $r=0.38$, $p=0.03$, respectively), the Boston naming test ($r=0.39$, $p=0.017$).

The presence of single asymptomatic lacunar foci was correlated with the following tests: MMSE ($r=-0.32$, $p=0.028$), FAB ($r=-0.35$, $p=0.024$), «10 words» ($r=-0.39$, $p=0.02$), literal associations ($r=-0.36$, $p=0.031$), categorical associations ($r=-0.40$, $p=0.007$), line orientations ($r=-0.38$, $p=0.026$), clock drawing ($r=-0.36$, $p=0.035$), both blocks of the number and letter association test ($r=0.39$, $p=0.008$ and $r=0.38$, $p=0.026$ respectively), the Boston naming test ($r=0.34$, $p=0.04$).

In addition to determining the correlations, we calculated the OR of CD development for each of the detected pathological neuroimaging signs. The results of univariate logistic regression indicate that external and internal hydrocephalus, periventricular / subcortical LA and the presence of lacunar foci are additional factors that increase the risk of CD in patients with arrhythmias (Table II).

Thus, the pathological processes that develop in the vascular system in arrhythmias cause damage to the actual substance of the brain with the formation of angioencephalopathy. The morphological substrate of these disorders is small focal and diffuse changes mainly in the deep parts of the brain.

DISCUSSION

The main morphological substrate of CD in patients with arrhythmias is white matter damage in the frontal lobes of the brain, which causes dysfunction of these parts and manifested by subcortical and periventricular leukoariosis. The consequence of such changes is the functional isolation of the frontal lobes due to disruption of their connections with other cortical and subcortical cerebral structures [7].

The changes detected during the neuropsychological examination in patients with arrhythmias, as well as the nature of brain changes according to spiral CT (moderately expressed LA, single lacunae in the absence of pronounced brain atrophy) give grounds to assume the presence subcortical frontal dysfunction as the main mechanism of CR development. The basis of frontal dysfunction probably lies in the damage of various parts of the brain (due to the formation of «silent» lacunae), as well as the disruption of associative connections between the frontal lobe and the visual hump, basal ganglia, and other parts of the brain [15].

In patients with arrhythmias in the presence of CD, compared to patients without CD, «silent» lacunar infarcts in the frontal lobe of the brain, leukoariosis around the bodies of the lateral ventricles, as well as signs of an atrophic process were detected on spiral CT scans. Therefore, taking into account the more pronounced CD in patients with arrhythmias, it is possible to assume that it is the above-mentioned changes in the brain that play a leading role in the development of cognitive deficits.

Neuroimaging changes in patients with arrhythmias were manifested by mild atrophic changes in the cortex, internal hydrocephalus, and a decrease in the density of the brain matter of the periventricular area, which depended on the duration of the arrhythmia, its severity, the variability of the daily rhythm, and episodes of increased blood pressure. Atrophic changes and internal hydrocephalus occurred more often in patients with moderate CD ($p=0.04$).

In patients with CD, compared to patients without CD, CT scans of the brain showed lacunar foci with predominant localization in the parietal and frontal lobes of the brain, periventricular and subcortical leukoariosis, signs of an atrophic process.

We established inverse correlations between the severity of leukoariosis / lacunar foci and the results of most neuropsychological tests. The results of uni-

variate logistic regression indicate that external and internal hydrocephalus, periventricular and subcortical leukoariosis, and the presence of lacunar foci are additional factors that increase the risk of CD in patients with arrhythmias.

Neuropsychological changes detected in patients with arrhythmias, as well as the nature of changes in the brain according to spiral CT (moderately expressed leukoariosis, isolated lacunae in the absence of pronounced brain atrophy), suggest the presence of subcortical frontal dysfunction as the main mechanism of CD development. The basis of frontal dysfunction probably lies in the damage of various parts of the brain (due to the formation of «silent» lacunae), as well as the disruption of associative connections between the frontal lobe and the visual hump, basal ganglia, and other parts of the brain. The results of our study confirm the connection between CD and structural changes in the brain (leukoariosis, lacunar infarcts, and subcortical brain atrophy), previously shown in a number of works [16].

CONCLUSIONS

1. The increase in the severity of cognitive deficits in patients with heart rhythm and conduction disorders is associated with atrophic changes at the cortical-subcortical level (OR 1.61, CI 1.14–2.2, $p=0.008$), accompanied by the phenomena of internal replacement hydrocephalus (OR 1.84, CI 1.16–2.64, $p=0.007$), leukoariosis [periventricular (OR 3.57, CI 1.54–5.82, $p=0.006$) and subcortical (OR 5.68, CI 2.21–9.62, $p<0.001$)] and lacunar foci (OR 4.68, CI 1.92–7.54, $p=0.003$), with a predominant localization in the frontal-temporal-occipital lobes, in the area of the visual hump and basal ganglia of both cerebral hemispheres.
2. Leukoariosis, localized subcortically, leads mainly to a violation of mnemonic function, periventricular – to disorders of attention and praxis. With widespread leukoariosis, a whole complex of cognitive disorders is revealed, among which there is a violation of speech function, thinking and memory. The combination of leukoariosis with the expansion of the ventricular system of the brain leads to a deterioration in such indicators as praxis and attention.

REFERENCES

1. Blumenthal JA, Smith PJ, Mabe S et al. Lifestyle and neurocognition in older adults with cognitive impairments. *Neurology*. 2019;92:212–23. doi: 10.1212/WNL.0000000000006784.
2. Livingston G, Sommerlad A, Orgeta V. Dementia prevention, intervention, and care. *Lancet*. 2017;390:2673–734. doi: 10.1016/S0140-6736(17)31363-6.

3. Mishchenko TS. Kognitivnyye narusheniya: aktual'nost', prichiny, diagnostika, lecheniye, profilaktika. [Cognitive impairment: relevance, causes, diagnosis, treatment, prevention]. *Healthy Ukraine. Thematic issue "Neurology, Psychiatry, Psychotherapy"*. 2017;1(40):15–7. (in Russian).
4. Golovchenko Yul, Goreva GV, Slobodin TM et al. Kliniko-neyropsykhologichne spivstavlennya kohnityvnoho defitsytu iz pokaznykamy systemnoyi ta tserebral'noyi hemodynamiky pry syndromi pomirnykh kohnityvnykh porushen' [Clinical and neuropsychological manifestations of cognitive deficits as indicators of systemic and cerebral hemodynamics in the syndrome of mild cognitive impairment]. *Collection of scientific workers of NMAPE named after P.L. Shupyk*. 2015;24(2):241–8. (in Ukrainian).
5. Dotsenko NYa, Boev SS, Shekhunova IA et al. Narusheniye kognitivnoy funktsii u bol'nykh s arterial'noy gipertenziiyey i dopolnitel'nymi faktorami riska, podkhody i ikh korrektsii [Impaired cognitive function in patients with arterial hypertension and additional risk factors, approaches and their correction]. *Therapia*. 2016;10(113):11–5. (in Russian).
6. Sviridova NK. Kohnityvni ta emotsiyno-osobystisni porushennya u khvorykh na hipertenzivnu entsefalopatiyu. Stan mozkovoho krovoobihu pry arterial'niy hipertenzii (naukovyy ohlyad ta osobysti sposterezheniya) [Cognitive and emotional-personal disorders in patients with hypertensive encephalopathy. State of cerebral blood circulation in arterial hypertension (scientific review and personal observations)]. *International neurological journal*. 2016;1(79):123–30. (in Ukrainian).
7. Rivard L, Khairy P. Mechanisms, clinical significance, and prevention of cognitive impairment in patients with atrial fibrillation. *Can. J. Cardiol*. 2017;33:1556–64. doi: 10.1016/j.cjca.2017.09.024.
8. Chen LY, Norby FL, Gottesman RF. Association of atrial fibrillation with cognitive decline and dementia over 20 years: the ARIC-NCS (Atherosclerosis Risk in Communities Neurocognitive Study). *J. Am. Heart. Assoc.* 2018;7:37–73. doi: 10.1161/JAHA.117.007301.
9. Dietzel J, Haeusler KG, Endres M. Does atrial fibrillation cause cognitive decline and dementia? *Europace*. 2018;20:408–19. doi: 10.1093/europace/eux031.
10. Dages N, Chao Tze-Fan, Fenelon G et al. European Heart Rhythm Association (EHRA). Heart Rhythm Society (HRS). Asia Pacific Heart Rhythm Society (APHRS). Latin American Heart Rhythm Society (LAHRS) expert consensus on arrhythmias and cognitive function: what is the best practice? *Heart Rhythm*. 2018;1–24. doi: 10.1016/j.hrthm.2018.03.005.
11. Demenko TN, Chumakova GA, Veselovskaya NG. Osobennosti kognitivnykh funktsiy, kachestva zhizni i psikhologicheskogo sostoyaniya patsiyentov s raznymi formami fibrillyatsii predserdiy [Features of cognitive functions, quality of life and psychological state of patients with different forms of atrial fibrillation]. *Heart*. 2017;2:123–134. (in Russian).
12. Singh-Manoux A, Fayosse A, Sabia S. Atrial fibrillation as a risk factor for cognitive decline and dementia. *Eur. Heart J*. 2017;38:2612–8. doi: 10.1093/eurheartj/ehx208.
13. Belova AN. Shkaly, testy i oprosniki v nevrologii i neyrohirurgii: Rukovodstvo dlya vracheji i nauchnykh rabotnikov [Scales, tests and questionnaires in neurology and neurosurgery: A guide for doctors and researchers]. Moscow: Practical medicine. 2018, p.432. (in Russian).
14. Fazekas F, Barkhof F, Wahlund L. CT and MRI rating of white – matter lesions. *Cerebrovasc Dis*. 2002;13(2):31–6. doi: 10.1159/000049147.
15. Derevetska VG. Osoblyvosti strukturno-funktsional'nykh zmin holovnoho mozku u khvorykh na fibrylyatsiyu peredserd [Peculiarities of structural and functional changes of the brain in patients with atrial fibrillation]: autoref. thesis ... candidate of medical sciences: 14.01.15. Nervous diseases. Kharkiv. 2006, p.22. (in Ukrainian).
16. Lobzin VYu, Odinak MM, Emelin AYu et al. Osobennosti kognitivnykh narusheniy, progressirovaniya atrofii golovnoho mozga i tserebral'nogo gipometabolizma u bol'nykh-nositeley alleleya e4 gena apolipoproteina Ye [Features of cognitive impairment, progression of cerebral atrophy and cerebral hypometabolism in patients with the e4 allele of the apolipoprotein E gene]. Abstracts of the All-Russian Scientific and Practical Conference "Davidenkov Readings". St. Petersburg: Publishing house "Man and his health". 2014, p.136–7. (in Russian).

ORCID and contributionship:

Sergiy Stadnik: 0000-0002-9987-7069 ^{A-C}

Olena Radchenko: 0000-0003-1108-963X ^{B,D-F}

Orest Komarytsia: 0000-0002-5822-8281 ^{A,C,D}

Iryna Zhakun: 0000-0002-5729-1270 ^{E,F}

Angelica Filipyuk: 0000-0001-6641-0780 ^{E,F}

Nataliya Bek: 0000-0002-5822-1928 ^{E,F}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Sergiy Stadnik

Danylo Halatsky Lviv National Medical University

69 Pekarska st., 79010 Lviv, Ukraine

e-mail: deporss76@gmail.com

Received: 08.07.2022

Accepted: 14.04.2023

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

ORIGINAL ARTICLE

FAMILY INFLUENCE ON THE FORMATION OF CHILDREN'S MOTIVATION FOR A HEALTHY LIFESTYLE

DOI: 10.36740/WLek202306111

Grygoriy P. Griban¹, Olha S. Zablotska², Halyna A. Kolomoiets³, Natalia A. Lyakhova⁴, Iryna M. Nikolaieva², Iryna I. Shpak⁵, Olena V. Lobova⁵

¹ZHYTOMYR IVAN FRANKO STATE UNIVERSITY, ZHYTOMYR, UKRAINE

²ZHYTOMYR MEDICAL INSTITUTE OF ZHYTOMYR REGIONAL COUNCIL, ZHYTOMYR, UKRAINE

³STATE SCIENTIFIC INSTITUTION "INSTITUTE FOR MODERNIZATION OF THE CONTENT OF EDUCATION", KYIV, UKRAINE

⁴POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

⁵KYIV MEDICAL UNIVERSITY, KYIV, UKRAINE

ABSTRACT

The aim: To study the family influence on the formation of children's motivation for a healthy lifestyle.

Materials and methods: The medical and sociological study among parents was conducted to assess their children's adherence to the principles of a healthy lifestyle and the influence of the family on the formation of children's motivation for a healthy lifestyle. The survey was conducted using a specially designed questionnaire using Google Forms. The design of the questionnaire was typical and contained the following structural components: addressing the respondent, obtaining informed consent to participate in the survey, and blocks with targeted questions (25 questions in total). The research involved 150 parents (including 54.7 % (82 people) of women and 45.3 % (68 people) of men).

Methods: bibliosemantic, system-oriented analysis and logical generalization, medical and sociological (questionnaire), statistical data processing.

Results: It has been found that positive attitudes towards a healthy lifestyle prevail in the families of the respondents (44.0 %), 42.0 % of parents indicated that their family members regularly adhere to a healthy lifestyle. Herewith, 48.0 % are interested in teaching their children about a healthy lifestyle. The main motives that most parents form in their children regarding a healthy lifestyle are maintaining and promoting health (38.0 %), improving physical condition (16.0 %), and creating a healthy family (10.0 %). However, almost a third of parents do not instill responsibility for their children's life and health due to a lack of time and knowledge about a healthy lifestyle.

Conclusions: To foster a positive attitude toward a healthy lifestyle in children, parents should set their example, create favorable conditions for a healthy lifestyle, and follow traditions related to active recreation, sensible nutrition, and the absence of bad habits. Children's motivation for a healthy lifestyle is the main responsibility of the family.

KEY WORDS: health, healthy lifestyle, motivation, family, parents, children

Wiad Lek. 2023;76(6):1400-1405

INTRODUCTION

Health is the highest value of every individual and society as a whole. The World Health Organization (WHO) defines "health" as a state of adequate physical, spiritual, and social well-being and not merely as the absence of disease or infirmity. The achievement of this state of well-being depends not only on the influence of factors that directly determine it (heredity, quality of medical care, environmental conditions, etc.) but also on the understanding by the population of different age groups, including children, of the value of their health and the conscious adherence to the principles of a healthy lifestyle [1, 2].

Childhood is the most favorable age for learning certain norms and patterns of behavior, accumulating

the necessary knowledge and skills, understanding needs and motives, and identifying key life priorities. Establishing motivation for a healthy lifestyle involves directing parents' work to form children's conscious positive attitudes toward personal hygiene, morning exercises and motor activity, sensible and balanced nutrition, responsible attitude to their health, etc. [3, 4].

Today, a significant portion of the world's population does not adhere to the principles of a healthy lifestyle, resulting in an increasing percentage of children and youth with bad habits, obesity, physical inactivity, dysfunction, and diseases of organs and body systems. Negative lifestyle patterns are becoming a model for the younger generation, which jeopardizes not only their

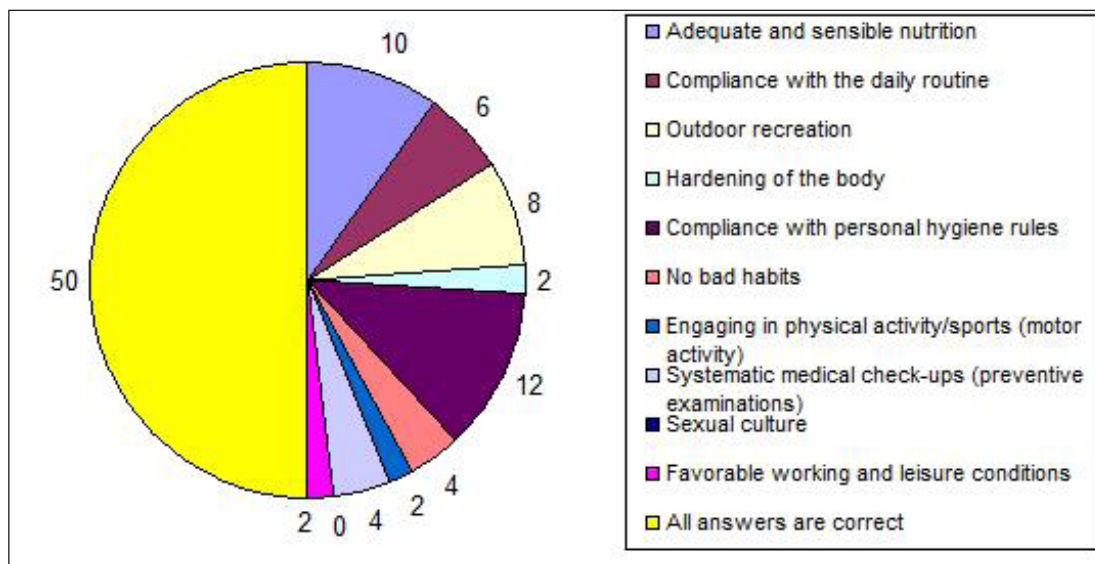


Fig. 1. Distribution of parents' answers about their understanding of the essence and principles of a healthy lifestyle

health but also the health of the world's population as a whole. With this in mind, the role of parents in motivating children to adopt a healthy lifestyle is growing.

THE AIM

The aim is to study the family influence on the formation of children's motivation for a healthy lifestyle.

MATERIALS AND METHODS

The research was conducted in 2020-2022 at Zhytomyr Medical Institute of Zhytomyr Regional Council and Zhytomyr Ivan Franko State University. Methods: bibliosemantic, which included an analytical review of sources of scientific information on the research topic (12 sources from the scientometric databases Index Copernicus, Scopus, PubMed, and others were investigated); system-oriented analysis and logical generalization – to formulate conclusions based on the results of the research; medical and sociological – for questioning parents; statistical processing method – for processing the experimental data obtained in the course of the research.

The research involved 150 parents (including 54.7 % (82 people) of women and 45.3 % (68 people) of men). The medical and sociological study among parents was conducted to assess their children's adherence to the principles of a healthy lifestyle and the influence of the family on the formation of children's motivation for a healthy lifestyle. The survey was conducted using a specially designed questionnaire using Google Forms. The design of the questionnaire was typical and contained the following structural components: addressing the respondent, obtaining informed consent to participate in the survey, and blocks with targeted questions (25

questions in total). The questionnaire was anonymous without any references to the authors of the article in the answers. The results were used for scientific purposes only. Questionnaire was assessed by the experts in this field (2 professors and 4 associate professors) and was approved by the Academic Council of Zhytomyr Ivan Franko State University (Protocol No. 14 dated 26.08.2020). Consent to voluntary participation in the survey was obtained from all the respondents involved in the study. This research followed the regulations of the World Medical Association Declaration of Helsinki – ethical principles for medical research involving human subjects.

RESULTS

Motivation is an incentive to act, a dynamic process of physiological and psychological plan that governs human behavior and determines its organized nature, activity, and stability, the ability of a person to actively meet his or her needs [5]. Scientists [6, 7] identify the following motivational components of a healthy lifestyle and health promotion in children: *at the level of physical health* (striving for physical perfection, attitude to one's own health as the highest social value, physical development, general physical working capacity, body hardening, observance of a rational daily routine, fulfillment of personal hygiene requirements, sensible and balanced nutrition); *at the level of mental health* (development of mental processes, presence of self-regulation, adequate self-esteem, absence of character accentuations and bad habits); *at the level of spiritual health* (coherence of universal and national moral and spiritual values, presence of a positive ideal, diligence, sense of beauty in life, nature, art); *at the level of social well-being* (formed civic responsibility for

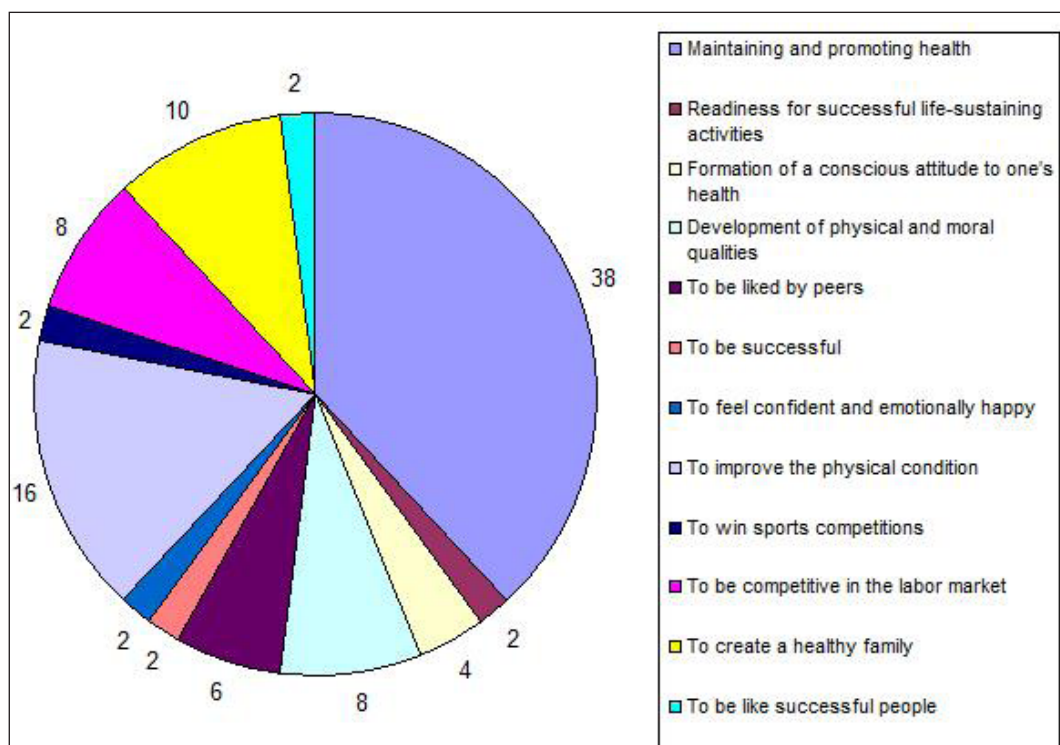


Fig. 2. A healthy lifestyle motives that parents form in their children

the consequences of an unhealthy lifestyle, positively directed communication skills, kindness in attitude to people, ability to self-actualization, self-regulation, and self-education).

The survey revealed that young respondents (25-44 years old) prevailed among the parents surveyed – 76.0 % (114 people); middle-aged parents (44-60 years old) – 24.0 % (36 people); more than half of the respondents (61.4 %) have higher education. The results of parents’ answers to the questionnaire about their knowledge and understanding of the essence and principles of a healthy lifestyle are presented in Fig 1.

These results show that most parents understand the essence of a healthy lifestyle. At the same time, it was found that only 44.0 % of respondents have a positive attitude towards a healthy lifestyle in the family, 36.0 % found it difficult to answer, 14.0 % were neutral, and 6.0 % were negative. Moreover, only 20.0 % of respondents provided an affirmative answer regarding the importance and necessity of adhering to the principles of a healthy lifestyle in the family, the remaining 28.0 % do not see the need for this, 22.0 % say that this issue does not concern them, and 30.0 % said that they found it difficult to provide a specific answer. The majority of respondents (58.7 %) believe that their children need knowledge about a healthy lifestyle. However, only 42.0 % of parents confirmed that they and other family members regularly lead a healthy lifestyle, 40.0 % sometimes lead a healthy lifestyle, and 18.0 % do not follow a healthy lifestyle at all.

When parents were asked what motivates them to follow the principles of a healthy lifestyle, the answers were distributed as follows: 30.0 % of parents believe that a healthy lifestyle helps prevent and eliminate bad habits, 28.0 % want to be a role model for their children, 24.0 % want to maintain and improve their health, 10.0 % want to alleviate existing diseases, and 6.0 % want to prevent diseases. And only 2.0 % of parents said that the main motivation for a healthy lifestyle is their responsibility for their health. Among the motives that parents form in their children to ensure their commitment to a healthy lifestyle, the main ones are maintaining and promoting health – 38.0 %, improving physical condition – 16.0 %, creating a healthy family – 10.0 % and others (Fig 2).

The analysis of parents’ responses to the most effective methods for teaching children to maintain a healthy lifestyle showed that the most effective method is the parents’ example. Among the main elements of their behavior that, according to the respondents, are a model for children’s perception of a healthy lifestyle, are the following: adherence to the rules of balanced and regular nutrition – 42.0 %; systematic exercise – 12.0 %; giving up bad habits – 8.0 %; outdoor recreation – 2.0 % (3 people). Only 10.0 % of parents talk to their children but do not follow the principles of a healthy lifestyle. It is worth noting that 26.0 % do nothing to help their children take responsibility for their health. Based on this, we believe that parents, as role models for their children, should not only be aware of health issues but also directly demonstrate a healthy lifestyle in practice.

It was also found that more than half (52.0 %) of the surveyed parents systematically pay enough attention to promoting their children's health, one-third of the respondents, namely 30.0 %, sometimes take an interest in their children's general condition, and 18.0 % do not devote the necessary time, arguing that they have no time for their children. The results of the survey on the measures parents use to promote their children's health show that the main measures, in their opinion, are: proper nutrition – 36.0 %, outdoor walks – 22.0 %, sports (attending sports clubs, etc.) – 16.0 %. Some respondents prefer to harden children by going to the pool, rubbing, etc. (12.0 %), conducting systematic medical examinations (10.0 %), and using massages as a means of promoting children's health (4.0 %).

It was found that only one-third of respondents (32.0 %) said they regularly do morning exercises with their children, while the other part of respondents said they sometimes or not at all do morning exercises (34.0 % each). The vast majority of respondents (46.0 %) believe that their children need 6-8 hours of sleep for a good night's rest; 42.0 % say 9 hours or more; 12.0 % say less than 6 hours. According to expert recommendations, children aged 6 to 12 should sleep 9 to 12 hours, and adolescents (13-18 years old) should sleep 8 to 10 hours. Therefore, based on these results, we conclude that not all parents are sufficiently informed about the specifics of the recommended sleep duration. It was found that 50.0 % of parents partially adhere to the balance and regularity of nutrition in the family; 20.0 % do not adhere to these principles and only 30.0 % claim to adhere to good nutritional behavior. At the same time, 57.3 % of respondents emphasized that there are no overweight or obesigenic relatives in their families; 42.7 % said that there are overweight and obese people in their families.

It is known that the types of activities children do in their free time also have a certain impact on their health. Thus, it was found that 30.0 % of children spend most of their free time playing games on their phones or computers, 22.0 % communicate on social media, 28.0 % go in for sports, 10.0 % relax outdoors, 6.0 % watch movies, and 4.0 % read books. Thus, most children spend their free time without benefit to their health.

It was found that 52.0 % of respondents' families have no bad habits. However, 36.0 % reported smoking in the family, and 12.0 % reported drinking alcohol. There must be no cases of drug use in the families of the surveyed respondents. At the same time, only 20.0 % of respondents would like to get rid of bad habits, 4.0 % did not express such a desire, 24.0 % said they were indifferent, and 52.0 % repeatedly confirmed the absence of bad habits in their families.

Among the reasons for parents' lack of attention to their children's health, the main reason is lack of time due to high professional workload (48.0 %). Other reasons include lack of knowledge and skills (22.0 %). Only one-third (30.0 %) of parents surveyed said they spend enough time on their children's health. It is worth noting that none of the parents surveyed indicated that they were not interested in their children's health.

DISCUSSION

The analytical review of scientific sources [8, 9] shows that health as a multidimensional phenomenon integrates various aspects – physical, mental, spiritual, and social. Scientists believe that a healthy lifestyle integrates the relationship between lifestyle and human health, and combines all the conditions that ensure the normal functioning of a person in professional, social, and domestic spheres. A healthy lifestyle expresses a person's attitude and guidelines for the development and improvement of individual and public health.

According to scientists [10, 11], among all periods, childhood is the most favorable for the formation of healthy lifestyle principles, because it is at this age that a child becomes aware of his or her "Ego". The task of parents is not to overload the child with a stream of ready-made information but to provide an opportunity to reflect and listen to their bodies. Only under such conditions can the acquired knowledge about a healthy lifestyle be used by children in various unexpected situations and transformed into their skills in real life. In middle preschool age, children form an idea of health as "not a disease" (they show a negative attitude to illness based on their experience). Nevertheless, children do not realize what it means to be healthy and feel healthy. As a result, an attitude towards health is formed as something abstract. In children's understanding, being healthy means not getting sick. That is, in middle preschool age, children begin to realize threats to their health from the external environment, as well as in their actions [12].

According to studies of the age dynamics of the importance of health and a healthy lifestyle, their priority role is most often noted among representatives of the older generation. The hierarchy of children's values is dominated by games and communication with peers, i. e. children's understanding of the role of physical, mental, and social health and the appropriate lifestyle is still in its infancy [3].

Fostering the need for a healthy lifestyle in children should be accompanied by the acquisition of a set of necessary skills and habits of caring for themselves, their bodies, and caring for others, in a special inter-

nal state associated with a sense of satisfaction and comfort. Experts recommend that parents make a list of healthy lifestyle skills that they are guaranteed to be able to instill in their children. At the same time, it is necessary to analyze existing habits, both good and bad, and help eliminate them. It is necessary to take into account the best family experience in the process of developing healthy lifestyle skills in children. The family should have a "fashion" for health among parents and all family members. When forming a child's motivation for a healthy lifestyle, the family should be guided by the algorithm referred to as "from habit to need, from the need to a healthy lifestyle".

CONCLUSIONS

Adherence to a healthy lifestyle is a pressing issue today. The quality of health directly depends on many factors, including a person's healthy lifestyle and motivation. Motivating children to adopt a healthy lifestyle and making them responsible for their health is the main obligation of the family.

As a result of a sociological study among parents, we found that even though 50.0 % of respondents understand the essence of a healthy lifestyle, only 20.0 % of respondents consider it necessary to form the motivation for it. For the most part, positive attitudes towards a healthy lifestyle prevail in the families of the respondents (44.0 %), 42.0 % of parents indicated that their family members regularly adhere to a healthy lifestyle. Herewith, 48.0 % are interested in teaching children about a healthy lifestyle. However, in our opinion, these figures are insufficient and indicate that a

healthy lifestyle in a family is secondary to other factors that affect health.

It is worth noting that parents, in addition to the motives for a healthy lifestyle, such as preventing or getting rid of bad habits, and maintaining and promoting their health, said that they intend to be role models for their children. Based on the latter statement, the main motives that most parents form in their children regarding a healthy lifestyle are maintaining and promoting health (38.0 %), improving physical condition (16.0 %), and creating a healthy family (10.0 %). However, almost a third of parents do not instill responsibility for their children's life and health. The lack of time and insufficient attention to children's health, according to parents, is caused by professional workload and lack of knowledge about a healthy lifestyle. These factors confirm that parents are interested in the health of their children, but for the reasons mentioned above, they cannot devote sufficient time to it. We believe that parents are role models for their children, and therefore they should not only be aware of health issues but also directly adhere to a healthy lifestyle.

Thus, fostering children's motivation for a healthy lifestyle requires considerable effort and willingness on the part of parents. To foster a positive attitude towards a healthy lifestyle in children, parents should set their example, create receptive conditions for a healthy lifestyle, follow traditions related to active recreation, exercise, practicing a healthy diet, avoiding bad habits, and involving all family members in a healthy lifestyle.

Prospects for further research are aimed at studying the motivation of children and adolescents to follow healthy lifestyle rules.

REFERENCES

1. Mukdad L, Shapiro NL. Establishing Healthy Lifestyle Choices Early: How to Counsel Children and Their Parents. *Otolaryngol Clin North Am.* 2022;55(5):1111-1124. doi:10.1016/j.otc.2022.06.013.
2. Pantiuk TI, Pantiuk MP, Kvas OV et al. Healthy lifestyle principles formation of children aged 6-7. *Wiad Lek.* 2021;74(10 pt 1):2477-2481.
3. Marconcin P, Matos MG, Ihle A et al. Trends of Healthy Lifestyles Among Adolescents: An Analysis of More Than Half a Million Participants From 32 Countries Between 2006 and 2014. *Front Pediatr.* 2021;9:645074. doi:10.3389/fped.2021.645074.
4. Münzel T, Münzel H, Geipel P et al. Educating Children for a Healthy Lifestyle. *Eur Heart J.* 2019;40(25):2000-2003. doi:10.1093/eurheartj/ehz419.
5. Maximova K, Ambler KA, Rudko JN et al. Ready, set, go! Motivation and lifestyle habits in parents of children referred for obesity management. *Pediatr Obes.* 2015;10(5):353-360. doi:10.1111/ijpo.272.
6. Martin A, Booth JN, Laird Y et al. Physical activity, diet and other behavioural interventions for improving cognition and school achievement in children and adolescents with obesity or overweight. *Cochrane Database Syst Rev.* 2018;3(3):CD009728. doi:10.1002/14651858.CD009728.pub4.
7. Zhelanov DV, Palamar BI, Gruzieva TS et al. Value-motivational component of a healthy lifestyle of modern university students: the real state and logic of formation. *Wiad Lek.* 2021;74(5):1079-1085.
8. Weil AR. Children's Health. *Health Aff (Millwood).* 2020;39(10):1663. doi:10.1377/hlthaff.2020.01647.
9. Leffers JM. Climate Change and Health of Children: Our Borrowed Future. *J Pediatr Health Care.* 2022;36(1):12-19. doi:10.1016/j.pedhc.2021.09.002.

10. Richards D, Caldwell PH, Go H. Impact of social media on the health of children and young people. *J Paediatr Child Health*. 2015;51(12):1152-1157. doi:10.1111/jpc.13023.
11. Grey EB, Atkinson L, Chater A et al. A systematic review of the evidence on the effect of parental communication about health and health behaviours on children's health and wellbeing. *Prev Med*. 2022;159:107043. doi:10.1016/j.ypmed.2022.107043.
12. Skouteris H, Hill B, McCabe M et al. A parent-based intervention to promote healthy eating and active behaviours in pre-school children: evaluation of the MEND 2-4 randomized controlled trial. *Pediatr Obes*. 2016;11(1):4-10. doi:10.1111/ijpo.12011.

The study was carried out according to the plan of the research work of Zhytomyr Ivan Franko State University for 2014-2024 on the theme of "Theoretical and methodological bases of improving the educational process of physical education at higher educational institutions" (state registration number 0114U003978).

ORCID and contributionship:

Grygoriy P. Griban: 0000-0002-9049-1485^A

Olha S. Zablotska: 0000-0002-0850-5754^B

Halyna A. Kolomoiets: 0000-0002-4315-3977^D

Natalia A. Lyakhova: 0000-0003-0503-9935^E

Iryna M. Nikolaieva: 0000-0002-6866-7587^B

Iryna I. Shpak: 0009-0008-2304-7756^C

Olena V. Lobova: 0000-0003-4252-8690^F

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR**Grygoriy P. Griban**

Zhytomyr Ivan Franko State University

40 Velyka Berdychivska st., 10002 Zhytomyr, Ukraine

tel: +380973341092

e-mail: gribang@ukr.net

Received: 19.12.2022

Accepted: 22.05.2023

A - Work concept and design, **B** - Data collection and analysis, **C** - Responsibility for statistical analysis, **D** - Writing the article, **E** - Critical review, **F** - Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

ORIGINAL ARTICLE

BRONCHIECTASIS IN ADULT PATIENTS: CLINICAL PECULIARITIES AND APPROACHES TO THE TREATMENT

DOI: 10.36740/WLek202306112

Viktoriia Rudnyk, Nataliia Chaplynska, Liubov Skrypnyk

IVANO-FRANKIVSK NATIONAL MEDICAL UNIVERSITY, IVANO-FRANKIVSK, UKRAINE

ABSTRACT

The aim: To perform a clinical analysis of bronchiectasis in adults, to analyze the effectiveness of nebulizer therapy with hypertonic NaCl solution with hyaluronic acid

Materials and methods: All patients were performed clinical-functional examination (MRC dyspnea index, Sp O₂, 6-minute walking test, external respiration function); calculated the index BODE, analyzed the SGRQ, studied the results of sputum. Statistical data analysis was performed using the Microsoft Excel for Microsoft 365 MSO 16.0.13530.2040418 package of statistical functions.

Results: The main symptom in 100% of cases was chronic cough with production of sputum. Patients were concerned about shortness of breath (91.7%), episodic hemoptysis (29.2%), systemic symptoms (fatigue, weight loss). Hypertonic NaCl solution has a direct mucolytic effect, osmotic and anti-edematous effect. Protection of the mucous membrane of the respiratory tract makes hyaluronic acid an ideal additional component of hypertonic saline solution. All patients showed a positive effect of treatment immediately. After 2 weeks, the respiratory rate decreased, the FEV₁ index increased at 8.6 (p<0.05), SpO₂ increased up to 93.75 ± 7.13%, the number of points according to the SGRQ decreased, BODE index also decreased

Conclusions: Leading clinical signs of bronchiectasis were: a chronic cough with daily sputum production (100% of patients), shortness of breath (91.7%). The use of nebulizer inhalations decreased shortness of breath at 17.6% (p<0.05), improved external respiratory function indices (FVCL increased at 9.7% (p<0.01), FEV₁ at 8.6% (p<0.01)) and blood oxygen saturation increased at 4.9% (p<0.05)). The offered complex increased tolerance to physical exertion (the 6-minute walk test and 4-year survival (BODE prognostic index)

KEY WORDS: treatment, bronchiectasis, nebulizer inhalations

Wiad Lek. 2023;76(6):1406-1412

INTRODUCTION

Bronchiectasis (BE) – is an acquired or congenital, segmental pathological enlargement of the bronchial lumens with changes in the anatomical structure of the bronchial wall due to destruction and/or disruption of neuromuscular tone due to inflammation, fibrosis and hypoplasia of the structural elements of the bronchi [1]. Bronchiectasis has a variety of etiologies. It can be idiopathic (in 35-57% of cases), and can be secondary to many diseases (allergic bronchopulmonary aspergillosis, cystic fibrosis, mycobacterial infection, immunodeficiency, chronic obstructive pulmonary disease, bronchial asthma, etc.). However, the most common factor is a respiratory infection [1, 2].

At present, there are no accurate world data on the epidemiology of bronchiectasis, and it is difficult to talk about the prevalence of bronchiectasis not associated with cystic fibrosis. It is known that with the advent of the era of antibiotic therapy, the frequency of their prevalence in the population has decreased. According

to the results of epidemiological study performed in the United States, the prevalence of bronchiectasis is approximately 4 per 100,000 young adults and 272 per 100,000 patients older than 75 years. There is an increase in the number of patients with bronchiectasis caused by non-tuberculous mycobacteriosis with lung damage [3, 4].

Clinical symptoms of the disease are usually characterized by a picture of chronic infectious inflammation of the respiratory tract, which has a wavy course with periodic exacerbations [2]. The degree of severity of the disease and the frequency of its exacerbations significantly affect the duration and quality of life of the patient. The quality of life of a patient with BE is comparable to the quality of life in severe chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis and other debilitating lung diseases. More than 70% of patients complain of daily cough with sputum in greater or lesser quantities, shortness of breath. In some cases, the disease is asymptomatic. Despite treatment,

about 50% of patients note that they had one or more exacerbations during the year, and every third patient with exacerbation requires hospitalization [4]. Complications of bronchiectasis include hemoptysis and persistent bronchial-obstructive disorders. Secondary amyloidosis and septic emboli in patients with bronchiectasis described in the past are very rare today [2, 5].

To date, the European and US regulators have not registered any medicine for the treatment of BE. Treatment is performed by analogy with that of cystic fibrosis, but research data and clinical experience suggest that the effectiveness of therapy is different and some special recommendations are needed for the management of patients with BE which is not caused by cystic fibrosis [3].

THE AIM

The aim of the study was to perform a clinical analysis of cases of bronchiectasis in adults and evaluate the effectiveness of nebulizer therapy with hypertonic NaCl solution in combination with hyaluronic acid.

MATERIALS AND METHODS

There was performed a prospective study. There were examined 24 patients with bronchiectasis who were treated at the Pulmonology Department № 1 of the UNPE "Regional Clinical Phthysiology-Pulmonology Center (Pulmonary Diseases Center)" in 2018-2019. The average age of patients was 47.23 ± 4.18 years.

The diagnosis was confirmed by computed tomography. All patients were performed clinical-functional examination, namely: determination of dyspnea index according to MRC [6], measurement of blood oxygen saturation SpO_2 , 6-minute test-walk [7], study of external respiration by spirometry, calculation of the prognostic index BODE [8], analysis of the SGRQ questionnaire [9], study of the results of a microbiological analysis of sputum.

The complex of treatment in addition to broad-spectrum antibacterial medicines (selected according to the results of antibioticogram of the sputum), bronchodila-

tors, anti-inflammatory agents, includes inhalation with a nebulizer of hypertonic sodium chloride solution in combination with hyaluronic acid (medicine containing 30 mg sodium chloride and 1 mg of sodium hyaluronate in 1 ml at a dose of 4 ml twice a day for 2 weeks). To assess the effectiveness of this treatment approach, patients were divided into 2 groups: Group I (n=12) – received traditional treatment, Group II (n=12) – additional inhalations of 3% NaCl solution in combination with sodium hyaluronate twice a day for 14 days.

Statistical data analysis was performed using the Microsoft Excel for Microsoft 365 MSO 16.0.13530.2040418 package of statistical functions. License ID: EWW_58c-c64b2-cc32-48b6-bd4b-cce379e20247_574357c00167ce3139. Session ID: F1221D8E-124A-49E5-892D-OBDA291BF859.

RESULTS

The presence of bronchiectasis in our examined adult patients in 11 (54.2%) cases was associated with frequent respiratory infections in childhood, which ran as bronchitis (45.5%), pneumonia (36.4%), measles (9.1%), whooping cough (9.1%). In adulthood, the main clinical symptom in 100% of cases was chronic cough with daily production of sputum. In addition, patients were concerned about shortness of breath (91.7%), episodic hemoptysis (29.2%), systemic symptoms (fatigue, weight loss). An objective picture was also characteristic: deformation of fingers in the form of "drumsticks" (41.7%), barrel-shaped chest (58.3%), auscultatory manifestations in the form of foci of tiny- or medium-bubbling wet rales over certain areas of lungs (mostly lower lobes) in all studied patients. In all patients, the diagnosis was confirmed by spiral computed tomography of the chest. There are some examples of these examinations of two of our patients in Fig. 1 and Fig. 2.

Indications for nebulizer therapy with hypertonic sodium chloride solution in combination with hyaluronic acid were: poor coughing of thick sputum against the background of oral and injectable use of various mu-

Table I. Study of the life quality according to SGRQ during the treatment of patients with bronchiectasis

Index	Group I		Group II	
	Before treatment	After treatment	Before treatment	After treatment
Symptoms	77.35±4.16	55.12±3.24 *	78.39±5.05	47.86±3.27 **
Activity	55.35±3.91	25.23±2.05 *	53.88±3.95	21.13±2.15 **
Influence	34.17±3.18	22.14±2.05 *	33.71±3.15	20.41±2.01*
General	52.58±3.77	39.68±3.07 *	53.43±3.75	34.24±3.07

Note: Significance of differences before and after treatment * $p < 0.01$

$p < 0.01$ – indices of groups I and II after treatment

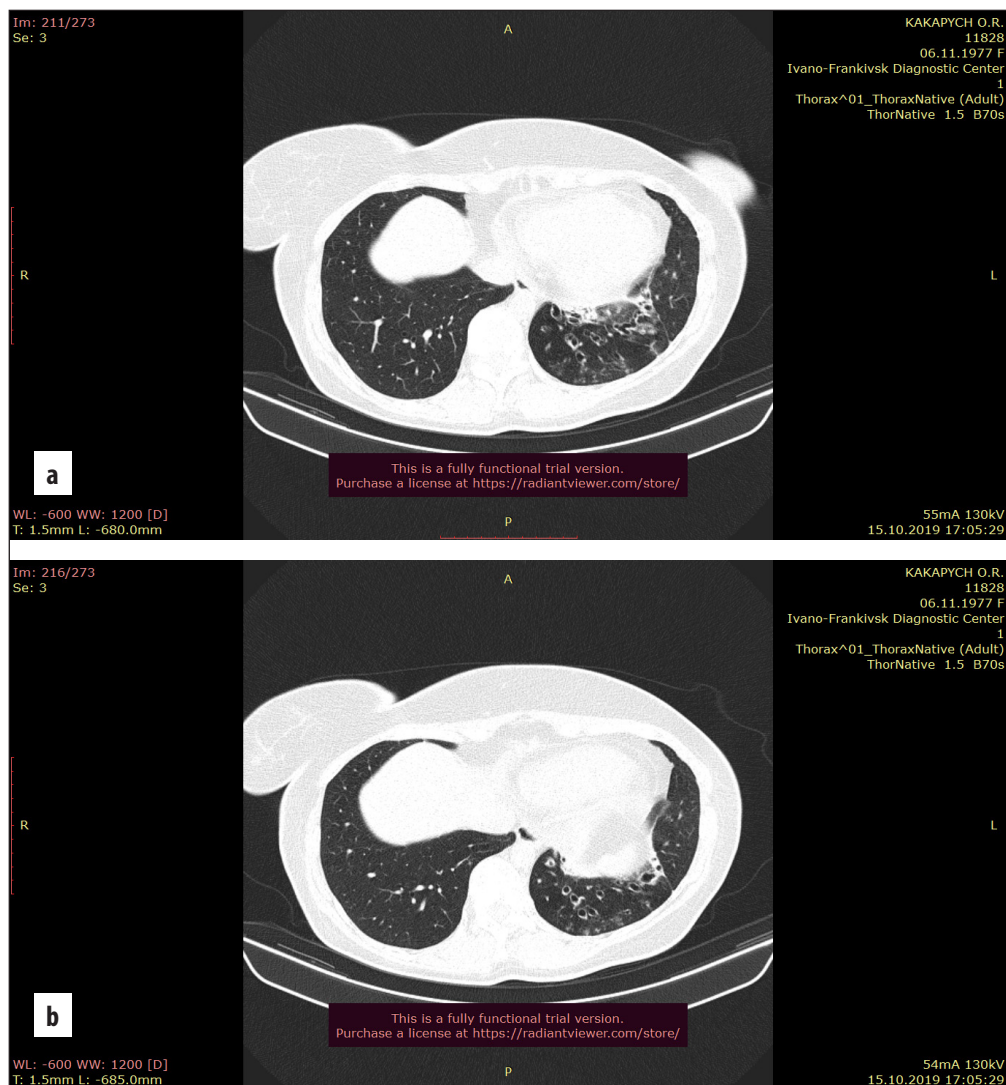


Fig. 1 (a, b). Spiral computed tomography of the chest organs of patient K., born in 1977, with bronchiectasis in the lower lobe of the left lung

coactive drugs. Hypertonic NaCl solution has a direct mucolytic effect, osmotic and anti-edematous effect, is able to change the viscosity of sputum, moisturize and cleanse the mucous membrane, improves epithelial function of airways, has anti-inflammatory and antibacterial properties, affects the formation of biofilms [10].

The second component of the medication is hyaluronic acid in the form of sodium hyaluronate, having a chemical structure, molecular weight and rheological properties similar to mucin – a component of bronchial mucus. Due to its water-binding properties, hyaluronic acid moisturizes the bronchial mucosa without impairing mucociliary transport. It has an anti-adhesive effect, inhibits the production of pro-inflammatory mediators, improves mucociliary clearance, participates in the repair and regeneration of the ciliated epithelium, increases local immunity, has an antioxidant effect. Protection of the mucous membrane of the respiratory tract from the irritating effect of salt in high concentrations, as well as moisturizing properties make hyaluronic acid an ideal additional component of hypertonic saline

solution [10, 11].

All patients in group II had a positive effect of treatment in the first few days, when the cough became more productive and the sputum became less thick and viscous. They noted an improvement in external respiratory function, namely an increase in VLC and FEV1. When comparing the effectiveness of traditional treatment with therapy with the inclusion of inhalations of hypertonic NaCl/sodium hyaluronate solution, a tendency to a more positive effect of this medicine on the above-mentioned indices (Fig. 3 A and B). After 2 weeks, shortness of breath significantly decreased, the rate of forced VLC increased at 9.7% ($p < 0.01$), FEV1 – at 8.6% ($p < 0.01$), SpO2 increased from $89.13 \pm 1.29\%$ up to $93.75 \pm 1.02\%$ ($p < 0.05$).

With the help of the questionnaire of St. George (SGRQ) the quality of life of patients with bronchiectasis was determined (Table I). The addition of nebulizer therapy with hypertonic sodium chloride solution in combination with hyaluronic acid was found to reduce scores in sections of the questionnaire such as symp-

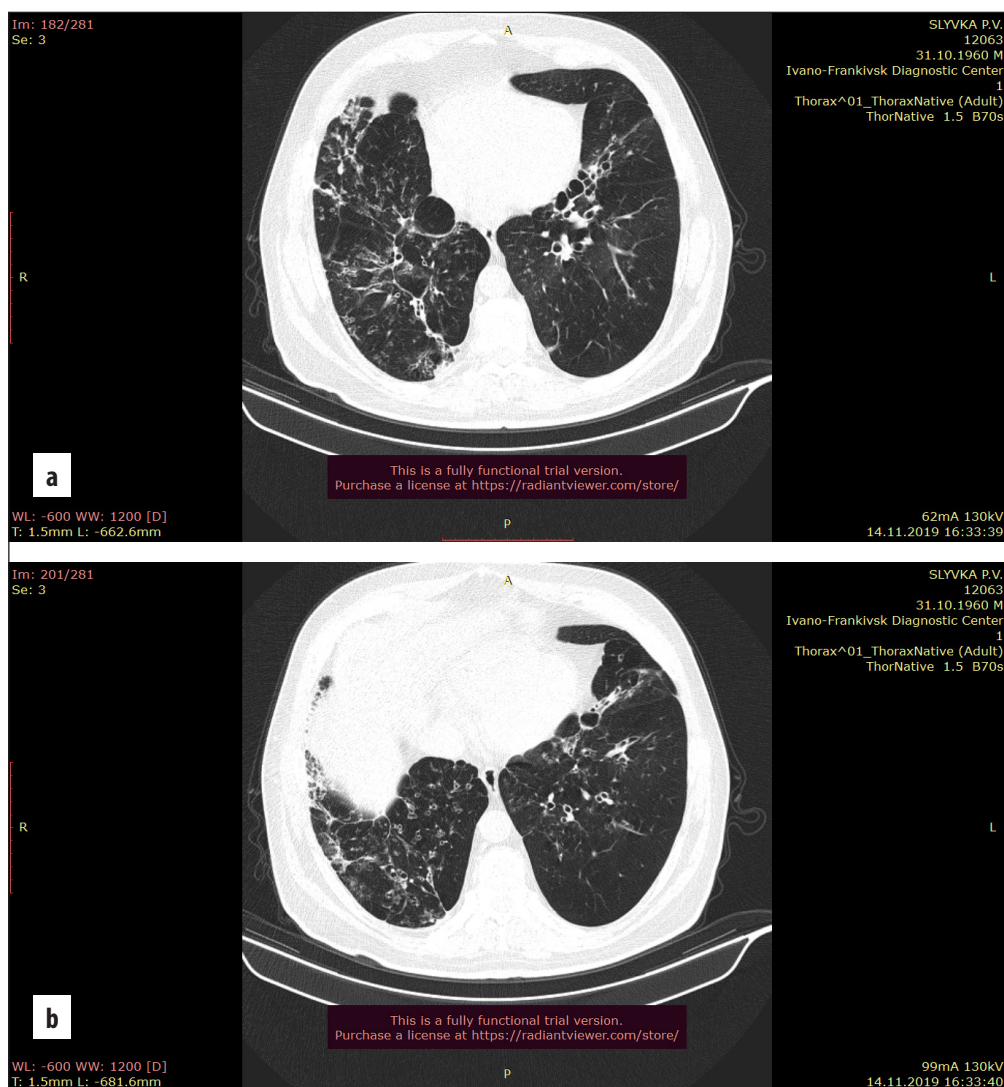


Fig. 2 (a, b). Spiral computed tomography of the chest organs of patient S., born in 1960, with bronchiectasis in both lungs

toms and physical activity. And this, in turn, indicates a decrease of manifestations of social and physical maladaptation in patients.

Assessment of exercise tolerance was performed by measuring the distance in a 6-minute walking test. In general, in patients of group II against the background of treatment with the inclusion of inhalation of 3% NaCl/sodium hyaluronate the distance has increased from 357.24 ± 6.27 m up to 391.81 ± 9.27 m ($p < 0.01$), an increase in walking distance was 34.57 m and was at 15.59 m higher ($p < 0.05$) than in the first group of patients.

BODE-index (BMI), Obstruction (FEV1), Dyspnea (Shortness of breath according to Modified Medical Research Council (MMRC)), Exercise (exercise tolerance in a 6-minute walking test) were calculated to determine individual risk of death or hospitalization. Among patients of group II of our study after the offered treatment, two (16.7%) scored 2.08 ± 0.67 points and moved from the rubric "3-4 points" to the rubric "1-2 points", which means an increase in approximate 4-year survival from 67% up to 80%.

DISCUSSION

The basis of conservative treatment of patients with bronchiectasis is effective sanitation of the tracheo-bronchial tree, which includes endoscopic methods in combination with rational antibiotic therapy and mucoactive therapy [1, 2, 5]. Actually, we've focused our attention on the last position and performed the study. After all, improvement of the evacuation of sputum plays one of the key roles in the management of patients with bronchiectasis. This is achieved with the help of physical methods (manual techniques, postural drainage, etc.) and medicinal means, in particular hypertonic sodium chloride solution. This agent, applied with the help of a nebulizer, contributes to the improvement of rheological properties and the evacuation of bronchial mucus due to several mechanisms, including the rehydration of mucus due to the increased osmosis of water under the influence of ions contained in the solution. These effects also help reduce the viscosity of bronchial mucus [3].

However, inhalation of only saline solution can induce the cough, chest tightness, bronchospasm, throat irri-

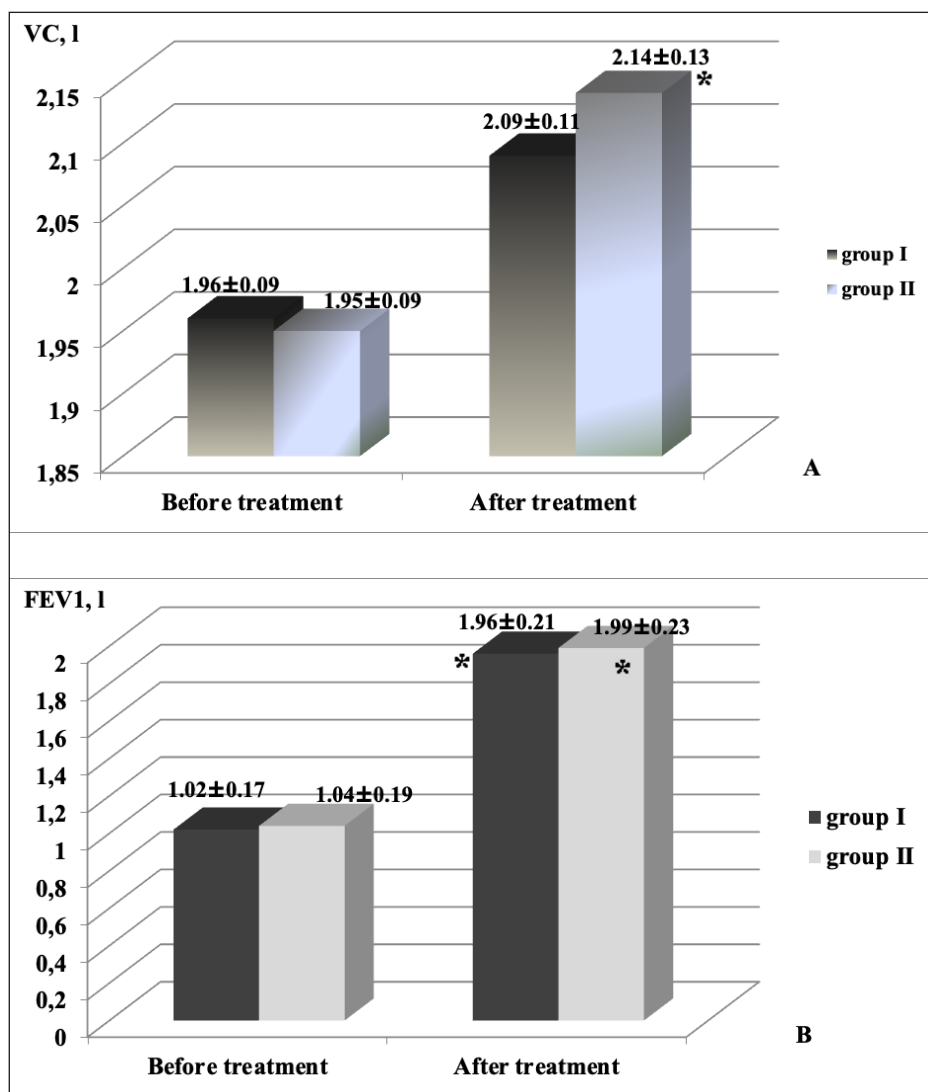


Fig. 3. Dynamics of spirometric indices of VC (A) and FEV1 (B) during the treatment of patients with bronchiectasis
 Note: reliability of the differences between and before treatment * p<0.01

tation, and a salty taste in the mouth in the patient. It was possible to solve this problem by supplementing the product with hyaluronic acid [3, 4].

Hyaluronic acid (HA, sodium hyaluronate) – is a hydrophilic mucopolysaccharide, chemically classified as a non-sulfonated glycosaminoglycan. HA is in every cell of the human body. Its highest concentration occurs in connective, epithelial and nervous tissues. HA is one of the main components of the extracellular matrix contained in many biological fluids (saliva, synovial fluid, etc.). It takes an active part in the proliferation and migration of cells. In the intercellular space, it binds liquid molecules, giving them a gel-like consistency. Since HA is a hydrophilic element, many people call it a “natural moisturizer” [10]. Due to hyaluronic acid, the activity of the inflammatory process in the mucous membrane of the respiratory tract decreases. At the same time, its swelling decreases and hydration occurs, which contributes to recovery. In addition, under the influence of HA, the rheological properties of sputum improve

(mucolytic action) and at the same time, mucociliary clearance (mucokinetic action) is restored, facilitating the evacuation of sputum from the respiratory tract, the restoration of bronchial patency, and the elimination of symptoms of bronchial obstruction. HA also reduces the unpleasant taste of hypertonic solution [11].

The above-mentioned effects of the combined nebulizer therapy using a hypertonic solution of NaCl/hyaluronic acid are confirmed by the results of our study. This is evidenced by the improvement of the function of external breathing and the reduction of the manifestations of broncho-obstruction according to the results of spirometry of patients having received the offered treatment scheme. In addition, they noted an increase in tolerance to physical exertion, a decrease in the manifestations of social and physical maladaptation, and an improvement in quality of life indices. The results of the study suggest a better prognostic survival in patients with bronchiectasis having received the offered treatment.

CONCLUSIONS

1. The leading clinical signs of bronchiectasis in adult patients were: a chronic cough with daily sputum production (100% of patients), shortness of breath (91.7%) and an auscultatory picture in the form of foci of tiny- or medium-vesicular moist rales over certain areas of the lungs (mainly the lower lobes) (100% of people).
2. The use of nebulizer inhalations of a hypertonic solution of sodium chloride in combination with hyaluronic acid in cases of impaired secretion and expectoration contributed to a decrease of disease symptoms, namely – shortness of breath at 17.6% ($p < 0.05$). The external respiratory function indices (FVCL increased at 9.7% ($p < 0.01$), FEV1 – at 8.6% ($p < 0.01$)) and blood oxygen saturation (SpO₂ increased at 4.9% ($p < 0.05$)) have improved.
3. According to the St. George questionnaire (SGRQ), it was found that the addition of nebulizer therapy with a hypertonic solution of sodium chloride in combination with hyaluronic acid to the treatment complex has improved the quality of life of such patients. This was reflected in a decrease in the number of points in such sections of the questionnaire as disease symptoms (at 38.9% ($p < 0.01$)) and physical activity (at 60.8% ($p < 0.01$)). And this, in turn, indicates a decrease in patients' manifestations of social and physical maladaptation.

4. The offered treatment complex contributed to an increase in tolerance to the physical exertion, as the distance of the 6-minute walk test has increased at 9.7% ($p < 0.01$) and 4-year survival at 13% ($p < 0.05$) according to the BODE prognostic index.

In the management of patients with bronchiectasis, the important components are early diagnosis of the disease and proper treatment, the directions of which are the prevention or treatment of bacterial infections, improvement of mucociliary clearance, effective sanitation of the respiratory tract.

PROSPECTS FOR FURTHER RESEARCH

Bronchiectasis has not been given due attention for a long time. To date, there are no international guidelines for the treatment of bronchiectasis in adult patients other than cystic fibrosis. However, the economic burden of this pathology can be compared with that of COPD and it increases with the increasing severity of the disease, increasing number of hospitalizations, increasing necessity for intensive care. Therefore, thorough research in this section of pulmonology is promising, in particular the study of therapeutic approaches and rehabilitation programs that would affect the chronic inflammatory process in the bronchi, would reduce the frequency of exacerbations and hospitalizations, improve the patients' quality of life.

REFERENCES

1. Anaev EKh. Modern approaches to the treatment of bronchiectasis in adults. *Practical pulmonology*. 2017; 4: 30-38.
2. National clinical guidelines. Suppurative lung diseases. <http://ksgs.mz.mosreg.ru/sites/default/files/doc/thoracic-surgeon-kr004.pdf>. [date access 15.12.2022].
3. Zaitsev AA, Sinopalnikov AI. Management of adult patients with bronchiectasis (based on the recommendations of the European Respiratory Society). *Practical pulmonology*. 2018; 4: 36-54.
4. Terpigorev SA. Bronchiectasis in clinical practice: current state of the problem. *Practical pulmonology*. 2017; 4: 28-39.
5. European Respiratory Society guidelines for the management of adult bronchiectasis. *European Respiratory Journal*. 2017; 50: 1700629. doi: 10.1183/13993003.00629-2017.
6. MRC Dyspnoea scale/MRC Breathlessness scale. <https://mrc.ukri.org/research/facilities-and-resources-for-researchers/mrc-scales/mrc-dyspnoea-scale-mrc-breathlessness-scale/#definition>. [date access 15.12.2022].
7. 6-min test – ATS Statement Guidelines for the Six-Minute Walk Test. <https://www.atsjournals.org/doi/10.1164/ajrccm.166.1.at1102>. [date access 15.12.2022].
8. Mosenifar Z. What is the BODE index, and how is used to estimate the prognosis of chronic obstructive pulmonary disease (COPD)? <https://www.medscape.com/answers/297664-7357/what-is-the-bode-index-and-how-is-used-to-estimate-the-prognosis-of-chronic-obstructive-pulmonary-disease-copd>. [date access 15.12.2022].
9. St. George's Respiratory Questionnaire (SGRQ). [<https://www.thoracic.org/members/assemblies/assemblies/srn/questionnaires/sgrq.php>]. [date access 15.12.2022].
10. Kovalenko SV. The use of Lorde Hyper solution in nebulizer therapy of patients with pulmonary profile. *Health of Ukraine of the 21st century*. 2016; 22 (395): 54-55.
11. Seliuk MM. Respiratory tract infections: treatment in the light of modern views. <http://www.health-medix.com/articles/mistetzvo/2019-07-11/5.pdf> [date access 15.12.2022].

ORCID and contributionship:

Viktoriia Rudnyk: 0000-0003-2582-8544^{B-F}

Nataliia Chaplynska: 0000-0002-5008-7453^{A-F}

Liubov Skrypnyk: 0000-0001-5630-2778^{B-F}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Viktoriia Rudnyk

Ivano-Frankivsk National Medical University
2 Halytska st., 76000 Ivano-Frankivsk, Ukraine
e-mail: nata.dubina.74@gmail.com

Received: 22.05.2022

Accepted: 14.04.2023

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

CAUSES OF ANXIETY DURING PLAY AS A FACTOR OF NEGATIVE IMPACT ON THE HEALTH OF PRESCHOOL AND SCHOOL CHILDREN

DOI: 10.36740/WLek202306113

Tetiana Miyer¹, Anna Klim-Klimaszewska², Svitlana Palamar¹, Olga Kotenko¹, Hennadii Bondarenko¹,
Liudmyla Nezhyva¹, Yurii Savchenko¹

¹BORYS GRINCHENKO KYIV UNIVERSITY, KYIV, UKRAINE

²HUMAN SIEDLCE UNIVERSITY OF NATURAL SCIENCES, SIEDLCE, POLAND

ABSTRACT

The aim: Generalization of the results of research by various scientists in the context of anxiety as a stable personality trait, determining the list of causes of anxiety during play in children of preschool and school age.

Materials and methods: The research was conducted within the framework of the agreement for international cooperation between Borys Grinchenko Kyiv University and University of Natural Sciences and Humanities in Siedlce. 400 people took part in the research from the Ukrainian side, 125 people from the Polish side, a total of 525 people. Of them: 130 (100/30) preschool children, 132 (105/27) primary school children, 130 (96/34) adolescents and 133 (99/34) young people.

The methodologies "CMAS Explicit Anxiety Scale" (adapted by A. Prihozhan) and "Personal Anxiety Scale" (A. Prihozhan) were used to achieve the stated goal of the research.

Results: Play as a social phenomenon has a positive impact on the health of preschool and school children. The positive impact is in identifying and resolving emotional and social issues. Negative effects on the health of preschool and school-age children have also been identified. This is the formation of anxiety as a stable personality trait. Three blocks of causes of anxiety in children of preschool and school age have been identified. The first block of reasons concerns the low level of organization of preparation for the game. The second block includes the reasons that are a consequence of the low level of the game process. Subjective experience of participation of children of preschool and school age in the game is reflected in the third block of reasons "Negative subjective result of the game".

Conclusions: The article summarizes scientific data on the need to take into account during play the levels of activity of preschool and school age children, their individual psychophysiological capabilities and the existing situational and personal anxiety. Also, three blocks of causes of anxiety during the game were identified (block I – during the preparation of the game; block II – during the game; block III – getting a negative subjective result in the game).

KEY WORDS: preparation for the game, participation in the game, negative subjective result of participation in the game

Wiad Lek. 2023;76(6):1413-1421

INTRODUCTION

A sign of modernity is the impact on a person of changing information flow, global and regional socio-economic transformations, manifestations of growing instability, changes in lifestyle and rhythm. These and other signs of modernity cause anxiety in people of all ages. On the one hand, any unknown situation that is perceived as dangerous, causes person negative feelings (anxiety, fear, panic). These negative feelings are a form of internal psychological tension and a factor that causes the formation of neurotic states or exacerbates existing ones. On the other hand, any serious ordeal pushes a person to rethink their life, their values, discover new abilities and talents, rethink the meaning of their existence, a sharp change in attitude

to themselves and the world, and change the direction of life. The described manifestations characterize human development in modern conditions. Of course, the negative impact of modern signs on the psyche of a child of preschool and school age is somewhat offset by the process of its gradual socialization. At the same time, the process of gradual socialization of the child is permeated with situations that cause the formation of the child's various personality traits, including anxiety.

The described manifestations characterize human development in modern conditions. Of course, the negative impact of modern signs on the psyche of a child of preschool and school age is somewhat offset by the process of its gradual socialization. At the same time, the process of gradual socialization of the child

is permeated by various situations. These situations cause the formation of various personality traits in the child, including anxiety. The described manifestations characterize human development in modern conditions. Of course, the negative impact of modern signs on the psyche of a child of preschool and school age is somewhat offset by the process of its gradual socialization. However, different situations permeate the process of gradual socialization. These situations cause the formation of the child's various personality traits, including anxiety.

Anxiety is the experience of emotional discomfort associated with anticipation of trouble, with a sense of danger. H. Miklyaeva [1] referred to the term "anxiety level" as a person's tendency to perceive most life situations as threatening, as well as individual sensitivity to stress. Taking into account the level of anxiety A. Prihozhan [2] analyze anxiety as a factor that can help mobilize mental reserves, stimulate search activity, and as a factor that outside the optimal values of anxiety negatively affect the child's behavior and activities.

Researchers have linked anxiety to various processes. According to L. Bozhovych [3], anxiety arises as a result of negative emotional experience, low self-esteem of their capabilities. A. Prihozhan [2] see the emergence of anxiety in the deepening of negative emotional experiences and in experiencing situations that may threaten the child's sense of self-worth. D. Elkonin [4], G. Kostyuk [5] attribute to the causes of anxiety and fears in younger students family and school environment, as well as communication with peers. According to the research's, in the senior preschool age anxiety can be formed as a stable personality trait and be part of the subjective component of the structure of self-regulation of child behavior.

THE AIM

The purpose of this work is to summarize the results of research by various scientists in the context of anxiety as a stable personality trait. Also, determine the list of causes of anxiety during play in children of preschool and school age.

Research hypothesis. Involving preschool and school age children in the game without taking into account the causes of anxiety during the preparation of the game, in the process of its implementation and in the context of receiving negative results from the game may have a negative impact on their health.

Tasks of research. 1. Summarize scientific data on play as a social phenomenon. Reveal the importance of the game process for preschool and school children. 2. To generalize scientific data on anxiety as a stable person-

ality trait and the period of trait formation in children. 3. Analyze the results of scientific research and summarize data on the levels of activity of preschool children and individual differences in psychophysiological capabilities of schoolchildren, which will serve as a basis for determining the conditions of anxiety in preschool and schoolchildren during play. 4. To summarize the results of the experiment in the blocks "Low level of organization of preparation for the game", "Low level of the game process" and "Negative subjective result of the game". 5. To draw conclusions about the causes of anxiety during play as a factor of negative impact on the health of preschool and school children.

MATERIALS AND METHODS

The set of methods is used in the work: theoretical (analysis, synthesis, comparison, systematization, generalization) and empirical (observations, conversations, questionnaires). Using theoretical methods, 23 scientific sources were analyzed, which were published in the period 1988-present in printed format.

Conducting research to identify the causes of anxiety during the game was organized in the following sequence:

- 1) acquaintance of the respondents of each age category with the new game. The game "Bear and Bunnies" was offered to preschool children, the game "Crucian and Pike" to primary school children, and the game "Shadow Leader" to adolescents and young people. During the games, special attention was paid to the emotional state of the children (at the beginning of the game, during it, after the end of the game). And how children reacted to the distribution of roles was also studied; how they interacted with other game participants; as expressed a desire to play with the same composition of participants (variable composition of participants).
- 2) involvement of respondents of each age category in the organization of the game. The children were asked to organize the games that they liked the most (liked by each of the respondents). At this stage of the research, special attention was paid to: children's attitude to the game initiatives of others; active performance of main and secondary roles in the game; change in emotional state in activity.
- 3) conducting conversation with of preschool children using the questions of the 1st block; surveying respondents of primary school children using the questions of the II block, adolescents and young people using the questions of the III block.

Three blocks of questions were developed for the research:

- *The first block* is a question for preschool children (Do you want to be a bear (main role) or a bunny (secondary role) in the game? Why? Do you always like the role you have to play? Why? You will be upset if you have to become a bunny (play a secondary role)? Why? Do you want to choose the role yourself or do you want adults to decide the role you will play in the game? Why? Are you interested in playing new games? Why? Do you want to play a new game with all the children or only with friends? Why? Do you always not want to play with all the kids, or just today? Do you cry while playing? Why? Do you remember why you cried? Do you want to play this game again? Why?).
- *The second block* are questions for primary school children (How do you think roles should be distributed in the game? Do you always like the distribution of roles in the game? What role in the game do you always want to play: main or secondary? Why do you always want to play main role in a game? Do you get upset when you have to play a secondary role? Are you interested in playing a new game with the whole class or just with your friends? Do you remember a game that made you really, really sad? Do you want to play that game today? Why? What can the game teach? What is your experience of the game, positive or negative?).
- *The third block* are questions for adolescents and young people (Does your mood depend on the role you have to play in the game? How do you think the roles in the game should be distributed? Do you always want to play the main role? Why? Are you interested in a new game with classmates or a new game with friends? Why? How often do you suggest a new game to classmates or friends? Do you remember a game in which you had a negative experience? Do you want to play that game again to gain a positive experience? Why? Do you think about knowledge and skills when you play a game? Do you think it is possible to play a game and study at the same time? What is your favorite game?).

The method of collecting information had certain differences for each category of respondents. Educators who worked with these children were involved in interviews with preschool respondents. Educators asked the questions of block I to each child individually and recorded their answers on a form that was developed according to the questions of block I. Teenagers and young men also took part in the questionnaire, prepared on the basis of the questions of the III block.

The research was conducted within the framework of the agreement for international cooperation between Borys Grinchenko Kyiv University and University of Natural Sciences and Humanities in Siedlce. 400 people

took part in the research from the Ukrainian side, 125 people from the Polish side, a total of 525 people. Of them: 130 (100/30) preschool children, 132 (105/27) primary school children, 130 (96/34) adolescents and 133 (99/34) young people.

The criterion for inclusion in the category of "respondents" was defined as studying in basic institutions of universities where students undergo pedagogical practice. The personal desire of each child was defined as the exclusion criterion. A sample of primary statistical data was obtained as a result of a specially targeted survey. The sample is representative, as it maximally reflects the properties and structure of the general population (those who have a certain level of education in Ukraine and Poland).

To research the causes of anxiety during the game, the coefficient (Kz) was used - the ratio of the sum of positive answers to the total number of questions. A negative answer (correlated with the words "I don't like") was evaluated with one point, a positive one (correlated with the words "I like") - zero. The maximum number of points is 10. If Kz was equal to 0.8-1.0 (the respondent received 8-10 points), which meant a high level of influence of the cause on the occurrence of anxiety during the game; Kz = 0.79-0.60 (5-7 points) - average level, Kz < 0.60 (less than 4 points) - low level.

The Kz coefficient was calculated according to the formula:

$$K = \frac{X_{\Pi} \times 100\%}{\Pi}, \text{ where:}$$

X_{Π} - the number of negative answers of all respondents of the age group;

Π - the maximum possible number of negative answers in the group;

$\Pi = (\text{number of respondents}) \times (\text{number of questions})$.

RESULTS

In this article, we consider the occurrence of anxiety during the game. We focus on the game, because the game is "a form of free expression of a person of any age, unfolds either in the form of competition or in the form of images (performance, representation) of certain situations, meanings, states" [6].

Regarding children of preschool and school age, scientists consider play as a social phenomenon, as the game arose in response to the "needs of children to become active members of society" (M. Stelmakhovich) [7]. The game arises from the living conditions of the child in society. In the game, the child is aware of the

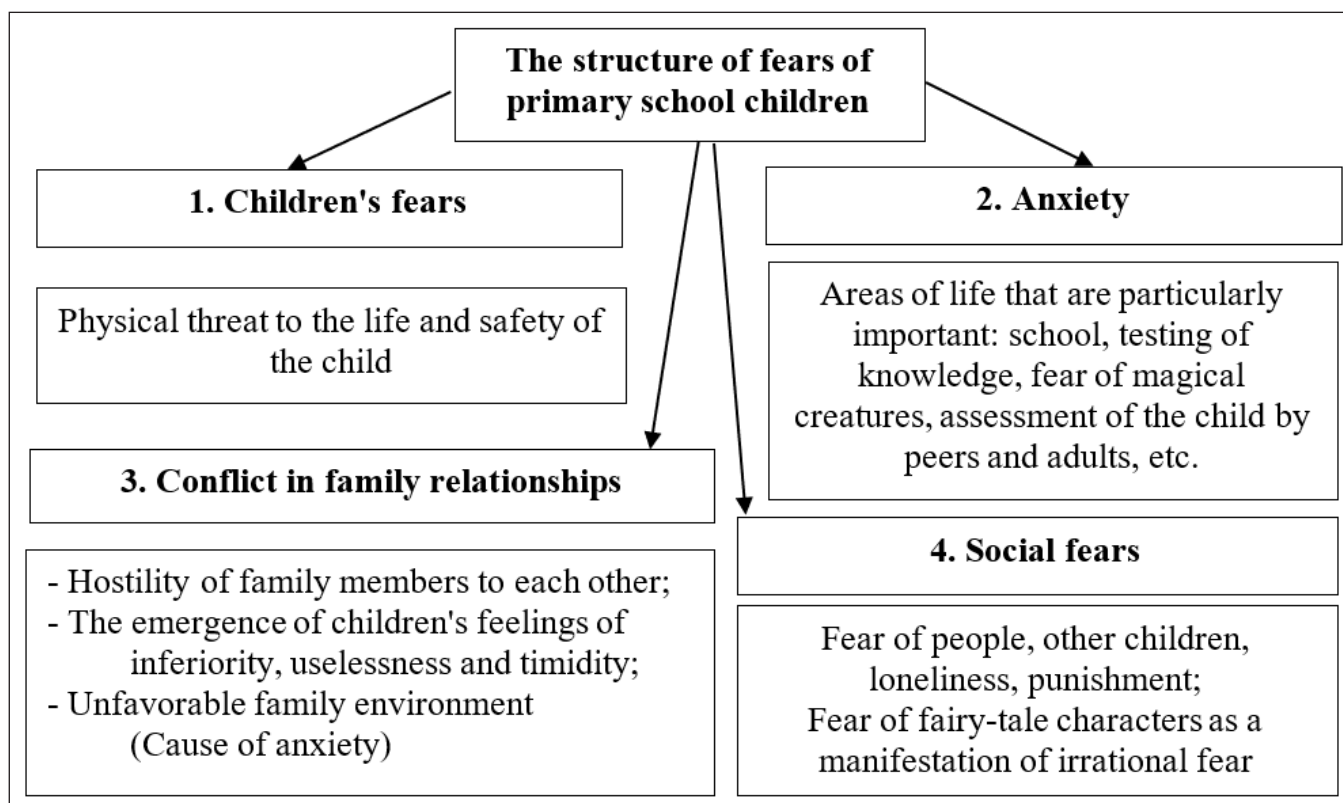


Fig. 1. Four-factor structure of fears of primary school children (Figure developed by the authors of the article based on the scientific work of H. Miklyaeva [1])

variety of human objects. Play is an activity through which children reproduce social relations between people, learn to transform reality, change the world (O. Bessarabova) [8].

Play is the main activity for preschool children. The child's need to influence the world, to become a subject of his activity is first formed and manifested in the game. According to S. Rubinstein [9], when a child plays a role, he is transformed into another person. In the course of the game, the child expands, enriches, deepens his own personality.

Play is the main form of active activity of the child. During the game, the preschool child meets his biological needs. The child implements the output of excess energy; satisfies the desire to become a leader; manifests itself as a person; checks own opportunities in collective activity; in a way manifests itself among peers; satisfies the need for rest, etc. (P. Blonsky [10], L. Bozhovich [3], D. Elkonin [4], G. Kostyuk [5]).

Scientists consider the game as a means of teaching school-age children (N. Anikieva [11], P. Podkasisty [12] and others), the formation of their cognitive activity (V. Zakharov [13], T. Shukurov [14]). Also, the game is a means of mental development and use of mental potential (J. Bruner) [15]. Play is an important method of forming social behavior and accumulating practical life experience of the child [7]. During the game, students can experiment with different situations, test their

abilities and skills, develop communication skills and learn social relationships and roles. For young people, the game becomes a form of self-affirmation in front of society [16].

We emphasize that the process of play can have different effects on children's health, namely:

1. Positive impact. The game helps to identify and solve emotional and social problems (According to Freud, the game is a symbolic repetition of a situation that in the past caused the child psychological trauma). Compared with traditional learning contributes to more effective development of skills [17].
2. Negative impact. Participation in the play process can cause anxiety in preschool and school-age children, i.e. have a negative impact on their health. This research focuses only on the negative impact of play on children's health, which is recorded as anxiety.

The analysis of scientific works was carried out in order to summarize information about anxiety as a stable personality trait that has developed in preschool and school age children. First of all, we singled out the work of D. Usyk [18]. The scientist's study concluded that anxiety, which in older preschool age acquires the quality of a stable personality trait and can be included in the subjective component of the structure of self-regulation of behavior.

In H. Miklyaeva's [1] research, anxiety was defined as one of the factors of the four-factor structure of fear (Fig 1).

H. Miklyaeva [1] studied the levels of anxiety and fear in younger students. The scientist found that children aged 8-9 years have an average level of anxiety. 49% of children showed a high level of fear of animals and an average level of fear of fairy-tale characters (49%), medical (52%), socially mediated (43%) and spatial (45%) fears; low level of fear of darkness and nightmares (50%) and fear of physical injury (50%).

Researchers also drew attention to gender differences in anxiety and fear. According to the results of research, boys have higher levels of anxiety and lower rates of autonomy of subjective regulation than girls (D. Usyk [18]). Primary school boys are more likely to show interpersonal anxiety, general anxiety, hostility in a family situation (H. Miklyaeva [1]). Girls are prone to medical fears, fear of physical injury, fear of death, fear of animals, fear of darkness and nightmares, spatial fears (H. Miklyaev [1]).

D. Usyk [18] established that the interaction of children in the plot-role has certain gender differences. Girls prefer domestic and professional plots. The boys like moving games with a less pronounced plot. In the game interaction, boys are more likely to conflict, talk less about the plot, roles and temporal parameters of the game.

Researchers are considering anxiety in the context of adolescents' and young people's understanding of the phenomenon of "my health." According to the research of O. Bogucharova [19], adolescents and young people, on the one hand, show a willingness to take responsibility for their health, and, on the other - understand the dependence of health on other factors (anxiety and fears, life satisfaction, positive experience, extroversion as a vector of activity). O. Bogucharova [19] notes that adolescents treat health as a list of a set of physical and mental characteristics, while young people associate health with the image of the physical self. High levels of positive values cause tension in adolescents and cause them to be almost constantly in a state of anxiety, which, in turn, leads to the further formation of anxiety as a personality trait. For young people, constant anxiety is weakened. O. Bogucharova [19] explains this process by the emergence of certain personal formations (freedom of choice, responsibility, autonomy, self-worth and life satisfaction) and the existing positive experiences that operate at the highest mental level - the level of subjectivity.

Also, the analysis of scientific works was carried out in order to summarize information on levels of activity. Anxiety during play can be caused by not taking into account the levels of activity inherent in preschool and school-age children. In the context of the above, we consider the results of M. Savchenko's [20] research to

be significant. The scientist identified sufficient, medium and low levels of activity of older preschool children during the game.

As a result of M. Savchenko's [20] research it was established that medium and low levels of activity predominate in children of older preschool age during play. Children with a low level of activity in the game do not show active actions when choosing a role and in the process of its implementation. They focus on other children's play ideas and do not offer their own ideas for organizing the game. Game actions depend on the toy or game attribute. The actions of children are monotonous. They often repeat the same actions with objects, because the plot of the game is missing. Children do not show persistence in achieving their own result in the game; do not follow the rules of conduct established by other players in the game. Instead of actively participating in the game, the children watched with interest the actions of other participants in the game.

The activity of middle-level children is aimed at realizing the role of play and expressing their own ideas about the game plan. Children try to realize the game idea. They independently determine the roles; participate in the distribution of roles in the game. Children follow certain rules of the game. They resent it when other players break the rules. Students are also interested in fulfilling a role that does not involve making independent decisions and influencing the overall course of the game.

Only 7% of children show a sufficient level of activity during play. According to M. Savchenko [20], children of this level of activity are characterized by: 1. Active actions aimed at realizing their own role in the game and activating other participants in the game. 2. Expression of own ideas on the organization of the game and the idea for the implementation of all its participants in the game. 3. Definition of roles in the game and their distribution among the participants of the game, expression of awareness in the implementation of their role. 4. Appropriate use of role speech; tendency to conflict in case of inconsistency of actions with partners and withdrawal from the role. 5. Do not need tips from adults to diversify and clarify the game activities. Children independently follow the rules of behavior in the game. They are persistent in achieving the result of the game. Children are able to control their own play activities and the actions of other participants in the game.

In relation to junior schoolchildren, we consider the work of M. Alekseeva [21] to be significant. The scientist determines the range of individual differences in the psychophysiological abilities of 1st grade students (including attention, memory, thinking, imagination, etc.) using a ratio of 1:15. This means that if the capabilities of the weakest

child are taken as one, then the capabilities of the strongest student will be equal to 15 units, i.e. will be 15 times higher. Indicators of children's abilities are very diverse.

This may be the number of repetitions required to memorize and reproduce the information. The amount of time it took to perform a certain action on your own, etc. M. Alekseeva [21] explains a certain range, first, the age differences of children (one child turned six years old, and the other children will soon turn 7 years old); secondly, children have different anatomical and physiological traits for future physical development; third, differences in the conditions of upbringing of children in preschool and school age.

According to L. Nozdrova's [22] research, differences in the readiness of junior schoolchildren for the learning process are significantly deepening. This is due to a number of factors.

1. Additional training of some students during the holidays.
2. Purposeful mastery of various techniques for organizing their working time.

We also consider significant the results of A. Sheiko's [23] research, which deals with the readiness of adolescents and young people to overcome critical situations. Critical situations can be caused by instability, dissatisfaction with the need for interpersonal communication, prestige and respect, insufficient formation of a stable image of "I", lack of experience in effective social interaction. According to the scientist's generalizations, mentally stable adolescents and young people show higher rates of self-organization, emotional intelligence, problem-orientation, and lower rates of situational and personal anxiety, motivation to achieve and focus on social support.

Mentally resilient adolescents and young people are characterized by greater self-organization, determination, and a tendency to imagine themselves as a strong person who has sufficient freedom of choice and acts in accordance with their goals. A. Sheiko [23] notes that critical situations that arise in the learning process lead to a statistically significant increase in the level of personal anxiety. While critical situations in everyday life affect the level of general stress, they cause significant changes in self-organization indicators.

We conducted an experiment to determine the causes of anxiety during the game. The survey of preschool children revealed the causes of anxiety at the stage of organizing the game.

1. The distribution of roles in the game without taking into account the wishes of game participants (78% of cases; $p0,001$).
2. Inconsistency of the game plot with the actual cognitive needs of the game participants (62% of cases).

Because of the analysis of the questionnaires of school-age children, another list of causes of anxiety during the game was established. For children of primary school age it is:

1. Appointment to the main roles of the same participants in the game (92% of cases; $p0,001$).
2. Lack of desire to play a secondary role in the game (54% of cases; $p0,001$).
3. Recalling the negative experience of participating in games (29% of cases; $p0,001$).

In adolescence, other reasons dominate, in particular:

1. Unwillingness to interact with a particular participant in the game (52% of cases; $p0,001$).
2. Inconsistency between the plot of the game and the actual cognitive needs of game participants (48% of cases; $p0,001$).

The causes of anxiety during the game in young people include.

1. The mismatch between the plot of the game and the actual cognitive needs of game participants (89% of cases; $p0,001$).
2. Unwillingness to interact with a particular participant in the game (45% of cases; $p0,001$).
3. Recalling negative experiences of participating in previous games (32% of cases; $p0,001$).

We also investigated the stage of children's participation in the game. Anxiety was recorded when preschool children were partially aware of the role to be played (68% of cases; $p0,001$). Primary school students experience anxiety when the role requires significant intellectual effort from them, which prevents them from enjoying the game process itself (73% of cases; $p0,002$).

Anxiety in adolescents is caused by the following factors.

1. Fulfilling the role requires the application of knowledge and skills that are formed at a low level (51% of cases).
2. External motivation to participate in the game (45% of cases; $p0,001$).

Anxiety in young people's is caused by two reasons.

1. Fulfilling the role requires significant intellectual effort from the participant of the game. This prevents enjoyment of the game process itself (43% of cases; $p0,001$).
2. Fulfilling the role requires the application of knowledge and skills that are formed at a low level (38% of cases; $p0,001$).

Anxiety in preschool children was also recorded as a result of negative experiences of participation in the game (58% of cases; $p0,001$). Primary school students felt anxious when they had negative associations with the game process (63% of cases; $p0,001$). Anxiety in adolescents is caused by lack of satisfaction with the

game process (72% of cases; $p < 0,002$) and lack of positive dynamics in personal development (48% of cases; $p < 0,001$). The causes of anxiety in young people include lack of satisfaction with the game process (70% of cases; $p < 0,001$). As well as the presence of the process of transferring negative emotions that arose during the game, to overt or covert confrontation in interpersonal interaction during school and extracurricular time (34% of cases; $p < 0,001$).

DISCUSSION

Play is the main activity of preschool children and one of the activities of primary school children, adolescents and young people. The wide range of use of the game in the process of teaching children is explained by the variety of its types (story-role play, educational game, business game, etc.) and the purpose of implementation. Compared to traditional learning, involving children in play has a positive effect on their mental development, helps to solve emotional and social problems. At the same time, the process of the game can cause anxiety in its participants and have a negative impact on their health.

Anxiety as a stable personality trait can be formed in older preschool age (D. Usyk [18]). Anxiety is included in the structure of self-regulation of behavior (H. Miklyaeva [1]). Primary school students are most likely to show anxiety in areas of life that are particularly important to them. This is school education, situations of testing knowledge, fear of magical creatures, evaluation of the child by peers and adults, etc. (H. Miklyaeva [1]). Adolescents and young people are characterized by an understanding of the dependence of health on anxiety and fears (O. Bogucharova [19]).

Medium and low levels of activity predominate in older preschool children. In particular, children with low levels of activity often observe the actions of other participants with interest instead of actively participating in the game. Medium-level children are interested in the implementation of role-playing actions and the implementation of the role, which does not provide for independent decisions that affect the overall course of the game (M. Savchenko [20]). The activity of primary school children in the game depends on individual psychophysiological capabilities. If the capabilities of the weakest child are taken as one, the capabilities of the strongest student will be almost 15 times higher. (M. Alekseeva [21]). Mentally stable adolescents and young people in comparison with the unstable show lower rates of situational and personal anxiety, achievement motivation and focus on seeking social support (A. Sheiko [23]).

Causes of anxiety during the game are divided into three blocks.

Block I – “Low level of organization of preparation for the game”. The block includes the following reasons: 1. The distribution of roles in the game without taking into account the wishes of game participants. 2. Appointment to the main roles of the same participants in the game. 3. Lack of desire to play a minor role in the game. 4. Mismatch between the plot of the game and the current cognitive needs of game participants. 5. Recalling the negative experience of participating in games. 6. Unwillingness to interact with a particular participant in the game.

Actions to eliminate the causes of anxiety at the level of the game preparation organization:

1. Take into account the wishes of children when assigning roles in the game. Avoid the occurrence of a conflict situation due to the child's reluctance to play a secondary role.
2. Do not assign the same players to the main roles.
3. Select the plot of the game taking into account the actual cognitive needs of the game participants.
4. Timely identify the negative experience of participating in the games that were held earlier, and promote the replacement of this experience with a positive one.
5. Take into account the reluctance of individual game participants to interact with each other.

- Block II – “Low level of the game”. The following reasons are included in the block: 1. Partial awareness of the participants of the game of the essence of the role. 2. Organization of the game without prior trial play of its plot. 3. Fulfilling the role requires significant intellectual effort from the participant of the game. This prevents from enjoying the gameplay itself. 4. Fulfilling the role requires the application of knowledge and skills that are formed at a low level. 5. External motivation to participate in the game. 6. Game participants do not want to communicate directly.

Actions to eliminate the causes of anxiety at the level of the game process:

1. To organize a test play of the plot of the game to eliminate the partial understanding of the essence of the role to be performed by the participants of the game.
2. Determine such a level of intellectual load during the game that will not prevent enjoyment of the process itself.
3. Use didactic materials that will help a game participant with a low level of knowledge and skills to enjoy the game process and master new knowledge and skills.
4. Transfer the external motivation of participation in the game to the internal one (I want to play because...)
5. Use your own example to show examples of possible communication between game participants.

- Block III – “Negative subjective result of the game”. The block includes the following reasons: 1. Getting a negative experience of participating in the game. 2. Lack of pleasure from the game process. 3. Lack of positive dynamics in personal development. 4. Formation of negative associations in the participants of the game. 5. Transfer of negative emotions that arose during the game, to overt or covert confrontation in interpersonal interaction in the educational and extracurricular time.

Actions to eliminate the causes of anxiety at the level of a negative subjective result of the game:

1. To prevent children from having a negative experience of participating in the game and negative associations with the game process.
2. End the game at the moment when the children are enjoying the game process.
3. To record positive dynamics in the personal development of children (for example, we learned to be attentive and overcome obstacles).
4. To prevent the transfer of negative emotions that arose during the game to overt or hidden confrontation in interpersonal interaction in educational and extracurricular time

CONCLUSIONS

In accordance with the purpose of the study, it was found that the game is used for the purpose of education, upbringing, development and socialization of children of preschool and school age. The originality of the study is that the game process is analyzed for the first time not in the context of a positive impact on children’s health, but in the context of the negative. In addition, for the first time, the causes of anxiety during the game are determined. These reasons are arranged in three blocks “Low level of organization of game preparation”, “Low level of the game process”, “Negative subjective result of the game”. The impact of the results of the game on the use of mental self-management techniques by adolescents and young people, which in turn has a positive effect on their health, remains controversial. And also questions about the presence of intrapersonal conflicts, which can be caused by subjective factors (emotional instability of teenagers and young men, low self-criticism, impulsivity, exaggerated harassment, depressive state) and objective factors (external influences, biorhythms, tense relations).

REFERENCES

1. Mikliaieva HM. Osobystisno-rolovy pidkhid u psikhokorektsii tryvozhnosti molodshykh shkoliariv. [Personality-role approach in psychocorrection of anxiety of junior schoolchildren] Avtor. dys. . . . kand. psykhn. nauk: 19.00.07 – pedahohichna ta vikova psikhohiia. Kharkiv. 2014, p.20. (In Ukrainian).
2. Prihozhan A. Psihologiya trevozhnosti. Doshkolnyiy i mladshiy shkolnyiy vozrast. [Psychology of anxiety. Preschool and primary school age] Sankt-Peterburg. Piter. 2007, p.35. (In Russian).
3. Bozhovich LI. Izbrannyye psihologicheskie trudyi. Problemyi formirovaniya lichnosti. [Selected psychological works. Problems of personality formation] Moskva: Mezhdunarodnaya pedagogicheskaya akademiya. 1995, p.209. (In Russian).
4. Elkonin DB. Psihologiya igryi. [Game psychology] Moskva: Pedagogika. 1978, p.304. (In Russian).
5. Kostiuk HS. Navchalno-vykhovnyi protses i psikhichniy rozvytok. [Educational process and mental development] Kyiv. 1989, p.297 (In Ukrainian).
6. Honcharenko S. Ukrainskyi pedahohichniy slovnyk. [Ukrainian pedagogical dictionary] Kyiv: Lybid. 1997; 374: 73. (In Ukrainian).
7. Stelmakhovych MH. Ukrainska narodna pedahohika. [Ukrainian folk pedagogy] Kyiv: IZMN. 1997, p.232.
8. Bessarabova OV. Hra yak zasib rozvytku piznavalnoi diialnosti u slabozorykh ditei [Play as a means of developing cognitive activity in visually impaired children]. Avtor. . . . dys. kand. ped. nauk: 13.00.03 – korektsiina pedahohika. Zaporizhzhia. 2011, p.20. (In Ukrainian).
9. Rubinshteyn SL. Osnovyi obschey psihologii. [Fundamentals of general psychology]. Sank-Peterburg: «Piter». 1999; 720:488. (In Russian).
10. Blonskiy PP. Psihologiya mladshhego shkolnika [Psychology of a younger student] Akademiya pedagogicheskikh i sotsialnyih nauk; Moskovskiy psihologo-sotsialnyiy institut. Moskva: Izd-vo “Institut prakticheskoy psihologii”. 1997, p. 575. (In Russian).
11. Anikeeva NP. Vospitanie igroy. [Education in game] Kniga dlya uchitelya. Moskva: Prosveschenie. 1987, p.144 (In Russian).
12. Pidkastyiy PI, Haydarov ZhS. Tehnologiya igryi v obuchenii i razvitii. [Game as a technology of learning and development] Uchebnoe posobie. Moskva: Rossiyskoe pedagogicheskoe agentstvo. 1996, p.272. (In Russian).
13. Zaharov VM. Intellektualnyie igryi kak sredstvo formirovaniya poznavatelnoy deyatelnosti uchaschihsya. [Intellectual games as a means of forming the cognitive activity of students] Avtoref. na soiskanie nauch. stepeni kand. ped. nauk: spets.13.00.01 «Teoriya i istoriya pedagogiki». Moskva. 1988, p.24. (In Russian).
14. Shukurov TA. Pedagogicheskaya sistema igrovyyih form organizatsii poznavatelnoy deyatelnosti shkolnikov. [Pedagogical system of game forms of organization of cognitive activity of schoolchildren] Avtoref. na soiskanie nauch. stepeni kand. ped. nauk: spets. 13.00.01 «Obschaya pedagogika». Dushanbe. 1999, p.48. (In Russian).
15. Bruner Dz. Igra, myshlenie i rech. [Play, thinking and speech] Perspektivyyi: voprosyi obrazovaniya. 1987;1:73–81. (In Russian).

16. Kulish IM. Chy potribno studentu hratsyia? Vykorystannia dydaktychnoi hry u pidhotovtsi fakhivtsiv riznykh spetsialnostei. [Does the student need to play? The use of didactic games in the training of specialists in various specialties] *Humanitarni nauky*. 2001; 2: 112–116. (In Ukrainian).
17. Neverkovich SD. Igrovye metodyi podgotovki kadrov. [Game training methods] *Uchebnoe posobie*. Moskva: Vysshaya shkola. 1995, p.207. (In Russian).
18. Usyk DB. Psykholohichni osoblyvosti samorehuliatcii povedinky starshykh doshkilnykiv u suzhetno-rolovii hri [Psychological features of self-regulation of behavior of senior preschoolers in a plot-role game]: avtor. dys. . . . kand psykhol. nauk: 19.00.07 – pedahohichna ta vikova psykholohiia. Kharkiv. 2013, p.20. (In Ukrainian).
19. Bohucharova OI. Zdorovia osobystosti u psykholohichnii perspektyvi. [Health of personality in the context of a psychological perspective] Kyiv. 2004, p.284. (In Ukrainian).
20. Savchenko MV. Vychovannia samostiinosti u ditei starshoho doshkilnogo viku v ihrovii diialnosti. [Education of independence in older preschool children in play activities] Avtoref. dys. . . . kand. ped. nauk: 13.00.08 – doshkilna pedahohika. Odesa. 2014, p.20. (In Ukrainian).
21. Aleksieieva MI. Motyvy navchannia uchniv. [Motives for student learning] *Posibnyk dlia vchyteliv*. Kyiv. 1974; 153: 50–52. (In Ukrainian).
22. Nozdrova OP. Dydaktychni ihry yak zasib vyrivniuvannia indyvidualno-piznavalnykh rozbizhnosti ditei 6 – 7 rokiv. [Didactic games as a means of equalizing individual and cognitive differences of children 6-7 years] *Pochatkova shkola*. 2007; 5: 50–53. (In Ukrainian).
23. Sheiko AO. Osoblyvosti proiavu psykhičnoi stiikosti osobystosti v yunatskomu vitsi pry podolanni krytychnykh sytuatsii. [Features of manifestation of mental stability of the person in the period of youth at overcoming of critical situations] Avtor. dys. . . . kand. psykhol. nauk: 19.00.07 – pedahohichna ta vikova psykholohiia. Kharkiv. 2014, p.20. (In Ukrainian).

ORCID and contributionship:

Tetiana Miyer: 0000-0002-2874-2925^{A-F}

Anna Klim-Klimaszewska: 0000-0001-7418-9983^{A-F}

Svitlana Palamar: 0000-0001-6123-241X^{A-F}

Olha Kotenko: 0000-0001-8967-8130^{A-C,E}

Hennadii Bondarenko: 0000-0001-5978-5138^{A-E}

Liudmyla Nezhyva: 0000-0001-9520-0694^{A-C,E}

Yurii Savchenko: 0000-0003-3662-2787^{A-C}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Svitlana Palamar

Borys Grinchenko Kyiv University

18/2 Bulvarno-Kudryavska St., 04053 Kyiv, Ukraine

e-mail: svetlana_03@ukr.net

Received: 01.06.2022

Accepted: 18.04.2023

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article



Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

ORIGINAL ARTICLE

IMPACT OF MOTOR ACTIVITY ON THE DYNAMICS OF INTELLECTUAL WORKING CAPACITY AND MENTAL COGNITIVE PROCESSES IN STUDENTS

DOI: 10.36740/WLek202306114

Iryna Yu. Karpiuk¹, Tetiana K. Obeziuk¹, Maryna O. Demydenko¹, Iryna Yu. Zakharova¹, Olena V. Pidvalna¹, Oleksandr Ye. Salamakha¹, Iryna A. Holovanova²

¹NATIONAL TECHNICAL UNIVERSITY OF UKRAINE "IGOR SIKORSKY KYIV POLYTECHNIC INSTITUTE", KYIV, UKRAINE

²POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

ABSTRACT

The aim: To study the impact of physical exercises of different intensity on the dynamics of intellectual working capacity and mental cognitive processes in students.

Materials and methods: The research involved 293 students. The research was conducted in 2 stages. The 1st stage involved the study of the level of intellectual activity of students with sufficient (the experimental group, n = 76) and insufficient levels of their motor activity (the control group, n = 217). The 2nd stage provided for the determination of the dynamics of intellectual activity indicators in students (n = 76) before and after physical exercises of different intensity.

Results: It was found that students with sufficient motor activity are characterized by significantly better indicators of intellectual working capacity and mental cognitive processes than students with insufficient motor activity. It was found that low-intensity physical exercises of a recreational nature had a more positive effect on intellectual working capacity in the course of training sessions.

Conclusions: Organized motor activity and optimal physical exertion both during and after the end of intellectual functioning can directly affect the preservation and improvement of students' intellectual working capacity.

KEY WORDS: motor activity, physical exercises, intellectual working capacity, mental cognitive processes, students

Wiad Lek. 2023;76(6):1422-1427

INTRODUCTION

The significant intensification of the educational process in higher educational institutions (HEIs) of Ukraine, which is designed to ensure the high quality of training of future specialists for professional activities, has led in recent years to a significant intellectual overload of students and caused a decrease in their motor activity [1]. This negative trend has been significantly intensified during the period of regular transitions from full-time to distance (online) education. As a result of a heavy learning load with low motor activity (students spend most of their time sitting in classrooms or at computer and phone screens), negative changes began to occur in students' bodies, associated with a general deterioration in health, diseases (pathologies) of many organs and systems, excess weight gain, and problems in the psycho-emotional sphere (irritability, aggressiveness, isolation, poor health, etc.) [2]. The above factors hurt the indicators of intellectual working capacity (IWC) and

mental cognitive processes (MCP) of students: academic performance deteriorates, attention, memory, thinking decrease, and fatigue sets in quickly [3]. Fatigue is based on a decrease in the body's functional capabilities and reserves. Since students' learning activities by their nature belong to the types of mental and intellectual labor, one of the first signs of fatigue is a decrease in their IWC.

According to some scientists [4], an effective way to combat fatigue, and deterioration of the intellectual, as well as the physical working capacity of students is to increase the amount of their motor activity (MA) and physical exertion, including their rational dosage during the period of intense intellectual activity. It is proved that physical exercises (PEs) actively influence the effectiveness of students' learning, elements of IWC, and are used to prevent and eliminate mental fatigue in the conditions of intensification of educational activities [5].

Of particular interest among scientists is the question of the rational use of PEs to restore working capacity during intellectual functioning. According to experts [6], a high level of IWC is maintained provided that the optimal excitability of the corresponding cortical areas of the cerebral cortex is maintained. As a result of prolonged intellectual functioning, inhibitory processes occur in the higher parts of the brain, which cause a decrease in attention, memory, the ability to creatively analyze information, and result in errors. A periodic transition to performing physical exercises allows you to accelerate the recovery of IWC, relieve fatigue, and have a general health effect. However, scientists emphasize the need to take into account the amount of physical exertion and the time of exercise in the daily routine for IWC recovery. It is during intellectual functioning, according to scientists [7], that the negative effects of physical exertion are most often encountered. Heavy physical exertion results in a disruption of the nerve centers, to the creation of a new dominant system of inter-center connections in the higher parts of the brain. This can complicate further intellectual functioning which is based on a different mechanism. Significant muscle exertion can create persistent fatigue. If the following processes occur during intellectual functioning, productivity may decrease. Therefore, training sessions with heavy physical exertion should be carried out after the end of intellectual activity, at the end of the working day.

Scientists [8] note that the selection and duration of PEs in the process of intellectual activity depend on the nature of such functioning. If it consists of habitual intellectual operations that do not contain complex analytical components, then in this case, moderate exertions of increased duration and intensity will not cause a decrease in the productivity of the main work. However, if intellectual functioning is creative in nature and involves analyzing a wide range of information, then the system of inter-center connections should not be disrupted by switching to intense muscle activity. In this case, a positive effect is achieved by light PEs, the performance of which does not disturb the dynamic stereotype of the main work in the cortex.

According to experts [9], within the daily or weekly cycles of activities, in which mental work and other types of work alternate, there must be a place for training sessions aimed at improving physical fitness. Depending on the conditions, they can take the form of regular physical education training sessions, independent training, or athletic training. It is better to conduct training sessions with high physical activity in the afternoon so that complete recovery of IWC occurs during evening rest and night sleep.

THE AIM

The aim is to study the impact of physical exercises of different intensity on the dynamics of intellectual working capacity and mental cognitive processes in students.

MATERIALS AND METHODS

The research was conducted at the Department of Health and Sports Technologies of the National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute" (Kyiv, Ukraine) in 2021. The research involved 293 students (168 men and 125 women) of the first and second instructional years of technical specialties.

The research was conducted in 2 stages. The 1st stage involved the study of the level of intellectual working capacity as well as the indicators of attention and memory of students with sufficient (the experimental group, $n = 76$) and insufficient levels of motor activity (the control group, $n = 217$). The level of MA was determined by interviewing students and assessing their involvement in various forms of MA: a sufficient level involved systematic physical exercise throughout the day and week (morning physical exercises, physical education training sessions at the HEI, club training sessions by sports, independent training); insufficient level – irregular, occasional attendance of physical education training sessions at the HEI, absence of morning exercises, independent and club training sessions in the daily routine. The 2nd stage provided for the determination of the dynamics of IWC and MCP indicators in students ($n = 76$) before and after physical exercises of different intensity, which was determined by the value of HR. Thus, two groups of students were randomly created: the EG1 ($n = 38$) and the EG2 ($n = 38$). The EG1 had low-intensity training sessions (students' heart rate during the training sessions did not exceed 130-150 beats / min), and the EG2 had high-intensity training sessions (heart rate – 160-180 beats / min). The duration of the training sessions was 90 minutes.

We used the following scientific methods: theoretical analysis and generalization of scientific and methodological literature, testing of students' indicators of IWC and mental cognitive processes, and methods of mathematical statistics. The IWC was assessed by Anfimov's correction task (a form with 1480 characters (37 lines of 40 characters each) [10]. The test lasts 10 minutes. The task was to consistently cross out the letters C and K in the form (M). At the same time, it was necessary to process as many characters as possible (H) and make as few mistakes

Table I. The level of IWC and MCP indicators in students with sufficient (EG, n = 76) and insufficient (CG, n = 217) levels of MA (Mean ± SD), c. u.

The studied indicators	EG (n=76)	CG (n=217)	Level of significance (p)
Volume of information (number of processed characters)	1261.5±14.3	1235.2±6.7	>0.05
Number of mistakes made	14.6±0.95	18.1±0.68	<0.01
Work accuracy indicator	91.2±0.51	89.4±0.34	<0.05
Intellectual working capacity	1147.8±13.2	1099.3±7.5	<0.01
Scope of attention	7.3±0.15	6.9±0.11	<0.05
Visual memory	6.1±0.17	5.7±0.10	<0.05

Table II. Dynamics of students' IWC and MCP before and after training sessions with PEs of low (EG1, n = 38) and high (EG2, n = 38) intensity (Mean ± SD), c. u.

The studied indicators	EG1		p	EG2		p
	Before	After		Before	After	
Volume of information	1257.8±19.1	1255.2±20.3	>0.05	1268.1±18.7	1249.4±19.2	>0.05
Number of mistakes made	15.3±1.04	13.8±0.99	>0.05	14.1±1.02	16.5±1.07	>0.05
Work accuracy indicator	89.3±0.81	90.6±0.79	>0.05	90.4±0.94	87.4±0.90	<0.05
Intellectual working capacity	1119.4±22.7	1142.2±21.9	>0.05	1141.3±23.2	1086.9±24.1	>0.05
Scope of attention	7.1±0.32	7.3±0.30	>0.05	7.2±0.34	6.7±0.35	>0.05
Visual memory	5.9±0.39	6.0±0.37	>0.05	5.8±0.40	5.6±0.41	>0.05

as possible (O). A mistake is considered to be the omission of letters that should be crossed out, as well as incorrectly crossed-out letters. Based on the test results, we determined the rate of accuracy (A) and IWC: $A = M / (M + O) \times 100$; $IWC = A / 100 \times H$. The scope of attention and visual memory of students was assessed using the numerical operations method, the essence of which is to operate with certain volumes of information in the form of one-digit numbers. A 25-cell form with numbers from 1 to 40 (15 numbers were omitted) was used. According to the test conditions, the student should find and cross out the numbers missing in the test form as quickly as possible (1-minute test). After that, using another form, the students had to write down the difference between the crossed-out numbers they had to memorize and the number 10. The scope of attention and visual memory were assessed on a 9-point scale. During each subsequent test, the position and order of the letters in the correction task form and the numbers in the forms were changed.

The significance of the difference in the results of the students was determined during the studying based on the Student's test. The significance for all statistical tests was set at $p < 0.05$. All statistical analyses were performed with the SPSS software, version 21, adapted to medical and biological researches. This research followed the regulations of the World Medical Association Declaration of Helsinki. Informed consent was received from all students who took part in this research.

RESULTS

The analysis of the results obtained at the 1st stage of the research showed that most of the studied indicators in students with a sufficient level of MA were significantly ($p < 0.05$; $p < 0.01$) better than those with an insufficient level of MA (Table I). Thus, only in terms of the number of processed characters, the indicators of the EG and the CG do not have a significant difference ($p < 0.05$). The number of errors in the CG was higher than in the EG by 3.5 c. u.; the indicators of accuracy, IWC, the scope of attention, and visual memory were better in the EG by 1.8, 48.5, 0.4, and 0.4 c. u., respectively. This indicates that MA is an effective factor in improving students' IWC and MCP while studying at the HEI.

The comparative analysis of students' IWC and MCP indicators before and after the training sessions with low- and high-intensity PEs in the educational process (in the intervals between academic studies) shows that all the studied indicators either improved or did not change after PEs performance in the EG1, where training sessions with PEs were characterized by low intensity. The most qualitative changes ($p > 0.05$) were found in the reduction of the number of errors (by 1.5 c. u.), in the accuracy indicators (by 1.3 c. u.) and in IWC (by 22.8 c. u.) (Table II).

There was deterioration in all indicators in the EG2, where the training sessions with PEs were conducted with high intensity, in contrast to the EG1. The most pronounced changes were found in the indicators of accuracy (by 3.0 c. u., at $p < 0.05$), the number of errors

made during the processing of the correction task (by 2.4 c. u., at $p < 0.05$), IWC (by 54.4 c. u., at $p < 0.05$) and the scope of attention (by 0.5 c. u., at $p < 0.05$). The obtained results indicate that training sessions with PEs in the process of academic studies should not give a heavy load on students. However, low-intensity training sessions with a health-improving effect are quite effective in improving both students' IWC and MCP.

DISCUSSION

Physical education is an integral part of the formation of a harmoniously developed modern specialist. It is proved that systematic optimal training sessions with PEs contribute to health promotion, improvement of physical and intellectual working capacity as well as the quality of education of students [11]. Scientists argue that intellectual functioning and intellectual development require an appropriate physical condition of students, that is, intellectual activity directly depends on MA [12]. Scientists describe the dependence of intellectual functioning productivity on physical activity as follows: the effectiveness of intellectual functioning in conditions of low MA decreases by 50 % on the second day. During intellectual activity, blood flow to the brain vessels increases, peripheral vessels of the extremities constrict, and the vessels of the internal organs dilate, i. e., reactions are reversed from those characteristics of muscle exertion. During PEs performance, many impulses are sent to the cerebral cortex from all organs and systems, especially from muscles and the entire musculoskeletal system, the importance of which is extremely important for the recovery of fatigue, ensuring thinking processes and sustainable intellectual activity. Thus, motor activity and physical exertion are a prerequisite for successful, fruitful, and long-term intellectual activity [13].

Specialists [14] note that PEs used in the educational process has a double effect on the students' body: specific and nonspecific. The specific effect is manifested in the direct participation of the motor analyzer in various learning activities: the ability to hold a static posture; performing movements necessary for intellectual functioning, i. e. finger and hand movements while writing; eye movements, moving the torso in space; manipulating various objects. The nonspecific effect is that muscle activity causes an increase in the tone of the cerebral cortex, thus creating favorable conditions not only for the functioning of existing connections but also for the development of new ones. However, physical exercises have the most beneficial effect on students' bodies only within the limits of optimal load. Excessive motor activity in the process of studying (between academic studies) can hurt the body – the general condition worsens, the

activity of the nervous system is disturbed, recovery processes slow down, excessive fatigue and overstrain arise and accumulate. That is why it is necessary to perform PEs with high intensity after the end of the academic day so that the body can recover by the next day [15].

In the course of our research, we found that MA is an important factor not only in promoting students' health but also in improving their IWC and MCP: students who had a sufficient amount of MA had significantly better indicators of intellectual and mental functioning (attention, memory). At the same time, the use of optimal physical exertion in the students' working day routine performs the function of active rest and recreation to prevent their intellectual fatigue. Thus, PEs has a positive impact on the effectiveness of students' learning, on the indicators of their intellectual functioning and is a means of relieving negative emotions and intellectual fatigue. Our results confirmed the conclusions of scientists, where it was found that PEs in the process of intellectual functioning contributed to the improvement of mobility of nervous processes and thus created prerequisites for the longer preservation of IWC. At the same time, one should avoid excessive physical and emotional stress when performing PEs in the process of intellectual functioning, which can increase the excitability of the central nervous system and complicate further involvement in intellectual activity.

CONCLUSIONS

It was found that students who systematically engage in PEs and have a sufficient amount of MA have significantly ($p < 0.05$; $p < 0.01$) better indicators of IWC and MCP than students with insufficient MA. The difference between the EG and the CG in terms of the number of errors, accuracy, IWC, the scope of attention, and visual memory was 3.5, 1.8, 48.5, 0.4, and 0.4 c. u., respectively.

It was found that in the process of academic studies, low-intensity PEs of recreational nature had a more positive effect on the indicators of IWC. Thus, most of the indicators of students' intellectual functioning improved after training sessions in the EG1, in contrast to the EG2, where training sessions were of a training nature of high intensity. Such training sessions should take place only after the end of intellectual functioning. Thus, organized MA and optimal physical exertion during and after the end of intellectual functioning can directly affect the preservation and improvement of students' intellectual working capacity.

Prospects for further research are aimed at studying the impact of physical exertion of different intensity on the indicators of physical development and health of students.

REFERENCES

1. Sevil J, Práxedes A, Abarca-Sos A et al. Levels of physical activity, motivation and barriers to participation in university students. *J Sports Med Phys Fitness*. 2016;56(10):1239-1248.
2. Macilwraith P, Bennett D. Burnout and physical activity in medical students. *Ir Med J*. 2018;111(3):707.
3. Davies EB, Morriss R, Glazebrook C. Computer-delivered and web-based interventions to improve depression, anxiety, and psychological well-being of university students: a systematic review and meta-analysis. *J Med Internet Res*. 2014;16(5):e130. doi:10.2196/jmir.3142.
4. Wunsch K, Fiedler J, Bachert P, Woll A. The tridirectional relationship among physical activity, stress, and academic performance in university students: A systematic review and meta-analysis. *Int J Environ Res Public Health*. 2021;18(2):739. doi:10.3390/ijerph18020739.
5. El Ansari W, Suominen S, Draper S. Correlates of achieving the guidelines of four forms of physical activity, and the relationship between guidelines achievement and academic performance: Undergraduate students in Finland. *Cent Eur J Public Health*. 2017;25(2):87-95. doi:10.21101/cejph.a4387.
6. Cabeza-Ruiz R, Sánchez-López AM, Trigo ME, Gómez-Píriz PT. Feasibility and reliability of the assessing levels of physical activity health-related fitness test battery in adults with intellectual disabilities. *J Intellect Disabil Res*. 2020;64(8):612-628. doi:10.1111/jir.12756.
7. Van Cutsem J, Marcora S, De Pauw K et al. The effects of mental fatigue on physical performance: A systematic review. *Sports Med*. 2017;47(8):1569-1588. doi:10.1007/s40279-016-0672-0.
8. Taylor CB, Sallis JF, Needle R. The relation of physical activity and exercise to mental health. *Public Health Rep*. 1985;100(2):195-202.
9. Pageaux B, Lepers R. The effects of mental fatigue on sport-related performance. *Prog Brain Res*. 2018;240:291-315. doi:10.1016/bs.pbr.2018.10.004.
10. Khoroshukha M, Ivashchenko S, Bosenko A et al. Gender-associated effects of serological markers of blood groups on the development of attention function of young adolescent athletes. *Georgian Med News*. 2020;(304-305):103-111.
11. Beltrán-Velasco AI, Donoso-González M, Clemente-Suárez VJ. Analysis of perceptual, psychological, and behavioral factors that affect the academic performance of education university students. *Physiol Behav*. 2021;238:113497. doi:10.1016/j.physbeh.2021.113497.
12. Chen K, Liu F, Mou L et al. How physical exercise impacts academic burnout in college students: The mediating effects of self-efficacy and resilience. *Front Psychol*. 2022;13:964169. doi:10.3389/fpsyg.2022.964169.
13. El Ansari W, Stock C. Relationship between attainment of recommended physical activity guidelines and academic achievement: undergraduate students in Egypt. *Glob J Health Sci*. 2014;6(5):274-283. doi:10.5539/gjhs.v6n5p274.
14. Pfisterer J, Rausch C, Wohlfarth D et al. Effectiveness of Physical-Activity-Based Interventions Targeting Overweight and Obesity among University Students-A Systematic Review. *Int J Environ Res Public Health*. 2022;19(15):9427. doi:10.3390/ijerph19159427.
15. Keating XD, Guan J, Piñero JC, Bridges DM. A meta-analysis of college students' physical activity behaviors. *J Am Coll Health*. 2005;54(2):116-125. doi:10.3200/JACH.54.2.116-126.

This research was carried out according to the research work of National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute" for 2018-2023 on the theme of "Information technologies for assessing and correcting the state of health of students in higher educational institutions" (state registration number 0117U006954).

ORCID and contributionship:

Iryna Yu. Karpiuk: 0000-0002-9645-8256^A

Tetiana K. Obeziuk: 0000-0002-3502-3080^B

Maryna O. Demydenko: 0000-0003-3593-8309^D

Iryna Yu. Zakharova: 0000-0002-6478-1761^D

Olena V. Pidvalna: 0000-0002-8416-121X^C

Oleksandr Ye. Salamakha: 0000-0002-4798-9800^F

Iryna A. Holovanova: 0000-0002-8114-8319^E

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Iryna A. Holovanova

Poltava State Medical University

23 Shevchenko st., 36000 Poltava, Ukraine

tel: +380506147638

e-mail: natanew2017@ukr.net

Received: 10.10.2022

Accepted: 21.05.2023

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

ORIGINAL ARTICLE

THE IMPACT OF PROFESSIONAL STRESS ON THE MENTAL HEALTH OF LAW ENFORCEMENT OFFICERS

DOI: 10.36740/WLek202306115

Ivan M. Okhrimenko¹, Vadym V. Barko², Lesia V. Vavryk³, Vadym D. Chornous³, Svitlana S. Okhrimenko¹, Yuri V. Aleksandrov⁴, Larysa M. Onishchuk⁵

¹NATIONAL ACADEMY OF INTERNAL AFFAIRS, KYIV, UKRAINE

²STATE RESEARCH INSTITUTE OF THE MINISTRY OF INTERNAL AFFAIRS OF UKRAINE, KYIV, UKRAINE

³NATIONAL ACADEMY OF THE SECURITY SERVICE OF UKRAINE, KYIV, UKRAINE

⁴KHARKIV NATIONAL UNIVERSITY OF INTERNAL AFFAIRS, KHARKIV, UKRAINE

⁵NATIONAL UNIVERSITY «YURI KONDRATYUK POLTAVA POLYTECHNIC», POLTAVA, UKRAINE

ABSTRACT

The aim: To investigate the impact of professional stress on the mental health of law enforcement officers.

Materials and methods: The research involved two groups of law enforcement officers (aged 25-40): the first group with up to 7 years of service activities (n = 52), the second group – 8-15 years (n = 48). Research methods: bibliosemantic, questionnaire, testing, method of system analysis and generalization, mathematical and statistical.

Results: It was found that law enforcement officers of both groups identified indicators of a significant professional workload, lack of adequate rest, and the nature of communication with participants in professional relationships among the factors of professional stress. It is proved that the mental health of law enforcement officers deteriorates under the influence of professional stress with the experience of their professional activities. Law enforcement officers with 8-15 years of service experience have significantly ($p < 0.05-0.001$) worse indicators of anxiety, aggressiveness, motivation, personal detachment, impulsiveness, vigor, and work efficiency.

Conclusions: It was established that the professional stress of law enforcement officers is the result of an imbalance between the internal resources of the individual and the requirements of the external environment, embodied in the peculiarities of law enforcement activities. Law enforcement officers are characterized by the presence of professional stress of average and high severity, which increases with the experience of their service activities. A set of measures was proposed to provide psychological assistance to law enforcement officers to effectively counteract professional stress and improve their mental health.

KEY WORDS: professional stress, factors, mental health, law enforcement officers

Wiad Lek. 2023;76(6):1428-1435

INTRODUCTION

Stress is a very strong and prolonged psychological tension that occurs in a person in situations where his or her nervous system experience a significant emotional load. During stressful conditions, the human body strives to achieve relative stability, so psychophysiological changes occur in the human body under the influence of negative factors [1-3]. Able-bodied people who have to be exposed to stressors every day due to certain circumstances are most susceptible to stress. Therefore, scientists identify the development of professional stress as an important problem that affects productivity, as well as the state of human mental health [4-6].

Scientific research confirms the tendency for stress levels to increase among specialists in socio-economic professions, which include the professional activities of

law enforcement officers [7-10]. Its analysis shows that the typical characteristics of work that provoke stress on the nervous system of law enforcement officers are the excessive intensity of workloads, high responsibility for the final results of activities, a multiple system of professional relationships, etc. The activities of law enforcement officers are multifaceted and heterogeneous in their content, with irregular working hours, the emergence of systematic sources of stress (service conflicts, life crises, confrontation between personal and corporate values), and significant flows of service information being its integral elements. Moreover, law enforcement activities take place in conditions of constant manifestation of external stressors (instability of social dynamics, relations with the criminal environment, etc.), which hurts the performance and

mental health of law enforcement officers. Thus, scientists consider law enforcement to be one of the most nerve-wracking and stressful activities, the conditions of which lead to the formation of professional deformation of law enforcement officers. This manifests in protective reactions, maladjustment, negative experience, deterioration of health, etc. [11, 12]. That is why the search for ways to overcome professional stress in law enforcement officers is of significant scientific and applied importance since the negative impact of stress on their mental health leads to a decrease in the effectiveness of their law enforcement activities.

THE AIM

The aim is to investigate the impact of professional stress on the mental health of law enforcement officers. Objectives: 1) to identify the factors of professional stress in law enforcement officers; 2) to find out the impact of stress on their mental health during their service activities.

MATERIALS AND METHODS

The research involved two groups of law enforcement officers (aged 25-40) who attended advanced training courses at the National Academy of Internal Affairs (NAIA, Kyiv, Ukraine) in 2022: the first group with up to 7 years of service activities ($n = 52$), the second group – 8-15 years ($n = 48$). The criterion for the selection and formation of the study groups was the experience of law enforcement officers.

Research methods: bibliosemantic, questionnaire, testing, method of system analysis and generalization, mathematical and statistical. The bibliosemantic method was used to conduct an analytical review of scientific sources on the outlined range of issues (16 sources from the scientometric databases PubMed, Scopus, Web of Science Core Collection, Index Copernicus, and others were analyzed). The questionnaire method involved surveying police officers using a questionnaire developed by the author's team to study the factors of professional stress. The questionnaire contains 10 questions that assessed the frequency of the factors: a – never, b – sometimes, c – often, and d – always. The questionnaire was anonymous. The separate questionnaire was used to survey the managers of police units ($n = 39$) where the law enforcement officers involved in the research served to assess the impact of professional stress on the mental health of subordinate law enforcement officers in the course of their service activities. The questionnaire contains 13 statements-characteristics, according to which man-

agers assessed the mental health of subordinate law enforcement officers on a 5-point scale, where 1 point is a low level of characteristic manifestation, and 5 – a high level. Both questionnaires were anonymous. Both questionnaires were assessed by the experts in this field (5 professors and 7 associate professors) and was approved by the Academic Council of NAIA (Protocol No. 1 dated 12.09.2022). Consent to voluntary participation in the survey was obtained from all the cadets involved in the study.

Testing, as a method of scientific research, was used to assess the impact of professional stress on the mental health of law enforcement officers with different service experience. Two methods were used: 1) "Assessment of the Level of Professional Stress"; 2) "Inventory of Stress Symptoms" [13, 14]. The "Assessment of the Level of Professional Stress" method is based on the understanding of professional stress as an indicator of mental stress relevant at the time of measurement, which is interpreted as a level of threat to the employee's mental health. The examinee must indicate the frequency of occurrence of a particular stressful phenomenon in his or her professional activities. It contains 15 questions, for which the respondent gives 1 to 5 points for each proposed position. The data is processed by summing the scores. The higher the score, the higher the level of stress in the law enforcement officer's professional activities, and the greater the negative impact on his or her mental health. The level of professional stress is considered low if a law enforcement officer scores 15-30 points, average – 31-50 points, and high – 51-75 points. The "Inventory of Stress Symptoms" method allows one to assess the frequency of their occurrence and the degree of exposure of a law enforcement officer to the negative effects of stress. The subjects of interest were offered 20 stress symptoms to assess the frequency of their manifestations in their life-sustaining activities on a four-point scale: 1 – never, 2 – rarely, 3 – often, and 4 – always. Then the total number of points was calculated, which was used to determine the level of stress symptoms manifestation. The level of stress symptoms manifestation was considered low if the law enforcement officer scored up to 30 points, average – 31-45 points, high – 46-60 points, and very high – 61-80 points.

The method of system analysis and generalization was used to analyze the results obtained and formulate the conclusions of the research and practical recommendations for combating professional stress among law enforcement officers.

The methods of mathematical statistics were applied to correctly process the data and identify the difference between the indicators under study. The compliance of

the data distribution with the Gauss' law was assessed using the Shapiro-Wilk *W*-test. The authenticity of the difference between the indicators that were evaluated in percentages was determined by means of Chi-square (χ^2) Pearson's criterion (*T*). The authenticity of the difference between the indicators that were evaluated in points was determined by means of Student's test (*t*). The statistical significance for all statistical tests was set at $p < 0.05$. All statistical analyses were performed with the SPSS software, version 21, adapted to medical and biological researches. This research followed the regulations of the World Medical Association Declaration of Helsinki and ethical principles for medical research involving human subjects. Informed consent was received from all police officers who took part in this research.

RESULTS

The study results of the factors of professional stress occurrence in law enforcement officers with different service experience are presented in Table I.

It was found that the first group of respondents can be characterized by the occurrence of the following most significant factors of professional stress: 1) gaps in the management system of units and relations with the senior executives (often – 59.7 %); 2) high professional load, lack of adequate rest (often – 57.7 %, always – 19.2 %); 3) tension in communication with participants of professional relations (often – 53.8 %, always – 25.0 %); 4) insufficient salary (often – 53.8 %, always – 21.2 %); 5) the imperfection and constant changes in the legislation regulating law enforcement activities (often – 53.8 %, always – 23.1 %). The second group of law enforcement officers was characterized by: 1) heavy professional workload, lack of adequate rest (often – 52.1 %, always – 16.7 %); 2) insufficient salary (often – 50.0 %, always – 29.1 %); 3) tension in communication with participants of professional relations (often – 47.9 %, always – 18.8 %); 4) constant shortage of time (often – 47.9 %, always – 12.5 %); 5) the imperfection and constant changes in the legislation regulating law enforcement activities (often – 45.8 %, always – 22.9 %). The data obtained indicate that both groups of respondents to a greater or lesser extent highlight the indicators of heavy professional workload, lack of adequate rest, and the special nature of communication with participants of professional relations. At the same time, no significant difference ($p > 0.05$) was found between the groups for all the factors studied, which confirms the presence of factors of professional stress occurrence in the service activities of law enforcement officers with different experience.

The analysis of the results obtained using the "Assessment of the Level of Professional Stress" method indicates the presence of professional stress in law enforcement officers with different experience, which negatively affects their mental health (Table II).

It was found that only 3.8 % of law enforcement officers of the first group and 2.1 % of the second group have a low level of professional stress and, accordingly, a high level of mental health. This indicates that both groups of law enforcement officers are characterized by daily stressful service activities, a high level of reduced productivity, and the likelihood of complications in the physiological and mental spheres of activities. Law enforcement officers of the second group have an average level of professional stress (56.2%) (compared to the first group, where a high level of 55.8 % prevails). First of all, this can be explained by the fact that over the course of a longer service career (8-15 years), the emotionality of social interaction is gradually lost, and the facts of the surrounding reality and objects of professional communication are already perceived as quite typical and ordinary. There is a decrease in the degree of satisfaction with everyday activities. However, no significant difference was found between the indicators of both groups of law enforcement officers ($p > 0.05$).

The results obtained using the "Inventory of Stress Symptoms" method are presented in Table III.

It was found that only 1.9 % of respondents with up to 7 years of service experience and 2.1 % with 8-15 years of experience have low levels of professional stress symptoms manifestation. The vast majority of surveyed law enforcement officers with 8-15 years of experience (47.9 %) and those with up to 7 years of experience (38.5 %) were characterized by average levels of professional stress manifestation. On the other hand, 53.8 % of respondents with up to 7 years of service activities and 45.8 % with 8-15 years of service activities had a high level of professional stress symptoms manifestation ($p > 0.05$). Systematic stressful phenomena in the indicators of service activities cause excessive mental stress, provoke a deterioration of relations with colleagues and senior executives, and can gradually lead to emotional burnout and professional deformation as inevitable processes.

The survey of senior executives ($n = 39$) of police units confirmed our previous findings and showed that certain indicators of the mental health of subordinate law enforcement officers significantly deteriorate with the experience of their professional activities (Table IV).

It was found that law enforcement officers with up to 7 years of service experience are more anxious but better motivated, more productive, and vigorous; they have a strong interest in their career, sensitivity to colleagues

Table I. Factors of professional stress occurrence in law enforcement officers with different professional experience (%)

Factors of professional stress occurrence	Frequency of manifestation	Groups of law enforcement officers studied		Significance of the difference	
		The first group (up to 7 years of service, n = 52)	The second group (8-15 years of service, n = 48)	T	p
Imperfection and constant changes in the legislation regulating law enforcement activities	a	9.6	10.4	0.86	>0.05
	b	13.5	20.8		
	c	53.8	45.8		
	d	23.1	22.9		
High level of personal responsibility for the decision made in conditions of information uncertainty	a	7.7	16.7	5.13	>0.05
	b	28.8	33.3		
	c	48.1	39.6		
	d	15.4	10.4		
Riskiness of the functions performed	a	13.5	18.7	0.62	>0.05
	b	26.9	29.2		
	c	48.1	41.7		
	d	11.5	10.4		
High professional load, lack of adequate rest	a	5.8	6.3	1.28	>0.05
	b	17.3	25.0		
	c	57.7	52.1		
	d	19.2	16.7		
Constant shortage of time	a	9.6	6.3	1.91	>0.05
	b	23.1	33.3		
	c	51.9	47.9		
	d	15.4	12.5		
Tension in communication with participants of professional relations	a	7.7	10.4	8.43	>0.05
	b	13.5	22.9		
	c	53.8	47.9		
	d	25.0	18.8		
Constant interaction with representatives of the criminal world	a	11.5	12.5	1.47	>0.05
	b	32.8	14.6		
	c	44.2	43.7		
	d	11.5	29.2		
Insufficient salary	a	5.8	6.3	5.11	>0.05
	b	19.2	14.6		
	c	53.8	50.0		
	d	21.2	29.1		
Gaps in the management system and relations with senior executives	a	9.6	10.4	7.47	>0.05
	b	19.2	20.8		
	c	59.7	43.8		
	d	11.5	25.0		
Performing additional functions not provided for by functional responsibilities	a	5.8	12.5	4.70	>0.05
	b	25.0	33.3		
	c	50.0	41.7		
	d	19.2	12.5		

Legend: a – never; b – sometimes; c – often; d – always; T – the value of χ^2 – criterion; $T_{critical} = 9.50$; p – significance of the difference between the indicators of the study groups

Table II. The level of professional stress and mental health among law enforcement officers with different service experience (%)

Level of professional stress	Level of mental health	Groups of law enforcement officers studied		Significance of the difference	
		The first group (up to 7 years of service, n = 52)	The second group (8-15 years of service, n = 48)	T	p
Low	High	3.8	2.1	5.11	>0.05
Average	Average	40.4	56.2		
High	Low	55.8	41.7		

Legend: T – the value of χ^2 – criterion; $T_{critical} = 9.50$; p – significance of the difference between the indicators of the study groups

Table III. Indicators of stress symptoms manifestation in law enforcement officers with different service experience (%)

Level of stress symptoms manifestation	Groups of law enforcement officers studied		Significance of the difference	
	The first group (up to 7 years of service, n = 52)	The second group (8-15 years of service, n = 48)	T	p
Low	1.9	2.1	0.96	>0.05
Average	38.5	47.9		
High	53.8	45.8		
Very high	5.8	4.2		

Legend: T – the value of χ^2 – criterion; $T_{critical} = 9.50$; p – significance of the difference between the indicators of the study groups

Table IV. Assessment of mental health indicators of subordinate law enforcement officers with different professional experience by unit senior executives ($M \pm m$), points

Indicators characterizing the mental health of law enforcement officers	Groups of law enforcement officers studied		Significance of the difference	
	The first group (up to 7 years of service, n = 52)	The second group (8-15 years of service, n = 48)	t	p
Anxiety	3.9±0.18	3.2±0.20	2,60	<0.05
Sociability	3.7±0.16	4.1±0.19	1,61	>0.05
Aggressiveness	1.8±0.20	2.7±0.21	3,10	<0.01
Motivation	4.9±0.21	3.6±0.22	2,30	<0.05
Criticism in work	2.9±0.19	3.4±0.19	1,86	>0.05
Sensitivity to colleagues	3.5±0.18	3.0±0.20	1,85	>0.05
Personal detachment	2.1±0.22	3.1±0.19	3,44	<0.01
Impulsiveness	2.2±0.19	3.4±0.23	4,02	<0.001
Vigor	4.1±0.16	3.2±0.20	3,51	<0.01
Conflicting nature	2.6±0.17	3.1±0.19	1,96	>0.05
Responsibility	3.4±0.20	4.1±0.19	2,54	<0.05
Interest in career	4.6±0.16	4.2±0.18	1,66	>0.05
Work efficiency	4.2±0.17	3.4±0.21	2,96	<0.01

Legend: t – Student's t-test value; p – the significance of the difference between the indicators of the study groups

and objects of professional relationships; they are less prone to conflicts. On the other hand, law enforcement officers with 8-15 years of experience are more responsible, although they no longer have the same vigor and interest in their work, their attitude towards colleagues and work in general changes in some way; they become more impulsive, critical and aggressive, and show a certain indifference to career success. It can also be

argued that with the experience of service and under the influence of systematic stress, there is a gradual decline in the effectiveness and vigorous attitude of law enforcement officers, as well as their detachment from the professional environment. The comparative analysis of the two groups showed that law enforcement officers with 8-15 years of service experience had significantly ($p < 0.05-0.001$) worse indicators of anxiety, aggressive-

ness, motivation, personal detachment, impulsiveness, vigor, and work efficiency. All this gives us grounds to assert that the greater the experience of professional activities, the more pronounced the negative impact of professional stress on the indicators of mental health of law enforcement officers.

DISCUSSION

According to many scientists [2-3, 5, 7], stress is a nonspecific reaction of an organism in response to an unexpected and tense situation. At its core, this reaction reflects the emergency mobilization of an organism's internal resources to overcome an obstacle or protect itself from its harmful effects. Strong external stimuli (worries, negative emotions) caused by stress are very dangerous for the human nervous system. They can disrupt the balance, lead to the formation of foci of stagnant brain excitation, and this, in turn, contributes to the development of psychosomatic changes in the personality.

Some scholars [1, 4, 8-10] rightly note the negative impact of professional stress on employees in the form of health problems, low motivation, reduced occupational safety, etc. This is also confirmed by the analysis of literature [12, 15, 16], pointing to the processes of exhaustion, loss of well-being, and productivity among representatives of socio-economic professions, including law enforcement officers. Researchers [9, 11] have also established the connection between professional stress and changes in the functional state of the organism, various psychosomatic diseases, and somatoform disorders provoked by significant physical and mental workload. This is because stress can intensify and develop, causing some specific changes in the organism. Instead, the human psyche tries to protect itself from stress, prevent it, or suppress it. However, the capabilities of the organism have their limits, and therefore, they are quickly exhausted in the case of a strong and systematic stressful impact.

Based on the research, we developed practical recommendations for providing psychological assistance to law enforcement officers to effectively counteract professional stress and improve their mental health.

1. Within the framework of *the resource-management approach*, psychological assistance measures are aimed at mitigating the factors contributing to the emergence of professional stress in law enforcement officers during their service activities:

- organizational development and unification of working groups of employees;
- stimulation of a favorable atmosphere for the team functioning;

- competent management support for staff;
- effective management that is adequate to the stage of development of a particular law enforcement agency;
- defining standards of formal and informal behavior of law enforcement officers;
- fair personnel policy and qualification career development of personnel;
- clear and balanced system of incentives for law enforcement officers, etc.

2. As part of *the restorative approach*, psychological assistance includes measures to restore the psycho-energetic resources of law enforcement officers and overcome the negative effects of professional stress. This is facilitated by conducting various educational and rehabilitation training, using psychological relief rooms, organizing corporate holidays, etc. The main goal of such measures should be to create a comfortable psychological environment that would help restore physical and mental strength, develop an adequate assessment of work processes, practice conflict-free communication skills, creative thinking, etc.

CONCLUSIONS

It was found that law enforcement officers of both groups identified indicators of a significant professional workload, lack of adequate rest, and the nature of communication with participants in professional relationships among the factors of professional stress. It is proved that the mental health of law enforcement officers deteriorates under the influence of professional stress with the experience of their professional activities. Law enforcement officers with 8-15 years of service experience revealed significantly ($p < 0.05-0.001$) worse indicators of anxiety, aggressiveness, motivation, personal detachment, impulsiveness, vigor, and work efficiency.

It was established that the professional stress of law enforcement officers is the result of an imbalance between the internal resources of the individual and the requirements of the external environment, embodied in the peculiarities of law enforcement activities. Law enforcement officers are characterized by the presence of professional stress of average and high severity, which increases with the experience of their service activities. A set of measures was proposed to provide psychological assistance to law enforcement officers to effectively counteract professional stress and improve their mental health.

Prospects for further research are to investigate the effect of professional stress on the state of mental health of servicemen.

REFERENCES

1. Grupe DW, McGehee C, Smith C et al. Mindfulness training reduces PTSD symptoms and improves stress-related health outcomes in police officers. *J Police Crim Psychol.* 2021;36(1):72-85. doi:10.1007/s11896-019-09351-4.
2. Galanis P, Fragkou D, Katsoulas TA. Risk factors for stress among police officers: A systematic literature review. *Work.* 2021;68(4):1255-1272. doi:10.3233/WOR-213455.
3. Cieślak I, Kielan A, Olejniczak D et al. Stress at work: The case of municipal police officers. *Work.* 2020;65(1):145-152. doi:10.3233/WOR-193067.
4. Okhrimenko IM, Lyhun NV, Pryimak VP et al. Negative factors of management activities of the security and defence sector representatives and directions of their overcoming. *Wiad Lek.* 2021;74(4):891-895. doi: 10.36740/WLek202104115.
5. Patterson GT, Chung IW, Swan PW. Stress management interventions for police officers and recruits: A meta-analysis. *Journal of Experimental Criminology.* 2014;10:487-513. doi:10.1007/s11292-014-9214-7.
6. Bondarenko V, Okhrimenko I, Piaskovskiy V et al. Scientific tools for forming professional competence of patrol police officers. *International Journal of Evaluation and Research in Education.* 2022;11(2):687-695. doi: 10.11591/ijere.v11i2.21987.
7. Queirós C, Passos F, Bártolo A et al. Burnout and stress measurement in police officers: Literature review and a study with the operational police stress questionnaire. *Front Psychol.* 2020;11:587. doi:10.3389/fpsyg.2020.00587.
8. Schilling R, Herrmann C, Ludyga S et al. Does cardiorespiratory fitness buffer stress reactivity and stress recovery in police officers? A real-life study. *Front Psychiatry.* 2020;11:594. doi:10.3389/fpsyg.2020.00594.
9. Habersaat SA, Geiger AM, Abdellaoui S, Wolf JM. Health in police officers: Role of risk factor clusters and police divisions. *Soc Sci Med.* 2015;143:213-222. doi: 10.1016/j.socscimed.2015.08.043.
10. Civilotti C, Acquadro Maran D, Garbarino S, Magnavita N. Hopelessness in police officers and its association with depression and burnout: A pilot study. *Int J Environ Res Public Health.* 2022;19(9):5169. doi:10.3390/ijerph19095169.
11. Okhrimenko IM, Pasko OM, Prudka LM et al. The influence of modern sports technologies on health and professional activity of law enforcement officers. *Wiad Lek.* 2021;74(6):1365-1371. doi: 10.36740/WLek202106115.
12. Wu X, Liu Q, Li Q et al. Health-related quality of life and its determinants among criminal police officers. *Int J Environ Res Public Health.* 2019;16(8):1398. doi:10.3390/ijerph16081398.
13. Aleksandrov DO, Davydova OV. Diahnostyka osobystosti pratsivnyka OVS v systemi psykholohichnoho suprovodzhennya [Diagnosis of the personality of a law enforcement officer in the system of psychological support]. Kyiv: National Academy of Internal Affairs. 2015. (in Ukrainian).
14. Barrett GV, Miguel RF, Hurd JM et al. Practical issues in the use of personality tests in police selection. *Public Personnel Management.* 2003;32(4):45-57. doi:10.1177/009102600303200403.
15. Queirós C, Passos F, Bártolo A et al. Job stress, burnout and coping in police officers: Relationships and psychometric properties of the organizational police stress questionnaire. *Int J Environ Res Public Health.* 2020;17(18):6718. doi:10.3390/ijerph17186718.
16. Mojallal M, Simons RM, Quevillon RP, Hatwan ML. Associations of experiential avoidance with burnout, wellbeing, and productivity loss among police officers: The mediating role of negative and positive affect. *J Clin Psychol.* 2022;78(11):2260-2280. doi:10.1002/jclp.23371.

This scientific article was carried out according to the plan of the research work of the National Academy of Internal Affairs for 2020-2023 "Psychological, pedagogical and sociological support of law enforcement officers» (state registration number 0113U008196).

ORCID and contributionship:

Ivan M. Okhrimenko: 0000-0002-8813-5107^{B,D}

Vadym V. Barko: 0000-0002-3836-2627^A

Lesia V. Vavryk: 0000-0002-0175-1880^F

Vadym D. Chornous: 0000-0002-9239-5382^C

Svitlana S. Okhrimenko: 0000-0002-9013-9780^{B,D}

Yurii V. Aleksandrov: 0000-0002-5871-8344^F

Larysa M. Onishchuk: 0000-0002-5411-149X^{C,F}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Ivan M. Okhrimenko

National Academy of Internal Affairs

1 Solom'yanska Square, 03035 Kyiv, Ukraine

tel: +380679903905

e-mail: ivango-07@ukr.net

Received: 17.12.2022

Accepted: 22.05.2023

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

ORIGINAL ARTICLE

DYNAMICS OF STUDENTS' PHYSICAL WELL-BEING INDICATORS DURING QUARANTINE RESTRICTIONS

DOI: 10.36740/WLek202306116

Oleksandr O. Sabirov, Zoia V. Syrovatko, Viktoriia M. Yefremenko, Nataliia Ye. Havrylova, Olena K. Syrotynska, Anna Yu. Chekhovska, Oleksandr D. Mokhunko
NATIONAL TECHNICAL UNIVERSITY OF UKRAINE "IGOR SIKORSKY KYIV POLYTECHNIC INSTITUTE", KYIV, UKRAINE

ABSTRACT

The aim: To study the dynamics of students' physical well-being and physical fitness during the quarantine restrictions caused by the COVID-19 pandemic.

Materials and methods: The research involved 263 students (148 men and 115 women) aged 18-20. Depending on the volume of physical activity performed by students during quarantine restrictions, they were divided into three groups (with sufficient, high, and low volume). The physical well-being of students was determined by the method proposed by Ye. A. Pyrohova. The level of physical fitness was determined by the results of students' performance of the exercises.

Results: The most pronounced negative changes in physical well-being indicators were found in group C students (both men and women), whose volume of motor activity during quarantine restrictions was low. Among the physical qualities, the level of endurance of students was the most negatively affected.

Conclusions: It was found that physical exercises have a positive effect on students' physical well-being during quarantine restrictions. The rational use of physical education makes it possible to mobilize the reserve motor capabilities of the students' body, offset the negative impact of low motor activity and sedentary lifestyle during quarantine restrictions, and help maintain the physical well-being and level of physical fitness at the proper level.

KEY WORDS: physical activity, physical well-being, physical fitness, students

Wiad Lek. 2023;76(6):1436-1442

INTRODUCTION

Training of competitive, highly qualified, harmoniously developed, and healthy professionals is one of the main tasks facing higher educational institutions (HEIs) in Ukraine. "Physical Education" is one of the main academic subject areas in higher educational institutions that contributes to the effective solution of this task and was a compulsory academic subject until 2015. At the same time, according to scientists [1, 2], the health and fitness level of student youth has rapidly deteriorated over the past decade. The concept of reforming the sphere of physical education in higher educational institutions, which was aimed at improving the catastrophic situation with the state of health of young people, in practice first manifested itself in a decrease in the number of ECTS credits allocated for teaching the academic subject area referred to as "Physical Education", then in an attempt to organize it as an elective (extra-credit academic subject without final control and inclusion in the curriculum and compulsory attendance). This was manifested in the fact that in many Ukrainian HEIs, the academic load for physical education during the 1-2 instructional years was reduced to two hours per week,

and the academic subject was transferred to the status of an educational component of students' choice or removed altogether in the senior instructional years. The works of scientists [3, 4] indicate that the transition from compulsory academic training sessions to a system of voluntary participation of students in physical education has led to a significant decrease in the involvement of students in specially organized motor activity in the conditions of studying in HEIs and a deterioration in their health and physical fitness. As a result, the level of motor activity of most modern youth does not meet the established age-related physiological norms and is no more than 20 %, i. e. 1/5 of the proper level, which is one of the lowest in Europe [5].

The situation worsened even more with the onset of the COVID-19 pandemic and forced quarantine measures [6, 7]. According to experts [8], in the conditions of extremely limited motor activity during the introduction of quarantine measures, when students are forced to spend all their time only on mental activities, there is a situation where learning takes place "at the expense of health". However, the quality of higher education is equated with the quality of training of employable

specialists, which is ensured by the proper state of their health and is the main driver of progress in all spheres of society and the state. That is why the issue of preserving students' health and maintaining their physical well-being and fitness during quarantine restrictions cannot be considered outside the context of physical education. Scientists [9] argue that under quarantine restrictions, independent training sessions using all possible types of physical activities are the basis of students' physical education. Human physical activity is directly related to the body's ability to adequately respond to external threats in the form of viruses and to resist them with maximum efficiency [10]. Systematic exercise will improve physical and mental health, ensure that students' physical well-being and fitness are maintained at the proper level, and strengthen their immune system [11].

THE AIM

The aim is to study the dynamics of students' physical well-being and physical fitness during the quarantine restrictions caused by the COVID-19 pandemic.

MATERIALS AND METHODS

The research involved 263 students (148 men and 115 women) of the main division aged 18-20 years who entered the National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute" (Kyiv, Ukraine) in 2019 at the Faculty of Radio Engineering, Faculty of Chemical Engineering and Faculty of Electric Power Engineering and Automatics. The research was conducted during 2020-2021. Depending on the volume of physical activity performed by students during quarantine restrictions, they were divided into three groups (with sufficient, high, and low volume): group A (77 men and 56 women) – students who performed physical exercises only within the distance course referred to as "Physical Education: Distance Learning", conducted by teachers of the Department of Health and Sports Technologies, twice a week for 90 minutes each (sufficient volume); group B (39 men and 32 women) – students who performed physical exercises within the framework of the specified course and additionally (independently or in sports clubs) in the amount of 5-6 hours or more (high volume); group C (34 men and 27 women) – students who for various reasons (laziness, lack of interest, lack of desire, mood, lack of time, etc.) did not perform physical exercises either within the specified course or additionally (low volume). The students were divided into groups based on the results of a survey conducted at the end of quarantine.

A questionnaire created by the authors of this article was used for the survey in accordance with the re-

quirements of the Code of Ethics of National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute". The questionnaire contains 5 questions and is aimed at studying the amount of motor activity of students during quarantine. The questionnaire was assessed by the experts in this field (2 professors and 4 associate professors) and was approved by the Academic Council of National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute" (Protocol No. 11 dated 28.07.2020). The survey was anonymous. Consent to voluntary participation in the survey was obtained from all the students involved in the study.

The physical well-being of students was assessed by indicators of their body weight, body length, age, heart rate, and blood pressure and was determined by the formula of the physical well-being index (PW-BI) proposed by Ye. A. Pyrohova [12]: $PW-BI = (700 - 3 \cdot HR - 2.5 \cdot BP_{avg} - 2.7 \cdot age + 0.28 \cdot body\ weight) / (350 - 2.6 \cdot age + 0.21 \cdot body\ length)$, where BP_{avg} is the average blood pressure (mm Hg), which was determined by the formula: $BP_{avg} = ((SBP - DBP) / 3) + DBP$, where SBP is systolic blood pressure and DBP is diastolic blood pressure. The ranking of physical well-being levels by PW-BI was carried out according to Table 1.

The level of physical fitness was determined by the results of students' performance of the following exercises: 100 m run (speed qualities), pull-ups (males), push-ups (females) (strength qualities), 3000 m run (males), and 2000 m run (females) (endurance). The assessment was conducted under the Regulations on State Tests and Standards for Assessment of Physical Fitness of the Population of Ukraine. The testing took place in the morning. The uniform was sportswear. The study of the level of physical well-being and physical fitness of students was conducted before the introduction of quarantine restrictions and after their cancellation. The duration of quarantine restrictions is 6 months.

The methods of investigation: questionnaire survey, testing, methods of mathematical statistics, theoretical analysis and generalization of the scientific and methodological literature: 19 sources on the topic of the article from the scientometric databases PubMed, Scopus, Web of Science Core Collection and others were analyzed. Statistical processing of the obtained results was carried out by methods of variation statistics using the STATISTICA 6.1 software package (number AGAR909E415822FA). The compliance of the data distribution with the normal law (Gauss' law) was assessed using the Shapiro-Wilk W-test. The results were presented as $(M \pm m)$, where M is the arithmetic mean, m is the error of the arithmetic mean. The authenticity of the difference between the indicators of students of studied groups was determined by Student's t-test. The

Table I. The ranking of physical well-being levels by PW-BI, c.u.

Well-being levels	Range of PW-BI values
Low	≤ 0.375
Below average	0.376–0.525
Average	0.526–0.675
Higher than average	0.676–0.825
High	≥ 0.826

Table II. Dynamics of students’ physical well-being indicators during quarantine restrictions (males – n = 148, females – n = 115), M ± m

Studied indicators	Groups	Gender	n	Stages of quarantine restrictions		Significance of the differences		
				Before	After	t	p	
Body weight, kg	A	m	77	73.5±1.23	74.8±1.37	0.71	>0.05	
		f	56	57.3±1.19	58.1±1.21	0.47	>0.05	
	B	m	39	73.8±1.42	74.2±1.45	0.20	>0.05	
		f	32	57.5±1.29	57.8±1.30	0.16	>0.05	
	C	m	34	73.7±1.36	75.9±1.40	1.13	>0.05	
		f	28	57.9±1.31	59.6±1.33	0.91	>0.05	
	HR, bpm	A	m	77	72.5±0.52	72.7±0.53	0.11	>0.05
			f	56	70.1±0.61	70.2±0.60	0.12	>0.05
B		m	39	71.3±0.58	70.8±0.56	0.62	>0.05	
		f	32	69.8±0.64	69.8±0.63	0.00	>0.05	
C		m	34	72.4±0.55	72.9±0.56	0.64	>0.05	
		f	28	70.6±0.68	71.3±0.70	0.72	>0.05	
PW-BI, c.u.		A	m	77	0.651±0.005	0.643±0.005	1.13	>0.05
			f	56	0.662±0.006	0.656±0.006	0.71	>0.05
	B	m	39	0.684±0.006	0.695±0.006	1.30	>0.05	
		f	32	0.691±0.006	0.705±0.005	1.79	>0.05	
	C	m	34	0.632±0.007	0.613±0.006	2.06	<0.05	
		f	28	0.647±0.006	0.629±0.006	2.12	<0.05	

Legend: M – arithmetic mean, m – error of the arithmetic mean, m – male students, f – female students, t – Student’s t-test value, p – significance of the difference between the indicators of studied groups before and after the quarantine restrictions

level of threshold statistical significance of the research results was chosen as $p < 0.05$.

This study complies with the ethical standards of the Act of Ukraine “On Higher Education” No. 1556-VII dated 01.07.2014 and the Letter from the Ministry of Education and Science of Ukraine “On the Academic Plagiarism Prevention” No. 1/11-8681 dated 15.08.2018. Also, this study followed the regulations of the World Medical Association Declaration of Helsinki – ethical principles for medical research involving human subjects. Informed consent was received from all individuals who took part in this research.

RESULTS

An important criterion for human health and physical working capacity is the level of physical well-being,

which is determined by a set of factors, among which the main ones are cardiovascular system indicators and body weight. These indicators are most adversely affected by quarantine restrictions, in particular low motor activity, and have the greatest impact on the physical well-being index. The results of the analysis of the dynamics of these indicators and the physical well-being index are presented in Table II.

The most pronounced negative changes in the physical well-being indicators of students are observed in group C (both among male and female students). Thus, during the period of self-isolation, male students increased their body weight by 2.2 kg ($p > 0.05$), and female students – by 1.7 kg ($p > 0.05$). Heart rate deteriorated by 0.5 and 0.7 bpm, respectively ($p > 0.05$). Body weight indicators also slightly deteriorated in groups A and B but the difference between initial and

Table III. Dynamics of students' physical fitness indicators during quarantine restrictions (males – n = 148, females – n = 115), M ± m

Physical qualities	Groups	Gender	n	Stages of quarantine restrictions		Significance of the differences		
				Before	After	t	p	
Speed qualities, s	A	m	77	14.4±0.09	14.6±0.10	1.49	>0.05	
		f	56	16.8±0.10	16.9±0.11	0.67	>0.05	
	B	m	39	14.3±0.12	14.3±0.13	0.00	>0.05	
		f	32	16.4±0.11	16.5±0.12	0.61	>0.05	
	C	m	34	14.5±0.13	14.7±0.13	1.09	>0.05	
		f	28	16.8±0.12	17.1±0.13	1.70	>0.05	
	Strength qualities, times	A	m	77	9.5±0.54	9.1±0.56	0.51	>0.05
			f	56	13.2±0.63	13.1±0.61	0.11	>0.05
B		m	39	10.2±0.49	10.4±0.51	0.28	>0.05	
		f	32	13.5±0.71	13.6±0.73	0.10	>0.05	
C		m	34	9.2±0.52	7.6±0.50	2.22	<0.05	
		f	28	12.8±0.65	10.9±0.67	2.04	<0.05	
Endurance, s		A	m	77	837.3±11.08	875.7±11.64	2.39	<0.05
			f	56	703.6±9.96	745.1±10.23	2.91	<0.05
	B	m	39	826.2±12.37	848.4±12.86	1.24	>0.05	
		f	32	689.5±10.18	712.7±10.67	1.57	>0.05	
	C	m	34	852.8±12.62	896.5±12.91	2.42	<0.05	
		f	28	709.4±11.07	758.9±11.58	3.09	<0.05	

Legend: M – arithmetic mean, m – error of the arithmetic mean, m – male students, f – female students, t – Student's t-test value, p – significance of the difference between the indicators of studied groups before and after the quarantine restrictions

final data was not significant ($p > 0.05$) and was smaller compared to group C. No significant changes in heart rate were observed in groups A and B ($p > 0.05$). It is important to note that the greatest changes during the quarantine period were in students' PW-BI: PW-BI deteriorated insignificantly ($p > 0.05$) in group A by 0.008 c. u. among men and by 0.006 c. u. among women; this indicator improved insignificantly ($p > 0.05$) by 0.011 c. u. and 0.014 c. u., respectively in group B; PW-BI deteriorated significantly ($p < 0.05$) by 0.019 c. u. and 0.018 c. u., respectively in group C. At the same time, in groups A and C, both before and after the end of quarantine restrictions, the PW-BI was at an average level, and in group B it was above average. This shows that physical exercises have a positive effect on the physical well-being of students during quarantine restrictions.

The analysis of the dynamics of students' physical fitness indicators during quarantine restrictions showed that the least influence was on the indicators of the development of speed qualities among the studied physical qualities, and the greatest – endurance (Table III). The most expressed negative changes took place in group C among the studied groups of students.

Results in the 100 m run deteriorated by 0.1-0.3 s in all groups, but did not change significantly during the

research period ($p > 0.05$). In terms of strength exercises, there was an insignificant ($p > 0.05$) deterioration in the students' indicators, both men and women, by 0.3 and 0.1 times, respectively in group A; strength indicators even improved by 0.2 and 0.1 times ($p < 0.05$), respectively in group B, and they deteriorated significantly ($p < 0.05$) by 1.6 and 1.9 times, respectively in group C. Negative dynamics are observed in all studied groups of students when it comes to endurance exercises but the difference between the initial and final data is not significant ($p > 0.05$) in group B, and it is significant ($p < 0.05$) in groups A and C. However, while the indicators in the 3000 m and 2000 m run deteriorated by 38.4 s and 41.5 s, respectively in group A, the situation deteriorated by 43.7 s and 49.5 s, respectively in group C. This shows that quarantine restrictions and distance learning hurt students' physical fitness in general and their endurance level in particular.

DISCUSSION

The task of higher education today is to prepare a healthy, educated personality with a high level of culture, capable of critical and creative thinking, proficient in terms of self-development, professional and personal self-actualization. However, according to experts [5, 13], today in

Ukraine there is a steady deterioration in the health and physical fitness of students, a low level of their physical culture, a lack of need and habit of regular motor activity, and insufficient involvement of young people in physical exercise during their extracurricular activities. A particularly sharp decline in students' motor activity is observed during quarantine restrictions. Studies conducted by experts [14] have shown that the transition of the education system to a remote mode due to quarantine restrictions has increased the burden on all participants in the educational process (teachers, students, parents), which has led to changes in their health, both mental and physical. According to scientists [15], during the quarantine period, a decrease in motor activity is usually associated with an irrational student's daily routine: when studying educational material remotely, the time when students are forced to maintain an uncomfortable static position while sitting at their workplace and limit their natural physical activity increases. A negative consequence of reduced motor activity is the exacerbation of symptoms of existing chronic diseases and the deterioration of the main functional systems of the body. There is weakness and lethargy of the muscles, impaired general cerebral circulation, venous stasis in the lower extremities, and decreased body working capacity [16].

Experts strongly recommend maintaining an active lifestyle during quarantine, as much as possible in conditions of limited movement, following the usual daily routine, and staying physically active. Physical activity is an important component of disease prevention, strengthening the immune system, and improving its ability to respond to pathogens [17]. People who regularly performed moderate physical activity had a much higher chance of a mild course of the disease in case of coronavirus infection. Physical activity also helps reduce the risks of cardiovascular disease, diabetes, hypertension, and depression [18].

According to the authors [15], who studied physical activity during COVID-19, in the spring of 2020, people's daily activity decreased by about 12 % on average worldwide compared to the spring of 2019. The most popular types of motor activity during the quarantine restrictions were walking and stationary bicycle riding. The number of stair-climbing workouts has increased dramatically. Compared to 2019, when more than half of all indoor training sessions were strength training,

in the spring of 2020, about half of all training sessions were focused on cardio. In addition, scientists [19] have found that people who led the most active lifestyles began to devote even more time to sports during quarantine. Conversely, people who led a sedentary lifestyle began to move even less. That is, the choice of motor activity during quarantine in favor of one's health and healthy lifestyle is a conscious choice of students who must understand the importance of their physical well-being and its impact on their quality of life and working capacity. People who lead an active lifestyle become more resilient and competitive than those who neglect motor activity and exercise. The results of our research confirmed the findings of many scientists that students who maintained a high level of personal motor activity and at least a sufficient level had a better level of physical well-being and physical fitness indicators after the quarantine restrictions abolishment than students whose motor activity was low.

CONCLUSIONS

The dynamics of students' physical well-being and physical fitness indicators during the quarantine restrictions caused by the COVID-19 pandemic were investigated. The most pronounced negative changes in physical well-being indicators (body weight, heart rate, PW-BI) were found in group C students (both men and women), whose volume of motor activity during quarantine restrictions was low. Among the physical qualities of students, the least affected during the quarantine period were indicators of speed qualities development, and the greatest – endurance. It was found that quarantine restrictions negatively affect the physical well-being and physical fitness of students. It was found that physical exercises have a positive effect on students' physical well-being during quarantine restrictions. The rational use of physical education makes it possible to mobilize the reserve motor capabilities of the students' body, offset the negative impact of low motor activity and sedentary lifestyle during quarantine restrictions, and help maintain the physical well-being and level of physical fitness at the proper level.

Prospects for further research are aimed at studying the dynamics of indicators of students' mental and physical health during the self-isolation period.

REFERENCES

1. Kljajević V, Stanković M, Đorđević D et al. Physical Activity and Physical Fitness among University Students-A Systematic Review. *Int J Environ Res Public Health*. 2021;19(1):158. doi:10.3390/ijerph19010158.
2. Sevil J, Práxedes A, Abarca-Sos A et al. Levels of physical activity, motivation and barriers to participation in university students. *J Sports Med Phys Fitness*. 2016;56(10):1239-1248.

3. Griban GP, Kuznietsova OT, Lyakhova NA et al. Dynamics of students' fitness level while differentiating physical education classes in accordance with their health and nosology of diseases. *Wiad Lek.* 2021;74(3 cz 2):641-646.
4. Griban GP, Kosheleva OO, Mitova OO et al. Physical development of students as an indicator of the physical education system functioning in the educational institution. *Wiad Lek.* 2022;75(6):1446-1452. doi:10.36740/WLek202206104.
5. Długosz P, Liszka D, Bastrakova A, Yuzva L. Health Problems of Students during Distance Learning in Central and Eastern Europe: A Cross-Sectional Study of Poland and Ukraine. *Int J Environ Res Public Health.* 2022;19(16):10074. doi:10.3390/ijerph191610074.
6. Castañeda-Babarro A, Arbillaga-Etxarri A, Gutiérrez-Santamaría B, Coca A. Physical activity change during COVID-19 confinement. *Int J Environ Res Public Health.* 2020; 17(18): 6878. doi: 10.3390/ijerph17186878.
7. Romero-Blanco C, Rodríguez-Almagro J, Onieva-Zafra MD et al. Physical activity and sedentary lifestyle in university students: Changes during confinement due to the COVID-19 Pandemic. *Int J Environ Res Public Health.* 2020;17(18):6567. doi:10.3390/ijerph17186567.
8. Sepúlveda-Loyola W, Rodríguez-Sánchez I, Pérez-Rodríguez P et al. Impact of social isolation due to COVID-19 on health in older people: Mental and physical effects and recommendations. *J Nutr Health Aging.* 2020; 24(9): 938-947. doi: 10.1007/s12603-020-1469-2.
9. Luciano F, Cenacchi V, Vegro V, Pavei G. COVID-19 lockdown: Physical activity, sedentary behaviour and sleep in Italian medicine students. *Eur J Sport Sci.* 2021;21(10):1459-1468. doi:10.1080/17461391.2020.1842910.
10. Wilson OWA, Holland KE, Elliott LD et al. The Impact of the COVID-19 Pandemic on US College Students' Physical Activity and Mental Health. *J Phys Act Health.* 2021;18(3):272-278. doi:10.1123/jpah.2020-0325.
11. Boukrim M, Obtel M, Kasouati J et al. Covid-19 and Confinement: Effect on Weight Load, Physical Activity and Eating Behavior of Higher Education Students in Southern Morocco. *Ann Glob Health.* 2021;87(1):7. doi:10.5334/aogh.3144.
12. Mykhailiuk EL. Functional tests in sports medicine: methodical recommendations. Kyiv. 2005, p.38.
13. Bergier J, Tsos A, Popovych D et al. Level of and Factors Determining Physical Activity in Students in Ukraine and the Visegrad Countries. *Int J Environ Res Public Health.* 2018;15(8):1738. doi:10.3390/ijerph15081738.
14. Guo YF, Liao MQ, Cai WL et al. Physical activity, screen exposure and sleep among students during the pandemic of COVID-19. *Sci Rep.* 2021;11(1):8529. doi:10.1038/s41598-021-88071-4.
15. Rogowska AM, Kuśnierz C, Pavlova I, Chilicka K. A Path Model for Subjective Well-Being during the Second Wave of the COVID-19 Pandemic: A Comparative Study among Polish and Ukrainian University Students. *J Clin Med.* 2022;11(16):4726. doi:10.3390/jcm11164726.
16. Rogowska AM, Ochnik D, Kuśnierz C et al. Satisfaction with life among university students from nine countries: Cross-national study during the first wave of COVID-19 pandemic. *BMC Public Health.* 2021;21(1):2262. doi:10.1186/s12889-021-12288-1.
17. Goicochea EA, Coloma-Naldos B, Moya-Salazar J et al. Physical Activity and Body Image Perceived by University Students during the COVID-19 Pandemic: A Systematic Review. *Int J Environ Res Public Health.* 2022;19(24):16498. doi:10.3390/ijerph192416498.
18. Ochnik D, Rogowska AM, Kuśnierz C et al. A Comparison of Depression and Anxiety among University Students in Nine Countries during the COVID-19 Pandemic. *J Clin Med.* 2021;10(13):2882. doi:10.3390/jcm10132882.
19. Kitamura N, Abbas K, Nathwani D. Public health and social measures to mitigate the health and economic impact of the COVID-19 pandemic in Turkey, Egypt, Ukraine, Kazakhstan, and Poland during 2020-2021: situational analysis. *BMC Public Health.* 2022;22(1):991. doi:10.1186/s12889-022-13411-6.

This research was carried out according to the research work of National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute" for 2018-2023 on the theme of "Information technologies for assessing and correcting the state of health of students in higher educational institutions" (state registration number 0117U006954).

ORCID and contributionship:

Oleksandr O. Sabirov: 0000-0002-8652-0052^A

Zoia V. Syrovatko: 0000-0002-5752-9445^B

Viktoriiia M. Yefremenko: 0000-0002-7723-5161^B

Nataliia Ye. Havrylova: 0000-0001-6630-5657^D

Olena K. Syrotynska: 0000-0003-0371-1601^C

Anna Yu. Chekhovska: 0000-0002-0675-5004^E

Oleksandr D. Mokhunko: 0000-0002-0793-2922^F

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Zoia V. Syrovatko

National Technical University of Ukraine

"Igor Sikorsky Kyiv Polytechnic Institute"

37 Peremohy Avenue, 03056 Kyiv, Ukraine

tel: +380984757293

e-mail: physical_education_2020@ukr.net

Received: 11.06.2022

Accepted: 27.05.2023

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

ORIGINAL ARTICLE

INDICATORS OF DENTAL HEALTH AND LOCAL IMMUNITY IN YOUNG ADULTS WHO HAVE SUFFERED FROM CORONAVIRUS INFECTION

DOI: 10.36740/WLek202306117

Yulia G. Kolenko, Tetiana O. Timokhina, Olesya V. Lynovytska, Olena V. Cherkasova, Ilona S. Semenova
BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE

ABSTRACT

The aim: To determine the dental status and state of local immunity in young adults who have suffered from the coronavirus disease.

Materials and methods: The main group consisted of 30 people aged 20–22 years, who suffered from the coronavirus infection Covid19 6.1±1.2 months ago. The comparison group included 20 people who did not have a coronavirus infection. The control group consisted of 35 people, randomized by age and sex, who did not have signs of caries and periodontal tissue disease and did not have coronavirus disease. All patients were examined for dental status and local immunity.

Results: The analysis of indicators of dental status revealed the possibility of the existence of a relationship between the signs of acute SARS-Cov2 viral infection and the development of caries and periodontal tissue diseases. Significant changes in the local immunity of the oral cavity were found in the examined patients, which had a pathogenetic influence on the development and progression of caries and periodontal tissue diseases: a significant increase in the level of Ig G, as well as a probable decrease in the concentration of SIg A relative to the comparison group, a probably higher normative value of pathogenic small- and medium-molecular CICs with a significant decrease in the level of physiological large-sized CICs relative to the comparison group, a decrease in the content of anti-inflammatory IL-4, as well as increased concentration of pro-inflammatory cytokines.

Conclusions: Young adults who have suffered a coronavirus infection during the last 6 months have significantly higher caries prevalence, bleeding index, PMA index and hygiene index, halitosis, which indicates deeper tissue damage and tooth pathology with the formation of dentition defects than in the comparison group. Indicators of local immunity of the oral fluid have a deep and specific character.

KEY WORDS: caries, coronavirus disease, young adults, local immunity, cytokines, secretory immunoglobulin A, circulating immune complexes

Wiad Lek. 2023;76(6):1443-1449

INTRODUCTION

Since December 2019, the novel coronavirus disease 2019 (COVID-19) has spread rapidly around the world, causing various complications that can be fatal [1-3]. The impact of the transmitted coronavirus disease on various organ systems is of considerable interest today [4].

The pathogenesis of COVID-19 involves selective virulence and pathogenicity factors that are specific to β -CoV viruses in general or unique to the SARS-CoV-2 virus that caused the COVID-19 pandemic. One of its pathogenic strategies is the ability of the virus to provoke aggression of the immune system against its own tissues in the form of autoimmune and auto-inflammatory processes, which is considered a unique feature of the survival of β -CoV in the body of an infected person [5].

In general, diseases of the oral cavity are considered as signs of SARS-CoV-2 infection: [6]. Preliminary observations indicate the expression of ACE-2 in the epithelial

cells of the oral cavity and raised the question of its ability to contribute to the fact that the periodontal pocket serves as a reservoir for severe infectious diseases, in particular, SARS-CoV-2 [7]. There are several potential sources of viral infection in these pockets, such as direct exposure of the gingival epithelial tissue to the oral environment or virus movement in the blood or via infected immune cells in the periodontium [8]. Natto prove the hypothesis that samples obtained from periodontal pockets or carious lesions will show positivity for SARS-CoV-2 and this may serve as an alternative means of detecting the virus, comparable to other methods such as nasopharyngeal swab, oropharyngeal swab and saliva examination [9].

SARS-CoV-2 infection can cause changes in the organs and tissues of the oral cavity, which is associated with a significant representation of angiotensin-converting enzyme type 2 (ACE2) receptors in the epithelial cells of the oral mucosa, gums and fibroblasts of the periodontal ligament [10, 11]. Thus, the oral mucosa can

be a gateway for the virus and function as a reservoir for SARS-CoV-2. The role of mucous membranes in the implementation of the immune function explained by the fact that a large part of antigens enters the body, overcoming this physiological barrier [12].

S-IgA of saliva in combination with specific epitopes of cariogenic bacteria causes a site-specific immune response. [13-16]. Conditions associated with hypofunction of the salivary glands, impaired oral clearance, low pH of saliva, and changes in the composition of saliva often lead to a disturbance in the function and composition of the oral microbiota, which causes dysbacteriosis and the associated risk of oral diseases [16-18]. The levels of s-IgA in the saliva of caries patients fluctuate [19, 20]. Therefore, the heterogeneity of s-IgA levels in saliva observed due to regional differences, differences in age, types of teeth, and methods of detecting s-IgA in saliva [21].

At the same time, there are significant gaps in our knowledge regarding the interaction between patient immunity, the development and progression of major dental diseases, and SARS-CoV-2, although Wyllie et al. (2020) demonstrated that saliva analysis is an accurate screening tool for SARS-CoV-2 infection, equivalent to nasopharyngeal swab analysis [22]. Nowadays, saliva considered as unique sample for evaluating the secretory immunity of the oral cavity [23]. There is evidence that age affects immune functioning associated with periodontitis and (less studied) dental caries, however, the mechanistic changes in the functioning of the immune system are complex and not fully explored [24].

THE AIM

To determine the dental status and the state of local immunity in young adults who suffered a coronavirus disease.

MATERIALS AND METHODS

The main group consisted of 30 people aged 20-22 who had Covid19 coronavirus infection, mostly mild to moderate severity. The comparison group included 20 people who did not have a coronavirus infection. The control group consisted of 35 people, randomized by age and sex, who did not have signs of caries and periodontal tissue disease and did not have coronavirus disease. In the main group of patients, the duration from the moment when there was a disease with coronavirus disease to the moment of inclusion in the study was 6.1 ± 1.2 months.

The performed dental examination for these patients included: determination of the prevalence and inten-

sity of dental caries, Average of Decayed, Missing and Filled Teeth index (DMFT); Standard debit of seized, shooting, and imprinted text index (SD of DMFT); quality of restorations according to a modified version of the clinical and radiographic criteria of Hickel et al. (2010); halitosis was assessed using the Winkler WTCl (Winkler Tongue Coating Index) plaque index; the intensity of the inflammatory process in periodontal tissues was assessed by the papillary-marginal-alveolar index (PMA) (G. Parma, 1960; Masler, 1967); oral hygiene status Average of Oral Hygiene Index Score (OHIS) (OHI-S); degree of bleeding sulcus bleeding index (SBI). A specially developed questionnaire was made specifically to included 40 questions on oral care, living conditions, and diet.

To assess the state of local immunity of the oral cavity, the following were evaluated in the oral fluid: the phagocytic activity of neutrophils by the degree of absorption of latex particles with the calculation of the Hamburg phagocytic index and Wright's phagocytic number; the functional state of B-lymphocytes by examining the level of the main classes of immunoglobulins Ig G, Ig A, Ig M by the method of simple radial immunodiffusion in a gel according to G. Mancini et al., 1965; the concentration of circulating immune complexes (CIC) - by the method of precipitation in a solution of polyethylene glycol (PEG-6000) on a microspectrophotometer «Specol-21» (Germany) at a wavelength of 450 nm [24]; the level of cytokines was studied by the immunoenzymatic method according to the methods of the developing companies with kits certified in Ukraine.

The results of the descriptive analysis presented in the form of percentage distribution, mean value and standard deviation (SD). Chi-square and Fisher's exact test were used to determine any differences in the distribution of categorical variables. Because continuous variables did not follow a normal distribution, Kruskal-Wallis analysis of variance and the Mann-Whitney U test used to detect differences in means between two or three groups. The level of significance was set at $p < 0.05$. Pearson's correlation coefficient used for non-normally distributed data or Spearman's for non-normally distributed data to assess the correlation between measures. For interpretation, the Chaddock scale used: the strength of the relationship was determined by the value of the correlation coefficient r (0.00-0.29 - "very weak", 0.30-0.49 - "weak", 0.50-0.69 - "medium", 0.70-0.89 - "strong", 0.90-1.0 - "very strong"). Statistical data processing was also determined by the method of variational statistics using the Microsoft XP "Excel" application program package and the specialized "STATGRAPHICS Plus version 2.1" program.

Table I. Mean number of decayed surfaces (DS), decayed teeth (DT) and decayed filled surfaces (DFS) in persons who suffered from coronavirus disease ($p < 0.05$)

Indicators	Main (Mean (SD))	Control (Mean (SD))
DS	2,1 (3,0)	1.4 (2.6)
DT	1.2 (2.1)	0.8 (1.4)
DFS	25.9 (16.6)	11.6 (12.1)

Table II. Distribution of subjects according to the quality of the poorest dental restoration

Indicators	Main	Control
Individuals with restorations	24 (80%)	8 (40%)
Quality of poorest filling		
Good	1 (4,2%)	5 (65%)
Acceptable	14 (58,3%)	3 (37,5%)
Poor	7 (29,2%)	0
Unacceptable	2 (8,4%)	0

RESULTS

DENTAL STATUS OF THE EXAMINED PATIENTS

Tables I and II show some indicators of the dental status of the examined young adults who suffered from the coronavirus disease.

According to a modified version of the clinical and radiographic criteria described by Hickel et al. (2010), the quality of the restorations in the examined patients was recorded clinically and, if possible, radiographically.

During the clinical examination of patients of the main group, 16 (53.33%) patients were diagnosed with bleeding gums, and 12 (40.0%) patients were diagnosed with halitosis and bleeding gums.

Patients with bleeding gums had dental deposits, which were found in 11 (68.75%) of the examined. In the second place, it should be noted the presence of carious cavities and their irrational filling, which were found in 3 (18.75%) patients. Orthodontic pathology was detected in 2 (12.50%) persons.

The indicators of the condition of the gums in the patients were assessed as mild and moderate severity of gingivitis, the indicators of the PMA index were around $39.41 \pm 1.3\%$. The state of individual oral hygiene was mostly assessed as unsatisfactory: (OHI-S index was on average 1.8 ± 0.12 points). SBI index was on average 1.48 ± 0.1 points.

In 8 (66.6%) examinees with the clinical symptom of halitosis and bleeding gums, dental deposits are the main etiological factor affecting the periodontal tissues. Among local traumatic factors it should be noted the presence of carious cavities and their irrational filling, which occurred in 2 (16.66%) cases. Crowding of teeth was found in 1 (8.34%) examinee.

Indicators of the PMA index around $42.2 \pm 1.9\%$. The state of individual oral hygiene was mostly assessed as unsatisfactory: (OHI-S index around 2.10 ± 0.25 points). SBI index around 1.68 ± 0.33 points.

It has been found a direct correlation between the state of oral hygiene, the presence of caries on the contact and cervical surfaces of the teeth, and the prevalence of periodontal diseases (gingivitis) ($r=0.75$).

The report results of the main group of examinees intended to show the level of oral care, some aspects of eating behavior, some conditions and lifestyle that can affect oral care, the nature of changes in oral care after the coronavirus infection. From the survey data, 20% were senior students, 53.3% were junior students, and 26.6% were studying at a medical college. 70% worked as dental assistants. 43.3% of healthy eating behavior was noted by those individuals who had previously observed a nutrition schedule. From the questionnaire data, a direct correlation was found between the indicators of the change in the nature of nutrition after the transferred coronavirus infection with the increased KPV index ($r=0.63$; $p<0.001$). It was also found a statistically significant direct correlation between the number of meals per day and the intensity of dental caries ($r=0.91$; $p<0.001$). The respondents noted that they began to consume sweets more often after suffering a coronavirus infection, which is confirmed by a direct statistically significant correlation ($r=0.66$; $p<0.001$). Young adults living in a dormitory used sweets more often ($r=0.74$; $p<0.001$). Only 6.6% of respondents added vitamins and trace elements to their daily diet, and 83.3% started doing so only after contracting the coronavirus infection. Regarding the frequency of visits to the dentist: 53.3% visited annually, 46.6% - once or twice in the previous 5 years, the rest - as needed. 43.3% claim that they did not receive oral hygiene instructions from their dentist.

Table III. Indicators of local immunity in the oral fluid of examined patients (M±m)

Immunological indicators	Main group (n=30)	Comparison group (n=20)	Control group (n=35)
Ig G, g/L	2,75 ± 0,22*	1,96±0,23* x	1,03±0,04
Slg A, g/L	0,67 ± 0,01*	1,05 ± 0,02* x	1,29±0,03
CIC large (>19S), cu.	29,43±1,18*	36,08 ± 1,15*x	43,5±3,13
CIC middle (11-19S), cu.	51,46±1,97*	42,89± 1,16 x	36,32±2,18
CIC small (<11 S), cu.	31,42±1,06*	23,11 ± 1,14*x	15,83±1,44
TNF-α, pg/mL	88,6 ± 3,7*	63,9±3,1*x	42,3±4,9
IL-1β, pg/mL	87,6±2,6*	62,1±2,4 *x	39,42±4,5
IL-4, pg/mL	17,2±1,6 *	18,5±0,9 *x	25,42±3,3
IL-6, pg/mL	11,9±0,6	13,2±0,5	12,8±1,3
Phagocytic number	5,08±0,22 *	6,97±0,17 *x	9,53 ± 0,56
Phagocytic index, %	38,71±2,36 *	46,21±1,43 *x	52,82 ± 2,21

Notes: * – the difference between the indicator and the control group is significant ($p < 0.05$);

x - the difference in the indicator between the groups is significant ($p < 0.05$);

n - the number of patients.

Regarding daily teeth cleaning, the interviewees used the following set of tools: electric toothbrush, dental floss, brushes, mono-bundle brush, irrigator - 13.3%; manual toothbrush, dental floss, monobundle brush - 16.6%, manual toothbrush, dental floss - 36.6%, others - only manual toothbrush. 73.3% of the respondents noted that they did not take care of oral hygiene as usual during the illness due to coronavirus infection and during the first month after. 59% of them cited improper physical condition as the reason, 27.2% cited a temporary change in taste sensations.

From the data of the questionnaire survey, it can be concluded that the peculiarities of the course of the coronavirus infection can have a negative impact on individual oral hygiene care in the direction of its temporary deterioration.

INDICATORS OF LOCAL IMMUNITY IN THE EXAMINED PERSONS

The analysis of literary sources showed the leading role of local immunity of the oral cavity in the pathogenesis of dental diseases. Local immunity of the oral cavity is represented by the phagocytic activity of macrophages, specific bactericidal or bacteriostatic and virus-neutralizing activity of immunocompetent substances of the oral cavity, primarily cytokines present in the oral fluid. In addition, the T- and B immune systems play a significant role in the formation of the immune response.

Scientific works shows that phagocytosis is an important mechanism of resistance of the mucous membrane to various bacterial infections.

In the available literature, there are data on changes in indicators of local immunity in dental patients, especially in patients with generalized periodontitis. As it is known from the literature [2, 15, 25], TNF-α is considered

as the main mediator that initiates and prolongs the development of

Table III shows the results of examination of indicators of local immunity in examined patients.

The analysis of the data presented in Table III showed that in the main group of patients, found significant increase in the level of Ig G in the oral fluid, as well as a probable decrease in the concentration of Slg A relative to the comparison group. A violation of the ratio of the concentration of CICs with a probably higher normative value of pathogenic small- and medium-molecular CICs with a significant decrease in the level of physiological large-sized CICs compared to the comparison group was established. In both groups of patients, was detected a low level of IL-4 in the oral fluid. A decrease in the content of anti-inflammatory IL-4 is a compensatory immunological reaction to the development of dental caries. Established that the patients of the main group also had a probable increase in the concentration of pro-inflammatory cytokines TNF-α, IL-1β in the oral fluid, and an increase in the content of IL-6.

In patients from the comparison group with caries and periodontal tissue diseases, who did not suffer from coronavirus infection, immunological indicators, had the same direction changes, but their degree of expression was probably less.

The study of the phagocytic activity of phagocytes in the oral fluid established a significant inhibition of this function in all groups of patients.

DISCUSSION

Therefore, we conducted an examination of the condition and data of local immunity in young adults who suffered a mild and moderate coronavirus infection.

The analysis of indicators of dental status revealed that within 6 months after experiencing the coronavirus disease in the examined patients, its indicators significantly worsened: the prevalence of caries was significantly higher, the quality of restorations was unsatisfactory than in the comparison group, were detected halitosis and bleeding gums (chronic catarrhal gingivitis).

This indicates the existence of a relationship between the signs of acute SARS-CoV-2 viral infection and the development of caries and periodontal tissue diseases. In the studies of Matsuyama Y. et al. shows similar results: "A degree-cohort interaction criterion for caries using a difference-in-differences analysis showed that dental caries among the cohort exposed to COVID-19 showed a significant increase in caries" [26].

Data from Sari A. et al. (2021) report: "In general, diseases of the oral cavity are considered signs of SARS-CoV-2 infection: among 5342 respondents from 43 countries of the world (8.1% reported infection with COVID-19), 42.7% had oral manifestations" [6]. Natto et al. (2022) used real-time polymerase chain reaction (RT-PCR) to assess SARS-CoV-2 in periodontal carious pockets. From the scientists' data: "A total of 180 samples from 72 patients were examined by RT-PCR for amplification of the E and S genes of SARS-CoV-2. SARS-CoV-2 was present in 41.7% of patients with COVID-19 and periodontal pockets and in 16.7% with carious lesions".

The presented observations support the hypothesis that samples obtained from periodontal pockets or carious lesions will show positivity for SARS-CoV-2, and this may serve as an alternative means of detecting the virus, comparable to other methods such as nasopharyngeal swab, oropharyngeal swab and saliva examination. [9]. Due to the tropism of the virus to mucous membranes, Paradowska-Stolarz attempted to describe oral manifestations of SARS-CoV-2 infection. The author emphasizes that there are many oral symptoms in COVID-19, but the coexistence with the underlying disease is not fully established.

It is still not clear whether the oral symptoms are manifestations of the disease or its arise from a loss of immune response. Of the identified symptoms in the oral cavity, the most common are: dysgeusia (disturbance of taste), toothache, exacerbation of autoimmune diseases, herpes simplex, chicken pox viruses, ulcers and aphthous stomatitis [11].

From the answers that we have from questionnaire of the main group of examinees about the level of their oral care, some aspects of eating behavior, some conditions and lifestyle that can affect the care of the oral cavity after suffering a coronavirus infection, it follows that such changes are observed in the direction of

deterioration, which is confirmed by direct statistically significant correlations.

The use of the above-mentioned data can help the dentist in forming a further set of individual preventive measures in the development of dental caries and periodontal tissue diseases in young people who have suffered a coronavirus infection.

Significant changes in local immunity were found in the examined patients, which contributed to the pathogenetic role in the development and progression of the carious process and periodontal tissue diseases.

They were manifested by changes of different degrees of severity: in the main group of patients was found a significant increase in the level of Ig G in the oral fluid, as well as a probable decrease in the concentration of SIg A relative to the comparison group, a probably higher normative value of pathogenic small- and medium-molecular CICs with a significant decrease in the level of physiological large CICs size relative to the comparison group, a decrease in the content of anti-inflammatory IL-4, as well as an increased concentration of pro-inflammatory cytokines.

Zinchuk O.M. et al. showed that the vast majority of the examined (86.1%) had a high level of anti-coronavirus antibodies, which exceeded the limits of quantitative indication. At the same time, there was no statistically significant difference in the level of IgG to SARS-CoV-2 among patients and persons with an asymptomatic course of the infectious process [3].

In particular, research in recent years has shown that secretory immunoglobulin A (s-IgA) of saliva plays an important role in local immunity, preventing microbial adhesion to the surface of hard tooth tissues, neutralizing certain enzymes and bacterial toxins of cariogenic bacteria, and also synergizes with other saliva proteins, such as lactoferrin or lysozyme, preventing caries [13-15, 27, 28]. Salivary s-IgA levels in the group of children with caries were significantly lower than in healthy control children, and adults did not show significant differences [20].

According to the review of scientific literature Preshaw P.M. et al. notes about age-related changes in immune function in the context of periodontitis, which should not be considered a decrease in immune functioning: "A systematic literature search revealed aspects of innate immunity (antimicrobial peptides, neutrophils and NEO, dendritic cells, natural killer cells, Toll-like receptors) and adaptive immune response (B and T cells, secretory IgA and IgG), which may play a role in susceptibility to caries with age" [23].

It can be assumed that a history of coronavirus disease can be attributed both to local factors of the occurrence of caries and periodontal tissue diseases, as local immu-

nological factors in saliva change, and to general causes, as there are disorders in various somatic organs. In the available literature, there is little data about the global pandemic on the course of dental diseases, especially in young adults. Therefore, there is a need for a more detailed study of the impact of SARS-CoV-2. on the prevalence and parameters of dental diseases among young adults infected with COVID-19.

CONCLUSIONS

1. In young adults who have suffered a coronavirus infection during the last 6 months, the prevalence of caries and its intensity are significantly higher than in the comparison group, unsatisfactory quality of res-

torations, significantly higher values of the bleeding index, PMA index and hygiene index, halitosis, which indicates a significant deterioration of dental health in these individuals and the further development of a strategy for the prevention of hard dental tissues and periodontal disease for this category of patients.

2. A study of local immunity has shown that 6 months after suffering from the COVID-19 disease, pronounced changes persist in young adults. It consist in an imbalance of circulating immune complexes with a predominance of the content of small-sized pathogens, as well as an increased concentration of pro-inflammatory cytokines against the background of a decrease in the phagocytic activity of immunocompetent cells of the oral fluid.

REFERENCES

1. Trichlib VI, Tsurak NR, Belyaeva KP et al. Laboratory indicators in patients with mild new coronavirus infection COVID-19. *Act. infectious disease.* 2021;9(3):5-11.
2. Kiselyova GL, Voronova KV, Isaev VM. Diagnostic significance of detection of neutralizing antibodies to SARS-CoV-2. *Act. infectology.* 2021;9(1):24-27.
3. Zinchuk OM, Petrukh AV, Hrynchyshyn NI, Shvaevska KK. Peculiarities of humoral immune response in coronavirus disease (COVID-19). *Act. infectious disease.* 2021;9(1):33-36.
4. Centers for Disease Control and Prevention. Interim Guidelines for COVID-19 Antibody Testing in Clinical and Public Health Settings. 2019. <https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines>. [date access 05.02.2023].
5. Castro Dopico X, Ols S, Loré K, Karlsson Hedestam GB. Immunity to SARS-CoV-2 induced by infection or vaccination. *J Intern Med.* 2022;291(1):32-50. doi: 10.1111/joim.13372.
6. Sari A, Bilmez ZY. Effects of Coronavirus (COVID-19) fear on oral health status. *Oral Health Prev Dent.* 2021;19(1):411-423. doi: 10.3290/j.ohpd.b1870377.
7. Badran Z, Gaudin A, Struillou X et al. Periodontal pockets: A potential reservoir for SARS-CoV-2? *Med Hypotheses.* 2020;143:109907. doi: 10.1016/j.mehy.2020.109907.
8. Miller CS. Viruses: are they really culprits for periodontal disease? A critical review? *J Investig Clin Dent.* 2014;5(3):243. doi: 10.1111/jicd.12114.
9. Natto ZS, Afeef M, Bakhrebah MA et al. Can periodontal pockets and caries lesions act as reservoirs for coronavirus? *Mol Oral Microbiol.* 2022;37(2):77-80. doi: 10.1111/omi.12362.
10. Brandão TB, Gueiros LA, Melo TS et al. Oral lesions in patients with SARS-CoV-2 infection: could the oral cavity be a target organ? *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2021;131(2):e45-51. doi: 10.1016/j.oooo.2020.07.014.
11. Paradowska-Stolarz AM. Oral manifestations of COVID-19: Brief review. *Dent Med Probl.* 2021;58(1):123-6. doi: 10.17219/dmp/131989.
12. Surboyo MD, Ernawati DS, Budi HS. Oral mucosal lesions and oral symptoms of the SARS-CoV-2 infection. *Minerva Dent Oral Sci.* 2021;70(4):161-168. doi: 10.23736/S2724-6329.21.04493-9.
13. Hemadi AS, Huang R, Zhou Y, Zou J. Salivary proteins and microbiota as biomarkers for early childhood caries risk assessment. *Int J Oral Sci.* 2017;9(11):e1. doi: 10.1038/ijos.2017.35.
14. Maksymenko AI, Sheshukova OV, Kuz IO et al. The level of interleukin-18 in the oral fluid in primary school children with chronic catarrhal gingivitis and type I diabetes mellitus. *Wiadomosci Lekarskie.* 2021;74 (6):1336-1340. doi: 10.36740/WLek202106109.
15. Gao X, Jiang S, Koh D, Hsu CY. Salivary biomarkers for dental caries. *Periodontol 2000.* 2016;70(1):128-41. doi: 10.1111/prd.12100.
16. Danylevsky MF et al. Therapeutic dentistry: textbook in 4 volumes. 3rd edition. Kyiv: Medicine. Caries. Pulpit. Periodontitis. Oral sepsis. 2020, p.592.
17. Brandtzaeg P. Secretory IgA: designed for anti-microbial defense. *Front Immunol.* 2013;4:222. doi: 10.3389/fimmu.2013.00222.
18. Lyng Pedersen AM, Belstrøm D. The role of natural salivary defences in maintaining a healthy oral microbiota. *J Dent.* 2019;80(1):S3-12. doi: 10.1016/j.jdent.2018.08.010.
19. Shifa S, Muthu MS, Amarlal D, Rathna Prabhu V. Quantitative assessment of IgA levels in the unstimulated whole saliva of caries-free and caries-active children. *J Indian Soc Pedod Prev Dent.* 2008;26(4):158-61. doi: 10.4103/0970-4388.44031.

20. Haeri-Araghi H, Zarabadipour M, Safarzadeh-Khosroshahi S, Mirzadeh M. Evaluating the relationship between dental caries number and salivary level of IgA in adults. *J Clin Exp Dent*. 2018;10(1):e66-9. doi: 10.4317/jced.54271.
21. Wu Z, Gong Y, Wang C et al. Association between salivary s-IgA concentration and dental caries: A systematic review and meta-analysis. *Biosci Rep*. 2020;40(12):BSR20203208. doi: 10.1042/BSR20203208.
22. Wyllie AL, Fournier J, Casanovas-Massana A et al. Saliva or nasopharyngeal swab specimens for detection of SARS-CoV-2. *N Engl J Med*. 2020;383(13):1283-6. doi: 10.1056/NEJMc2016359.
23. Brandtzaeg P. Secretory immunity with special reference to the oral cavity. *J Oral Microbiol*. 2013;5. doi: 10.3402/jom.v5i0.20401.
24. Preshaw PM, Henne K, Taylor JJ et al. Age-related changes in immune function (immune senescence) in caries and periodontal diseases: a systematic review. *J Clin Periodontol*. 2017;44(18):S153-S177. doi: 10.1111/jcpe.12675.
25. Perederii VG, Zemskov AM, Bychkova NG, Zemskov VM. Immune status, principles of its assessment and correction of immune disorders. Kyiv: Health. 1995, p.211.
26. Khabchuk VS, Rozhko MM, Oliynyk RP et al. Effectiveness of early diagnosis of hidden forms of caries and monitoring of the dental status of children of different age groups. *Herald of Scientific Research*. 2017; 4:122-6.
27. Matsuyama Y, Isumi A, Doi S, Fujiwara T. Impacts of the COVID-19 Pandemic Exposure on Child Dental Caries: Difference-in-Differences Analysis. *Caries Res*. 2022;56(5-6):546-554. doi: 10.1159/000528006.
28. Słotwińska SM. Immunological aspects of dental caries. *Centr Eur J Immunol*. 2012;37(2):182-185.

Department of Dental Therapy. The topic of the research is «A multidisciplinary approach to the prevention and treatment of hard tooth tissues and periodontal diseases in persons of working age» (State registration number No. 0119U104010).

ORCID and contributionship:

Yulia G. Kolenko: 0000-0003-1659-3333 ^{A, B, F}

Tetiana O. Timokhina: 0000-0002-0220-0220 ^{A, B, D}

Olesya V. Lynovytska: 0000-0001-6723-6921 ^{C, E, F}

Olena V. Cherkasova: 0000-0001-7244-0476 ^{B, D}

Ilna S. Semenova: 0000-0002-3251-9101 ^{C, E}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Tetiana O. Timokhina

Bogomolets National Medical University

1 Zoologichna st., 03057 Kyiv, Ukraine

tel: +380961111122

e-mail: tanyatimokhina@gmail.com

Received: 11.09.2022

Accepted: 05.05.2023

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

ORIGINAL ARTICLE

PECULIARITIES OF FORMATION OF CADETS' PSYCHOLOGICAL RESILIENCE AND PHYSICAL READINESS FOR COMBAT STRESS

DOI: 10.36740/WLek202306118

Kostiantyn V. Prontenko¹, Ivan M. Okhrimenko², Olena O. Yevdokimova³, Kateryna R. Mannapova³,
Volodymyr M. Filonenko³, Iuliia L. Tverdokhvalova³, Liliia O. Bondarenko³

¹S.P. KOROLIOV ZHYTOMYR MILITARY INSTITUTE, ZHYTOMYR, UKRAINE

²NATIONAL ACADEMY OF INTERNAL AFFAIRS, KYIV, UKRAINE

³KHARKIV NATIONAL UNIVERSITY OF INTERNAL AFFAIRS, KHARKIV, UKRAINE

ABSTRACT

The aim: To investigate the impact of special physical training sessions on the formation of cadets' psychological resilience and physical readiness for the stress factors of future professional and combat activities.

Materials and methods: The research involved 96 cadets (men) in the 2nd training year of S. P. Koroliov Zhytomyr Military Institute (Ukraine) aged 18-20 years, who were divided into two groups: the experimental (E, n = 47) and the control (C, n = 49). The cadets of the E group studied according to the authors' program, and the C group cadets – according to the existing program. Cadets' psychological resilience was studied using psycho-diagnostic methods aimed at assessing their volitional qualities. Cadets' physical fitness was assessed by the tests of general and special physical training.

Results: It was found that the level of general physical training of the E and the C group cadets was significantly the same ($p > 0.05$) at the end of the research but in terms of special physical training and psychological readiness, the E group cadets had all indicators significantly ($p < 0.05-0.001$) better than those of the C group.

Conclusions: It has been proved that the special physical training sessions conducted according to the authors' program were more effective than the existing program in forming cadets' physical readiness and psychological resilience for stress factors of future professional and combat activities.

KEY WORDS: psychological resilience, physical readiness, physical training, combat stress, cadet

Wiad Lek. 2023;76(6):1450-1456

INTRODUCTION

The combat activities of the military personnel of the Armed Forces of Ukraine in the modern war are accompanied by many factors that are stressful (or psycho-traumatic) in nature and that negatively affect the psyche of soldiers, causing them a sense of fear, strong mental stress, lack of confidence in their abilities, and fatigue. The determining psycho-traumatic factors of combat activities are constant danger and threat to life as well as extremely high physical exertion [1, 2].

According to scientists [3], the main psycho-traumatic factors of combat activities are: a conscious feeling of a threat to one's life, the so-called biological fear of death, injury, pain, and disability; death of a fellow soldier in front of somebody's very eyes or the need to kill a person; lack of time, acceleration of the pace of action, suddenness, uncertainty, and novelty (factors of the combat situation); lack of adequate sleep,

peculiarities of hygiene and nutrition, etc. The cumulative impact of psycho-traumatic factors on military personnel is defined by the concept of "combat stress", which significantly changes the human psyche [4]. Combat stress is the process of mobilizing all available capabilities of the body, immune, protective, nervous, and mental systems to overcome a life-threatening situation. Combat stress is experienced by all servicemen in a dangerous combat situation, without exception. However, the degree of influence of stress factors on the psyche of each serviceman depends on his psychological preparedness, which is determined by the individual mental properties and moral qualities of the serviceman [5]. If the level of psychological preparedness corresponds to the level of danger, the serviceman retains the ability to perform his duties on a combat mission. If the level of mental preparedness of the serviceman does not correspond to the danger, fear, as a natural human reaction to danger, becomes

more pronounced. This begins to affect a person's mental and physiological functions [6].

Physical fatigue is also a powerful psychogenic factor that depresses the human psyche. It arises as a result of the impact on military personnel of the heavy physical exertion that accompanies modern combat activities [7]. Special physical training (SPT) plays an important role in the formation of the psychological readiness of servicemen to act in extreme conditions, increasing their psychological resistance to combat stress [8, 9]. This is because the means of SPT ensure the development and improvement of not only the physical but also the mental nature of a person. If properly applied, the means of SPT can significantly improve all components of the psychological readiness of servicemen including spiritual welfare, volitional qualities, and emotional stability. Physical exercises have the greatest impact on the will and emotional stability of servicemen [10]. Therefore, the development of SPT exercises should be systematic to form cadets' psychological resilience and physical readiness for combat stress.

THE AIM

The aim is to investigate the impact of special physical training sessions on the formation of cadets' psychological resilience and physical readiness for the stress factors of future professional and combat activities.

MATERIALS AND METHODS

The research involved 96 cadets (men) in the 2nd training year of the Faculty of Technical Types of Intelligence and Information Warfare of S. P. Koroliov Zhytomyr Military Institute (ZMI) (Ukraine) aged 18-20 years, who were divided into two groups: the experimental (E, $n = 47$) and the control (C, $n = 49$). The cadets of the E group studied according to the authors' improved work program of the academic subject area (WPASA) referred to as "Physical Education, Special Physical Training" (PESPT) (hereinafter – the author's program), and the C group cadets – according to the traditional WPASA on PESPT (hereinafter – the existing program). The research lasted from April to September 2022. The weekly volume of physical activities (in hours) in the E and the C groups was the same and amounted to 10 hours (morning physical exercises (MPes) – 6 times a week for 30 minutes, training sessions – 2 times a week for 2 hours, sporting and mass participation events (SMPEs) – 3 times a week for 1 hour). At the same time, the content of the MPes

and SMPEs did not differ in the E and the C groups; the only difference was in the content of practical training sessions. All training sessions in the E and the C groups were conducted by instructors of the Department of Physical Education, Special Physical Training and Sports of ZMI according to the schedule of training sessions.

Cadets' psychological resilience was studied using psycho-diagnostic methods aimed at assessing their volitional qualities: the "Study of Willpower" method (by M. M. Obozov); the "Study of Volitional Self-Regulation" method (by A. V. Zvierkov and E. V. Eidman); the "Study of Patience" method (by Ye. P. Ilin and Ye. K. Feshchenko) [11]. The "Study of Willpower" method includes 15 questions and aims to assess cadets' ability to use volitional efforts to overcome obstacles. Answers "yes" are worth 2 points; "don't know" or "sometimes" – 1 point; "no" – 0 points. If the sum of points was 0-12 points, then willpower was assessed as weak, with 13-21 points – medium, with 22-30 points – high. The "Study of Volitional Self-Regulation" method contains 30 statements and aims to determine the values of the volitional self-regulation index. Cadets answered questions or statements with "yes" or "no", and if the answer matched the key, they were awarded 1 point. The index of volitional self-regulation is high if the cadet scored 16 or more points, medium – 9-15 points, and low – 8 or fewer points. The "Study of Patience" method contains 18 statements and was scored 1 point if the answer matched the key. The level of patience is low if a cadet scored up to 6 points; medium – 7-11 points; high – 12 points or more.

Cadets' physical fitness was assessed by the tests of general physical training (GPT) (100 m run; pull-ups; 3 km run) and SPT (6x100 m shuttle run with a sub-machine gun, magazine pouch, and two magazines; 5 km cross-country run; throwing grenades at a distance; performing hand-to-hand combat techniques). The GPT exercises were tested in sports uniforms, and the SPT exercises were tested in military uniforms. Both the psychological resilience and physical readiness of cadets were tested twice: at the beginning (April) and at the end of the experiment (October) in 2022.

Research methods: theoretical analysis and synthesis of literature, pedagogical experiment, testing, methods of mathematical statistics. Theoretical analysis and synthesis of literature were used to find out the current state of the researched problem, systematize and generalize information to achieve the aim of the article (16 sources on the topic of the article from the scientometric databases PubMed, Scopus, Web of Science Core Collection, Index Copernicus, and others

Table I. The dynamics of the indicators of GPT and SPT of the E and C group cadets during the pedagogical experiment (Mean±SD)

Stages of the experiment	Studied groups		Significance of the difference, t; p
	E (n=47)	C (n=49)	
Indicators of GPT			
100 m run, s			
Before	13.3±0.08	13.2±0.09	0.83; p>0.05
After	13.3±0.09	13.1±0.08	1.66; p>0.05
Pull-ups, times			
Before	15.9±0.65	15.8±0.59	0.11; p>0.05
After	15.8±0.63	16.0±0.58	0.23; p>0.05
3 km run, s			
Before	755.1±5.94	758.9±5.86	0.39; p>0.05
After	759.4±6.02	751.7±5.79	0.79; p>0.05
Indicators of SPT			
6x100 m shuttle run, s			
Before	134.1±1.12	133.3±1.07	0.52; p>0.05
After	127.8***±1.05	130.9±1.04	2.10; p<0.05
5 km cross-country run, s			
Before	1457.2±6.57	1452.8±6.41	0.48; p>0.05
After	1431.7*±6.32	1449.6±6.27	2.01; p<0.05
Throwing grenades at a distance, m			
Before	35.6±1.16	36.2±1.09	0.38; p>0.05
After	40.9**±1.19	37.5±1.11	2.09; p<0.05
Performing hand-to-hand combat techniques, points			
Before	3.7±0.14	3.9±0.13	1.05; p>0.05
After	4.8***±0.13	4.0±0.12	2.26; p<0.05

Note to tables I and II: Mean – arithmetical average; SD – standard deviation; t – t-test value; p – significance of difference between the indicators of E and C group cadets due to the t-test; *, **, *** – significance of difference between the indicators of each group according to p<0.05, p<0.01, p<0.001 respectively

were investigated). Pedagogical experiment was used to test the effectiveness of the authors' program. Testing was used to assess the level of physical readiness and psychological stability of cadets of groups E and C. The significance of the difference in the results of the cadets was determined during the studying based on the Student's t-test and the dynamics of the results was investigated in both groups. The significance for all statistical tests was set at p<0.05. All statistical analyses were performed with the SPSS software, version 21, adapted to medical and biological researches.

This research followed the regulations of the World Medical Association Declaration of Helsinki. Also this research complies with the ethical standards of the Order of the Minister of Defense of Ukraine "On Approval of the Regulation on the Organization of Scientific and Technical Activity in the Armed Forces of Ukraine" No. 385 dated 27.07.2016. Informed consent was received from all students who took part in this research.

RESULTS

The purpose of cadets' physical training during war-time is to accelerate the formation of their psychological resilience and physical readiness for future professional and combat activities, to perform assigned service tasks, and to facilitate the solution of other tasks of their training and education. Therefore, taking into account the above, we have improved the traditional WPASA of ESPT by increasing the volume of SPT in the following sections, topics and means: overcoming natural obstacles in various ways (mountains, ravines, ditches, rivers, and marshland); hand-to-hand combat (a special place for the formation of cadets' volitional qualities and psychological resilience to engage in conditioned and semi-conditioned clashes); mountain training (ascent and descent on steeply inclined surfaces, arrangement and overcoming of single- and double-channel banksides, descent in various ways on different terrain, overcoming of banksides in various ways); military-applied swimming (in uniform, with

Table II. The dynamics of the indicators of psychological readiness of the E and C group cadets during the pedagogical experiment (Mean±SD), points

Stages of the experiment	Studied groups		Significance of the difference, t; p
	E (n=47)	C (n=49)	
"Study of Willpower" method			
Before	15,8±1.58	16.1±1.33	0.15; p>0.05
After	22.9**±1.48	18.5±1.26	2.26; p<0.05
"Study of Volitional Self-Regulation" method			
Before	15.1±1.07	14.9±1.03	0.13; p>0.05
After	19.3** ±0.89	16.7±0.91	2.04; p<0.05
"Study of Patience" method			
Before	12.9±0.92	12.4±0.81	0.41; p>0.05
After	16.7±0.85	14.2±0.75	2.21; p<0.05

models of weapons, using improvised means); tactical medicine (the main attention was paid to evacuation of the wounded in various ways); grenade throwing (for accuracy, for range, from a place, from a step, from running, from the knee, from the lying position, from behind shelters, etc.); combat army system (methods of movement with weapons, quick reloading of weapons, etc.); marches and accelerated marches (for 5, 10 and more km in full equipment); performing physical exercises for the formation of military-applied motor skills using improvised means (trees, tire casings, logs, terrain features, exercises with the weight of one's body and the body of a partner, etc.). Thus, the volume of SPT in the E group was increased to 90 %, respectively, 10 % was allocated to the GPT (track and field athletics and accelerated movement, gymnastics and athletic training, sports, and outdoor games, etc.). The level of GPT of the E group cadets, formed at the previous stages of their training, was maintained during the MPEs and SMPEs. In the C group, according to the existing program, 30 % of the time was allocated to SPT, and 70 % to GPT.

The real situation of modern combat was recreated according to the author's program during training sessions in bad weather and by using various means of simulation and naturalizing the combat situation: shooting, explosions, smoke, fires, screams, the smell of blood and meat, etc. Simulation tools have a strong emotional impact on the human psyche. Therefore, according to the author's program, we systematically used simulation tools in the SPT sessions, which contributed to solving the problems of cadets' psychological training.

The volitional qualities that are most important in the formation of cadets' psychological resilience to combat stress are courage, determination, perseverance, endurance (patience), self-control, and self-confidence. All of these qualities are effectively developed during the

performance of the SPT exercises that contain elements of novelty, risk, and danger: overcoming high-altitude obstacles; jumping over trenches and fences; hand-to-hand combat; accelerated marches with the simultaneous overcoming of obstacles; exercises with logs, carrying boxes, dragging bags; Commando crawling in difficult weather conditions; throwing grenades from different positions; overcoming elements of a tactical (psychological) obstacle course, etc.

The results of testing the level of GPT and SPT of the E and the C group cadets are given in Table I.

The analysis of Table I shows that there was no significant difference between the E and the C group cadets in all studied tests in terms of their GPT and SPT ($p > 0.05$) before the experiment. At the end of the research, it was found that the indicators of GPT in the C group, in contrast to the E group, tend to increase, but no significant difference between the groups' indicators was also found ($p > 0.05$) at the end of the experiment. This indicates that training sessions according to the author's program allow maintaining the level of cadets' GPT in the E group at the achieved level. In terms of the SPT indicators, we found significantly ($p < 0.05$) better results in the E group at the end of the experiment, compared to the C group, in 6x100 m shuttle run – by 3.1 s; in 5 km cross-country run – by 17.9 s; in grenade throwing – by 3.4 m; in hand-to-hand combat – by 0.8 points. Moreover, all the studied indicators significantly ($p < 0.05-0.001$) increased during the experiment in the E group. The obtained results allow us to state that the SPT sessions conducted according to the author's program have a much greater effect on the formation of cadets' physical readiness for future professional and combat activities.

The analysis of cadets' psychological readiness showed that all studied indicators of the groups did not differ significantly ($p > 0.05$) before the experiment (Table II). The E group cadets showed significantly bet-

ter indicators by all three methods at the end of the experiment – by 4.4, 2.6, and 2.5 points, respectively ($p < 0.05$). At the same time, all methods revealed a tendency to improve performance in both groups, but the difference between the pre- and post-experiment scores was significant in the E group, unlike the C group ($p < 0.01$).

According to the results of the assessment of cadets' psychological readiness indicators, it was found that after the experiment the E group cadets differ from their peers in a high level of willpower, self-confidence, stability of intentions, the realism of views, developed sense of duty, proactive attitude, independence, self-sufficiency, high level of endurance and self-control.

DISCUSSION

Experts [12, 13] argue that psychological and physical readiness are the main components of the combat capability of servicemen. Psychological readiness is a state of mental, volitional, and emotional elements of the serviceman psyche that ensures the highest efficiency and reliability of their military and professional activities in a combat situation. Physical readiness for combat activities is manifested in the physical condition of servicemen, which ensures the successful performance of assigned tasks. These components are interconnected, so in no case should the importance of any component in the formation of cadets' readiness for combat stress be played down or underestimated.

According to scientists [14, 15], combat stress is manifested in the acceleration of the pulse, breathing, increase in body temperature of a serviceman, redness or pallor of the skin, intense sweating, dry mouth, muscle tremors, changes in external activity (number, frequency, and amplitude of movements), increased anxiety, vigilance, etc. There are significant changes in the motor activity of servicemen in a state of intense fear. They begin to perform actions irrationally, with much greater effort than usual. Depending on the strength of the stressor and the individual psychological preparedness of the soldier, his actions may become inhibited, unmotivated and inappropriate, or they may accelerate significantly, but become chaotic and therefore less accurate. The soldier begins to make significantly more mistakes when performing certain military and professional tasks. A significant excess of the level of danger over the level of mental preparedness of a serviceman can lead to his complete inability to control himself, respond to the requirements and orders of command-

ers, act according to the situation, and even move. A serviceman may forget to use his weapon in combat under the influence of intense fear. In such circumstances, fear can cause complete incapacitation of a serviceman, and sometimes the only reason for the death of servicemen or a unit [16].

Modeling of psychological difficulties is achieved through the use of various techniques and actions during the SPT sessions the implementation of which is associated with danger and risk. Such actions cause tension, excitement, and fear in cadets. Overcoming them forces them to rise above themselves and thus strengthen the emotional and volitional sphere. When conducting training sessions using emotionally stimulating actions, the main focus should be on developing the ability of cadets to consciously act in tense situations, to mobilize their will to achieve the maximum possible success in performing the tasks. Conducting training sessions according to the author's program showed its effectiveness, compared to the existing one, in forming cadets' psychological resilience and physical readiness for combat stress.

CONCLUSIONS

The influence of SPT sessions on the formation of cadets' psychological resilience and physical readiness for combat stress was studied. It was found that the level of GPT of the E and the C group cadets was significantly the same ($p > 0.05$) at the end of the research but in terms of SPT and psychological readiness, the E group cadets had all indicators significantly ($p < 0.05-0.001$) better than those of the C group. Thus, the E group showed significantly ($p < 0.05$) better indicators at the end of the experiment, compared to the C group in 6x100 m shuttle run – by 3.1 s; in 5 km cross-country run – by 17.9 s; in grenade throwing – by 3.4 m; in hand-to-hand combat – by 0.8 points; by three psycho-diagnostic methods – by 4.4, 2.6 and 2.5 points, respectively. Moreover, all the studied indicators increased significantly ($p < 0.05-0.001$) during the experiment in the E group, unlike the C group. It has been proved that the SPT sessions conducted according to the authors' program were more effective than the existing program in forming cadets' physical readiness and psychological resilience for stress factors of future professional and combat activities.

THE PROSPECT OF FURTHER RESEARCH

It is planned to investigate the impact of SPT sessions on the physical readiness and psychological resilience of the female cadets.

REFERENCES

1. Adler AB, Gutierrez IA. Acute Stress Reaction in Combat: Emerging Evidence and Peer-Based Interventions. *Curr Psychiatry Rep.* 2022;24(4):277-284. doi:10.1007/s11920-022-01335-2.
2. Killgore WD, Cotting DI, Thomas JL et al. Post-combat invincibility: violent combat experiences are associated with increased risk-taking propensity following deployment. *J Psychiatr Res.* 2008;42(13):1112-1121. doi:10.1016/j.jpsychires.2008.01.001.
3. Hines LA, Sundin J, Rona RJ et al. Posttraumatic stress disorder post Iraq and Afghanistan: prevalence among military subgroups. *Can J Psychiatry.* 2014;59(9):468-479. doi:10.1177/070674371405900903.
4. Delgado-Moreno R, Robles-Pérez JJ, Clemente-Suárez VJ. Combat Stress Decreases Memory of Warfighters in Action. *J Med Syst.* 2017;41(8):124. doi:10.1007/s10916-017-0772-x.
5. Gibbons SW, Hickling EJ, Watts DD. Combat stressors and post-traumatic stress in deployed military healthcare professionals: an integrative review. *J Adv Nurs.* 2012;68(1):3-21. doi:10.1111/j.1365-2648.2011.05708.x.
6. Tornero-Aguilera JF, Robles-Pérez JJ, Clemente-Suárez VJ. Effect of Combat Stress in the Psychophysiological Response of Elite and Non-Elite Soldiers. *J Med Syst.* 2017;41(6):100. doi:10.1007/s10916-017-0748-x.
7. Osório C, Jones N, Jones E et al. Combat Experiences and their Relationship to Post-Traumatic Stress Disorder Symptom Clusters in UK Military Personnel Deployed to Afghanistan. *Behav Med.* 2018;44(2):131-140. doi:10.1080/08964289.2017.1288606.
8. Moran DS, Evans R, Arbel Y et al. Physical and psychological stressors linked with stress fractures in recruit training. *Scand J Med Sci Sports.* 2013;23(4):443-450. doi:10.1111/j.1600-0838.2011.01420.x.
9. Taylor MK, Markham AE, Reis JP et al. Physical fitness influences stress reactions to extreme military training. *Mil Med.* 2008;173(8):738-742. doi:10.7205/milmed.173.8.738.
10. Konkright WR, O'Leary TJ, Wardle SL et al. Sex differences in the physical performance, physiological, and psycho-cognitive responses to military operational stress. *Eur J Sport Sci.* 2022;22(1):99-111. doi:10.1080/17461391.2021.1916082.
11. Neurova AB, Kapinus OS, Hrytsevich TL. Diagnostics of individual psychological properties of the personality. Lviv: National Academy of Sciences. 2016, p. 181.
12. Szivak TK, Kraemer WJ. Physiological Readiness and Resilience: Pillars of Military Preparedness. *J Strength Cond Res.* 2015;29(11):S34-S39. doi:10.1519/JSC.0000000000001073.
13. Orr R, Sakurai T, Scott J et al. The Use of Fitness Testing to Predict Occupational Performance in Tactical Personnel: A Critical Review. *Int J Environ Res Public Health.* 2021;18(14):7480. doi:10.3390/ijerph18147480.
14. Takla NK, Koffman R, Bailey DA. Combat stress, combat fatigue, and psychiatric disability in aircrew. *Aviat Space Environ Med.* 1994;65(9):858-865.
15. Tracie Shea M, Reddy MK, Tyrka AR, Sevin E. Risk factors for post-deployment posttraumatic stress disorder in national guard/reserve service members. *Psychiatry Res.* 2013;210(3):1042-1048. doi:10.1016/j.psychres.2013.08.039.
16. Ursano RJ, Colpe LJ, Heeringa SG et al. The Army study to assess risk and resilience in servicemembers (Army STARRS). *Psychiatry.* 2014;77(2):107-119. doi:10.1521/psyc.2014.77.2.107.

This scientific article was carried out according to the plan of the research work of the National Academy of Internal Affairs for 2020-2023 "Psychological, pedagogical and sociological support of law enforcement officers» (state registration number 0113U008196).

ORCID and contributionship:

Kostiantyn V. Prontenko: 0000-0002-0588-8753^{A,B}

Ivan M. Okhrimenko: 0000-0002-8813-5107^B

Olena O. Yevdokimova: 0000-0003-4211-7277^C

Kateryna R. Mannapova: 0000-0003-3754-4637^D

Volodymyr M. Filonenko: 0000-0003-2662-1705^D

Luliia L. Tverdokhvalova: 0000-0001-8431-0943^E

Liliia O. Bondarenko: 0000-0001-7975-9797^F

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Kostiantyn V. Prontenko

S.P. Koroliov Zhytomyr Military Institute
22 Mira Avenue, 10023 Zhytomyr, Ukraine
tel: +380675069142
e-mail: prontenko-kostya@ukr.net

Received: 09.12.2022

Accepted: 28.05.2023

A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

DEVELOPMENT OF COORDINATION ABILITIES IN 6-10 YEARS OLD BOYS WITH POSTURAL DISORDERS

DOI: 10.36740/WLek202306119

Oleksii V. Tymoshenko¹, Zhanna H. Domina¹, Valerii V. Trotsenko², Serhii V. Sembrat², Andrii O. Artiyushenko³, Oleksandr A. Tomenko⁴, Romana R. Sirenko⁵

¹UKRAINIAN STATE DRAGOMANOV UNIVERSITY, KYIV, UKRAINE

²HRYHORII SKOVORODA UNIVERSITY IN PEREIASLAV, PEREIASLAV, UKRAINE

³BOHDAN KHMELNYTSKY NATIONAL UNIVERSITY OF CHERKASY, CHERKASY, UKRAINE

⁴SUMY STATE PEDAGOGICAL UNIVERSITY NAMED AFTER A. S. MAKARENKO, SUMY, UKRAINE

⁵IVAN FRANKO NATIONAL UNIVERSITY OF LVIV, LVIV, UKRAINE

ABSTRACT

The aim: To develop, substantiate and experimentally test the methodology for the development of coordination abilities in 6-10 years old boys with postural disorders during their physical education training sessions.

Materials and methods: The experimental (EG) and the control groups (CG) were formed to organize the pedagogical experiment. The EG included 17 boys and the CG consisted of 19 boys. The EG was engaged in sports activities according the developed methodology and the CG followed the current school curricula on physical education.

Results: The methodology for the development of coordination abilities in 6-10 years old boys with postural disorders in the process of their physical education has been developed. Its peculiarity lies in the accentuated influence on the vestibular, motor and visual analyzers with the help of a system of exercises aimed at controlling movements in space in static positions and during movement.

Conclusions: The obtained results testify to the effectiveness of the developed methodology. The EG boys had significantly higher indicators of static balance and coordination abilities at body position change, as well as general coordination of movements ($p \leq 0.05$) at the end of the academic year than those of the CG. In addition, the number of 6-10 years old boys with various postural disorders decreased by 7.4% (from 26.8% to 19.4%).

KEY WORDS: body posture disorders, posture, coordination abilities, 6-10 years old boys, physical education

Wiad Lek. 2023;76(6):1457-1463

INTRODUCTION

According to scientists [1, 2], the degree of development and possibilities of improving children's motor sphere are limited by the presence of disorders in functional activity of sensory and physiological systems of the body, including disorders in the musculoskeletal system, which includes deviations in the development of posture. Deviations in the development of posture occupy one of the leading places in the structure of morbidity of school-age children, and, in addition to a significant cosmetic defect, they create the prerequisites for slowing down the pace of physical development, the emergence of pathological processes in the body. At the same time, the formation of the correct motor stereotype of posture depends on muscle tone and coordination of symmetrical trunk muscles, muscles that support the physiological curves of the spine, so the development of coordination of move-

ments of primary schoolers is a prerequisite for fixing physiologically correct body position when holding stable position and during movement [3, 4]. Skills of holding physiologically correct body positions in static and dynamic positions are formed due to constant application of precisely dosed tensions of muscular corset on the basis of training of different coordination movements [5].

Primary school age is favorable for the development of the majority of motor qualities and is an active period of motor function development; therefore, deviations in posture development at this age are unstable and successfully undergo pedagogical influence. Physical exercises that have a stabilizing effect on the spine, improve respiratory function and strengthen the muscles of the trunk are the main means used during physical education lessons for schoolers with postural disorders [6, 7].

In equal measure, modern pedagogical theory and practice lacks researches devoted to peculiarities of motor function development of primary school children with deviations in posture development along with sufficient elaboration of the problem of high schooler's posture formation, prevention and correction of its disorders by means of physical exercises. The question of the development of coordination abilities in primary school boys with postural disorders remains open, which requires scientific research.

THE AIM

The aim is to develop, substantiate and experimentally test the methodology for the development of coordination abilities in 6-10 years old boys with postural disorders during their physical education training sessions.

MATERIALS AND METHODS

The experimental (EG) and the control groups (CG) were formed to organize the pedagogical experiment. The EG included 17 boys and the CG consisted of 19 boys. The EG was engaged in sports activities according the worked out methodology for the development of coordination abilities in boys with postural disorders and the CG followed the current school curricula on physical education. The homogeneity of the groups of schoolers created for the pedagogical experiment was proved by the fact that the average results obtained during the study of the EG and CG schoolers at the beginning of the pedagogical experiment did not have a significant difference in all the studied indicators.

The following methods of the research were used: analysis and generalization of literature sources was used to study the relevance of the research topic and the actual state of development of the scientific question, to outline the algorithm of the research, theoretical substantiation of its results; pedagogical observation was implemented to study the real state of educational process of physical culture of primary schoolers, and special attention was paid to the quality of health-promoting tasks realization, in particular formation of posture and the development of coordination abilities in primary schoolers; the purpose of method of indices was to determine the type of postural disorders in schoolchildren by the method of indices: scoliotic posture according to the index of vertical curvature of the spine, kyphotic posture (stoop) according to the shoulder index; testing was used to check the level of coordination abilities manifestation in primary schoolers, in particular static and dynamic body balance, coordination of movements and coordination abilities at body position change.

The static balance of the body was determined using the modified Romberg test [8]. The ability to maintain balance was assessed as follows: holding the position of "attention" for less than 15 seconds – grade "1"; holding the position of "attention" for 15 seconds – grade "2"; raise the arms forward, stand for another 15 seconds – grade "3"; close the eyes (or lower the bandage) and stand for another 15 seconds – grade "4"; raise the head with eyes closed and stand for another 15 seconds – grade "5". The Yarotskyi test was used to determine dynamic balance [8]. The exercise was performed from a preparatory standing position with eyes closed, while the examinees began to continuously rotate their heads to one side at a rate of 2 movements per second. The time was recorded with an accuracy of 0.1 seconds from the beginning of rotation to the loss of balance. The test referred to as "Ten Eights" proposed by Yu. A. Kopylov [8] was used to determine the level of movement coordination. This coordination test provided for a schooler's performance of ten cycles of movements with tennis ball "in figure eight" between legs from an angle position with the legs straddled, passing the ball from hand to hand. As a result of the test performance by schoolers of the 1-4th grades, the performance time is estimated according to the relevant normative data: "excellent" – 10.0 - 16.0 seconds; "good" – 16.1 - 22.0 seconds; "satisfactory" – 22.1 - 22.8 seconds. Coordination abilities at body position change of schoolers were determined by means of the Burpee test [8]. A schooler was offered to perform a sequence of movements for 10 seconds: 1 – squat rest position; 2 – front plank; 3 – squat rest position; 4 – standing position. The final result of the test was to record the number of complete cycles and partial exercise performance for 10 seconds. Evaluation of partial performance was as follows: $\frac{1}{4}$ – motion execution on the count of 1; $\frac{1}{2}$ – motion execution on the count of 2; $\frac{3}{4}$ – motion execution on the count of 3. Integral indicator of coordination abilities in schoolers with deviations in posture development was estimated by the index of coordination abilities, calculated as difference in speed of 3 x 10 m shuttle run and 30 m run.

The pedagogical experiment lasted 1 year. The methods of mathematical and statistical data processing were used for quantitative and qualitative processing of digital research materials, for quantitative and qualitative processing of the obtained research results and determination of their reliability. The significance of the difference in the obtained results was determined during the studying based on the Student's test. The significance for all statistical tests was set at $p < 0.05$. The procedure for organizing the research was previously agreed with the Committee on compliance with Academic Integrity and Ethics of the Ukrainian State

Table I. Peculiarities of selection of load components in the process of coordination abilities development in primary schoolers with postural disorders

Components of the load	Methodological peculiarities of load planning and direction of impact
Complexity of movements	Wide range of coordination complexity: 30-60 % of individually accessible level.
Intensity of work	Gradual increase in intensity as the developmental effect accumulates. The intensity of a particular task depends on the type of coordination abilities and conditions of performance.
Duration of a separate motor task or a set	Wide range from 1-5 seconds to 180 seconds depending on the coordination complexity and intensity of the motor task.
Number of repetitions	From 5 to 10 times for short-term work (1-5 seconds). Reducing the number of repetitions (up to 1-2 times) as the duration of the exercise and their total number increases.
Duration and nature of rest	From 30 seconds to 2-3 minutes depending on the duration and intensity of the load until full recovery of efficiency and attention, as well as for psychological mood. The nature of rest is active, passive or combined.

Table II. Methodical peculiarities of application of exercises for coordination abilities development in primary schoolers with postural disorders

Type of coordination abilities	Peculiarities of physical loads planning
Static balance	Exercises of a static nature. Complexity: 30-60 % of the individual maximum. The intensity is low. Duration of a single exercise: 1-5 seconds or until balance disorder. Number of repetitions: up to 10-12 times. Change of conditions and methods of performance: limitation of visual control, support area, inclusion of accompanying movements. Rest between sets: 30-120 seconds, the character is active.
Dynamic balance	Exercises of a dynamic nature. Complexity: 30-60 % of the individual maximum. Intensity of a separate motor task: from low to medium. Duration of a single exercise or a series of exercises: up to 30 seconds or until the appearance of a balance disorder. Number of repetitions (depending on complexity and intensity): 2-8 times. Change of conditions and methods of performance: limitation of visual control, inclusion of accompanying movements, change of preparatory positions, tempo, direction, amplitude of movements. Rest between sets: 30-60 seconds. Character of rest: passive or combined.
Coordination of movements	Exercises of a dynamic nature. Complexity: 30-60 % of the individual maximum. Intensity of a separate motor task: average and above average. Duration of a single exercise or a series of exercises: up to 30-60 seconds or until the coordination of movements, interest or concentration of attention decreases. Number of repetitions (depending on complexity and intensity): up to 8 times. Change of conditions and methods of exercise performance: inclusion of accompanying or additional movements, change of preparatory positions, tempo, direction, amplitude of movements. Rest between sets: 60-180 seconds. Character of rest: passive or combined.
Coordination abilities at body position change	Exercises of a dynamic nature. Complexity: 30-60 % of the individual maximum. Intensity of a single task: average and above average. Duration of a single exercise or a series of exercises: 5-30 seconds or until coordination of movements, interest or attention decreases. Number of repetitions (depending on complexity and intensity): up to 8 times. Change of conditions and methods of performance: change of preparatory positions, orienting points, spatial boundaries, tempo, direction of movements. Rest between sets: 60-180 seconds. The character of rest is passive.

Dragomanov University. Prior consent to participate in the research was obtained from all the participants.

RESULTS

The educational process of physical education of primary schoolers includes the implementation of many tasks: educational, health-promoting and educational. Given that the health-promoting orientation of physical education of schoolers with poor health is a priority, and taking into account the connection between coordination of movements and the formation of a stereotype of schoolers' posture, the development of coordination abilities is the purpose of physical education of primary schoolers with postural disorders. The content, means,

methods and organizational forms of the educational process for the realization of the set purpose on the basis of determined principles and compliance with the necessary organizational and pedagogical conditions constitute the methodology for the development of coordination abilities in primary schoolers with postural disorders. Its peculiarity lies in the accentuated influence on the vestibular, motor and visual analyzers with the help of a system of exercises aimed at controlling movements in space in static positions and during movement. The content of the methodology was based on the principle of combined action on motor coordination and correction of muscle asymmetry, which consists in the variable use of physical loads associated with the reproduction of spatial, rhythmic, dynamic, plastic

Table III. Dynamics of coordination and motor abilities development in 6 primary schoolers with postural disorders (Mean \pm SD)

Studied indicators	Groups	Stages of the experiment		% increase in the indicator	p
		Before	After		
6-8 years old boys					
Static balance, points	CG	2.0 \pm 0.6	2.9 \pm 0.8	36.7	p > 0.05
	EG	1.8 \pm 0.3	4.0 \pm 1.2	75.9	p \leq 0.05
Dynamic balance, seconds	CG	20.6 \pm 1.1	21.2 \pm 0.8	2.5	p > 0.05
	EG	20.9 \pm 0.8	21.4 \pm 1.0	1.6	p > 0.05
Coordination abilities at body position change, times	CG	5.6 \pm 0.6	5.8 \pm 0.4	3.5	p > 0.05
	EG	5.4 \pm 0.4	6.2 \pm 0.5	13.8	p \leq 0.05
Coordination of movements, seconds	CG	20.9 \pm 0.2	21.2 \pm 0.3	2.6	p > 0.05
	EG	21.1 \pm 0.3	22.6 \pm 0.5	6.9	p > 0.05
9-10 years old boys					
Static balance, points	CG	2.1 \pm 0.7	2.8 \pm 0.9	28.6	p > 0.05
	EG	2.2 \pm 0.8	4.3 \pm 1.1	64.6	p \leq 0.05
Dynamic balance, seconds	CG	23.0 \pm 1.2	23.5 \pm 0.9	2.2	p > 0.05
	EG	22.8 \pm 1.0	23.4 \pm 1.1	2.6	p > 0.05
Coordination abilities at body position change, times	CG	6.0 \pm 0.3	6.3 \pm 0.5	4.9	p > 0.05
	EG	6.2 \pm 0.4	7.7 \pm 0.8	21.6	p \leq 0.05
Coordination of movements, seconds	CG	19.0 \pm 0.8	19.4 \pm 0.6	2.1	p > 0.05
	EG	19.2 \pm 0.6	21.3 \pm 1.1	9.9	p > 0.05

Note: Mean: arithmetical average; SD: standard deviation; p: the significance of the difference between the indicators of studied groups before and after the experiment

Table IV. Dynamics of the indicators of general coordination of movements in 6-10 years old boys with postural disorders in the conditions of the pedagogical experiment (Mean \pm SD)

Studied indicators	Groups	Stages of the experiment		% increase in the indicator	p
		Before	After		
6-8 years old boys					
Index of coordination abilities, seconds	CG	4.32 \pm 0.2	3.95 \pm 0.3	8.9	p > 0.05
	EG	4.34 \pm 0.3	3.76 \pm 0.2	14.3	p \leq 0.05
9-10 years old boys					
Index of coordination abilities, seconds	CG	4.03 \pm 0.3	3.72 \pm 0.2	8.0	p > 0.05
	EG	4.01 \pm 0.2	3.45 \pm 0.3	15.0	p \leq 0.05

Note: Mean: arithmetical average; SD: standard deviation; p: the significance of the difference between the indicators of studied groups before and after the experiment

characteristics of static positions or movements. Consideration of age peculiarities of physical development provided for ensuring biological need for movement, combined development of coordination abilities and formation of movement organs i. e. skeletal muscles, bones, tendons and articulo-ligamentous apparatus, planning adequate parameters of muscular apparatus loads, emphasis on symmetrical development of muscles of the right and the left sides of the trunk and limbs, as well as training of correct breathing during exercises (Tables I, II).

The obtained results in the process of conducting the formative stage of the pedagogical experiment testify

to the effectiveness of the proposed methodology for the development of coordination abilities in primary school boys with postural disorders (Table III). Thus, the EG children revealed significantly higher indicators of static balance and coordination abilities at body position change than the CG primary schoolers (p \leq 0.05). Flexibility of the EG and the CG boys significantly improved at the end of the pedagogical experiment (p \leq 0.05). As for the indicators of vestibular stability, ability of voluntary muscle relaxation and coordination of movements in the EG and the CG boys, they did not change significantly during the pedagogical experiment (p > 0.05).

The significant improvement of the indicators of general coordination of movements was revealed in the EG boys at the end of the pedagogical experiment (Table IV).

Thus, these results increased by 14.3 % in 6-8 years old schoolers and by 15.0 % in 9-10 years old schoolers at $p \leq 0.05$. The index of general coordination of movements improved insignificantly in boys of the control group: by 8.9 % in 6-8 years old schoolers and only by 8.0 % in 9-10 years old schoolers at $p > 0.05$.

It was established that the use of the worked out methodology for the development of coordination abilities in primary schoolers with postural disorders during the educational process of general secondary education institutions allows solving a number of issues relevant to the modern national school: increasing the level of development of coordination of movements and correction of deviations in the development of posture. Thus, it was found that the number of 6-10 years old boys who have various deviations in the development of posture, on average decreased by 7.4 % (from 26.8 % to 19.4 %).

DISCUSSION

The study of modern scientific researches allows us to say that physical culture with its main means of influence i. e. physical exercises is the only school subject that takes into account the biological need of schoolers in movement and has a health-promoting character [9, 10]. It was established that physical exercises that have a stabilizing effect on the spine, improve respiratory function and strengthen the muscles of the trunk are the main means used during physical education lessons for schoolers with postural disorders [11, 12]. There are active anatomical and physiological changes in the body of children in primary school age, the course of which is smooth without significant sex differences. It is characterized by complex morphofunctional, mental restructuring: high growth rates, weight gain, intensive changes in both structure and functions of individual organs and body systems. The presence of an incorrect dynamic stereotype of posture causes disturbances in the biomechanical structure of posture and movements, as the interaction of mechanisms responsible for the coordination of motor processes deteriorates. Children with deviations in the development of posture are characterized by a decrease in the tone of individual muscles, which is described by a violation of the interaction of individual muscle groups and reduced ability to muscle-articular sensitivity and movement control [13]. This explains the decrease in the level of manifestation of motor abilities of schoolers with postural disorders

and requires special attention to the development of their motor function.

It was revealed that deviations in posture development influence the development of motor function and limit possibilities of full motor development. To ensure the quality of motor activities and the formation of the motor fund of children, it is important to develop coordination abilities, which are characterized as innate prerequisites for the compliance of motor function with the biomechanical requirements of performing movements according to certain kinematic and dynamic parameters and allow choosing the optimal means of motor tasks solving [14]. Therefore, we have developed and substantiated the methodology for the development of coordination abilities in primary schoolchildren with postural disorders during physical education lessons. In addition, consideration of age peculiarities of physical development provided for ensuring biological need for movement, combined development of coordination abilities and formation of movement organs i. e. skeletal muscles, bones, tendons and articulo-ligamentous apparatus, planning adequate parameters of muscular apparatus loads, emphasis on symmetrical development of muscles of the right and the left sides of the trunk and limbs, as well as training of correct breathing during exercises.

CONCLUSIONS

The methodology for the development of coordination abilities in primary schoolers with postural disorders in the process of their physical education was developed and substantiated. Its peculiarity lies in the accentuated influence on the vestibular, motor and visual analyzers with the help of a system of exercises aimed at controlling movements in space in static positions and during movement. The content of the methodology was based on the principle of combined action on motor coordination and correction of muscle asymmetry, which consists in the variable use of physical loads associated with the reproduction of spatial, rhythmic, dynamic, plastic characteristics of static positions or movements. Differentiation of the content of physical loads was provided taking into account the type of postural disorders of boys, in particular the associated characteristic features of spinal asymmetry and informative varieties of coordination abilities.

The results of the formative stage of the pedagogical experiment testify to the effectiveness of the proposed methodology for the development of coordination abilities in primary school boys with postural disorders. Thus, the EG boys had significantly higher indicators of static balance and coordination abilities at body position

change, as well as general coordination of movements ($p \leq 0.05$) at the end of the academic year than those of the CG. As for the indicators of dynamic balance and coordination of movements in the EG and the CG boys, they did not change significantly during the pedagogical experiment ($p > 0.05$). In addition, the number of 6-10

years old boys with various postural disorders decreased by 7.4 % on average (from 26.8 % to 19.4 %).

Prospects for further research are to use the electromyography method to diagnose disorders of the vertical spine and to correct children's postural disorders in frontal plane.

REFERENCES

1. Permoda-Białozorczyk A, Olszewska-Karaban M, Permoda A et al. Evaluation of the Functional Status of the Posture Control System in Children with Detected Disorders in Body Posture. *Int J Environ Res Public Health*. 2022;19(21):14529. doi:10.3390/ijerph192114529.
2. Deconinck FJ, De Clercq D, Savelsbergh GJ et al. Differences in gait between children with and without developmental coordination disorder. *Motor Control*. 2006; 10(2): 125-142. doi:10.1123/mcj.10.2.125.
3. Yam TTT, Fong SSM, Tsang WWN. Foot posture index and body composition measures in children with and without developmental coordination disorder. *PLoS One*. 2022; 17(3): e0265280. doi:10.1371/journal.pone.0265280.
4. Chaves R, Baxter-Jones A, Gomes T et al. Effects of Individual and School-Level Characteristics on a Child's Gross Motor Coordination Development. *Int J Environ Res Public Health*. 2015;12(8):8883-8896. doi:10.3390/ijerph120808883.
5. Reyes AC, Chaves R, Baxter-Jones ADG et al. Modelling the dynamics of children's gross motor coordination. *J Sports Sci*. 2019;37(19):2243-2252. doi:10.1080/02640414.2019.1626570.
6. Cheng YTY, Wong TKS, Tsang WWN et al. Neuromuscular training for children with developmental coordination disorder: A randomized controlled trial. *Medicine (Baltimore)*. 2019;98(45):e17946. doi:10.1097/MD.00000000000017946.
7. Fong SSM, Guo X, Cheng YTY et al. A Novel Balance Training Program for Children With Developmental Coordination Disorder: A Randomized Controlled Trial. *Medicine (Baltimore)*. 2016;95(16):e3492. doi:10.1097/MD.0000000000003492.
8. Serhiienko LP. *Sportyvna metrolohiiia: teoriia i praktychni aspekty [Sports metrology: theory and practical aspects]*. Kyiv: KNT. 2010, p.773. (in Ukrainian).
9. Griiban GP, Tymoshenko OV, Arefiev VG et al. The role of physical education in improving the health status of students of special medical groups. *Wiad Lek*. 2020;73(3):534-540.
10. Molina-Garcia P, Mora-Gonzalez J, Migueles JH et al. Effects of Exercise on Body Posture, Functional Movement, and Physical Fitness in Children With Overweight/Obesity. *J Strength Cond Res*. 2020;34(8):2146-2155. doi:10.1519/JSC.0000000000003655.
11. Rusnak R, Potasova M, Littva V et al. World's COVID-19 anti-pandemic measures in the context of postural and spine disorders in primary school children in Slovakia. *Bratisl Lek Listy*. 2022;123(8):555-559. doi:10.4149/BLL_2022_088.
12. Morrison SC, Ferrari J, Smillie S. Assessment of gait characteristics and orthotic management in children with developmental coordination disorder: Preliminary findings to inform multidisciplinary care. *Res Dev Disabil*. 2013; 34(10): 3197-3201. doi:10.1016/j.ridd.2013.06.012.
13. Surkar SM, Harbourne R, Corr B et al. Exploration of a novel physical therapy protocol that uses a sensory substitution device to improve the standing postural balance of children with balance disorders. *Physiother Theory Pract*. 2022;38(5):637-647. doi:10.1080/09593985.2020.1786869.
14. Silva Batista MA, Almeida Honório SA, Jones GW et al. The influence of extra-curricular physical activities in the development of coordination in preschool children. *Minerva Pediatr (Torino)*. 2022;74(5):503-510. doi:10.23736/S2724-5276.17.04981-7.

This study was carried according to the research plan of the Faculty of Physical Education, Sports and Health of the Ukrainian State Dragomanov University in 2023-2024 in accordance with the theme "Monitoring, control and evaluation of learning results in physical culture, the basics of healthy lifestyle" (state registration number 0113U009185).

ORCID and contributionship:

Oleksii V. Tymoshenko: 0000-0002-5310-4941^A

Zhanna H. Domina: 0000-0002-8315-6590^{B,D}

Valerii V. Trotsenko: 0000-0003-1109-0534^C

Serhii V. Sembrat: 0000-0002-8589-6007^B

Andrii O. Artiyushenko: 0000-0002-2954-2714^D

Oleksandr A. Tomenko: 0000-0002-1097-965X^E

Romana R. Sirenko: 0000-0001-9100-4709^F

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Zhanna H. Domina

Ukrainian State Dragomanov University

9 Pirogova st., 02000 Kyiv, Ukraine

tel: +380668551916

e-mail: janne@ukr.net

Received: 03.01.2023

Accepted: 28.05.2023

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

ORIGINAL ARTICLE

INFLUENCE OF SEROLOGICAL MARKERS OF BLOOD GROUPS UPON THE DEVELOPMENT OF VISUAL MEMORY IN HIGH SCHOOLERS AND STUDENTS

DOI: 10.36740/WLek202306120

Mykhailo F. Khoroshukha¹, Grygoriy P. Griban², Anatolii I. Bosenko³, Natalia A. Lyakhova⁴, Alla M. Harlinska², Pavlo P. Tkachenko⁵, Anna A. Bondar⁶

¹BORIS GRINCHENKO KYIV UNIVERSITY, KYIV, UKRAINE

²ZHYTOMYR IVAN FRANKO STATE UNIVERSITY, ZHYTOMYR, UKRAINE

³THE STATE INSTITUTION "SOUTH UKRAINIAN NATIONAL PEDAGOGICAL UNIVERSITY NAMED AFTER K.D. USHYNKY", ODESA, UKRAINE

⁴POLTAVA STATE MEDICAL UNIVERSITY, POLTAVA, UKRAINE

⁵POLISSIA NATIONAL UNIVERSITY, ZHYTOMYR, UKRAINE

⁶VINNYTSIA INSTITUTE OF TRADE AND ECONOMICS OF STATE UNIVERSITY OF TRADE AND ECONOMICS, VINNYTSIA, UKRAINE

ABSTRACT

The aim: To investigate the influence of serological markers of blood groups of the ABO system upon the development of short-term visual memory in high schoolers and students.

Materials and methods: The research involved 13-16-year-old high schoolers (boys) (n = 139) who were involved in various sports: group A – speed and strength sports (n = 74); group B – endurance sports (n = 65). The control group consisted of 13-16-year-old high schoolers (n = 106) and 17-20-year-old students (n = 212) who were not engaged in sports. The study of short-term visual memory was conducted using the "Memory for geometric shapes" method.

Results: It was found that high schoolers and students with the O(I) blood group have the best associative coupling with the properties of short-term visual memory.

Conclusions: The use of serological markers of blood groups according to the ABO system is possible in the genetic prediction of the development of visual memory in high schoolers and students. Herewith, the associative coupling is more pronounced in juvenility than in adolescence.

KEY WORDS: serological markers, blood group, visual memory, high schoolers, students

Wiad Lek. 2023;76(6):1464-1469

INTRODUCTION

Not only individual and typological features of higher nervous activity (strength and functional mobility of nervous processes) but also the level of development of such mental properties of individuals as attention, thinking, and memory play great importance in ensuring effective physical and mental activity in sports that require from athletes quick and accurate assessment of situations, ability to think and make decisions in conditions of physical and emotional fatigue of their organisms, etc.[1-3].

It is known that the function of visual memory is an active process in various spheres of human activities, and in sports practice, like other mental functions (attention, logical thinking, time perception), it directly affects the effectiveness of sports activities [4-6]. In addition, from the results of our previous studies [7], we know about

the fact of the specific influence of the orientation of the training process on the development of the main mental properties of adolescents who were engaged in various sports. In particular, it was found that there was an improvement in visual memory function under the influence of endurance physical activity, while there were insignificant changes in the above-mentioned property under the influence of speed and strength loads.

In this regard, the issue of using serological markers of blood groups in the genetic prediction of the development of visual memory function in high schoolers and students engaged in various sports is relevant. The study of this problem is not only theoretical but also practical. Knowledge about the influence of serological markers of blood groups upon the development of visual memory can be used in the practice of genetic

Table I. Assessment of visual memory of high schoolers and students (in points)

Number of correct answers	14	13	12	11	9-10	7-8	5-6	4	3	2
Number of points	10	9	8	7	6	5	4	3	2	1

Table II. Indicators of visual memory function in 13-16-year-old high schooler athletes with different blood groups (not taking into account the specifics of sports), $X \pm m$, (n = 139)

No	Blood groups	n	Visual memory	
			Number of errors, pcs.	Score, points
1	O(I)	46	2.9±0.24	7,2±0,20
2	A(II)	43	3.4±0.28	6,9±0,22
3	B(III)	28	3.5±0.32	6,7±0,23
4	AB(IV)	22	3.5±0.33	6,7±0,26
Reliability of the difference		p1-p2	>0.05	>0.05
		p1-p3	>0.05	>0.05
		p1-p4	>0.05	>0.05
		p2-p3	>0.05	>0.05
		p2-p4	>0.05	>0.05
		p3-p4	>0.05	>0.05

Table III. Indicators of visual memory function in 13-16-year-old high schoolers with different blood groups who were engaged in speed and strength sports (group A), $X \pm m$, (n = 74)

No	Blood groups	n	Visual memory	
			Number of errors, pcs.	Score, points
1	O(I)	24	3.2±0.32	7.0±0.26
2	A(II)	23	3.8±0.38	6.6±0.27
3	B(III)	15	3.7±0.50	6.6±0.35
4	AB(IV)	12	3.6±0.48	6.7±0.36
Reliability of the difference		p1-p2	>0.05	>0.05
		p1-p3	>0.05	>0.05
		p1-p4	>0.05	>0.05
		p2-p3	>0.05	>0.05
		p2-p4	>0.05	>0.05
		p3-p4	>0.05	>0.05

psychological and pedagogical counseling of young people on the problems of their choice of sports and professional activities.

THE AIM

The aim is to investigate the influence of serological markers of blood groups of the ABO system upon the development of short-term visual memory in high schoolers and students.

MATERIALS AND METHODS

The research involved 13-16-year-old high schoolers (boys) (n = 139) of the Brovary Higher School of Physical Culture (Brovary, Kyiv oblast) (the experimental group)

who were engaged in various sports: group A (n = 74) – speed and strength sports (boxing, wrestling, track-and-field athletics: sprinting, hurdling, jumping, shot put and discus throwing); group B (n = 65) – endurance sports (skiing, cycling, swimming: 200, 400 and 1500 m). The control group consisted of 13-16-year-old high schoolers (n = 106) and 17-20-year-old students (n = 212) who were not engaged in sports. The research on the influence of serological blood group markers on the development of visual memory of high schoolers and students was conducted in the period from 2019 to 2022.

The study of individual characteristics of short-term visual memory was conducted using the “Memory for geometric shapes” method, which was proposed by M. V. Makarenko et al [8, 9]. During this test, the subject of interest was presented with forms depicting 7

Table IV. Indicators of visual memory function in 13-16-year-old high schoolers with different blood groups who were engaged in speed and strength sports (group B), $X \pm m$, (n = 65)

No	Blood groups	n	Visual memory	
			Number of errors, pcs.	Score, points
1	O(I)	22	2.6±0.35	7.5±0.31
2	A(II)	20	2.9±0.39	7.3±0.35
3	B(III)	13	3.3±0.38	6.8±0.32
4	AB(IV)	10	3.4±0.48	6.8±0.39
Reliability of the difference		p1-p2	>0.05	>0.05
		p1-p3	>0.05	>0.05
		p1-p4	>0.05	>0.05
		p2-p3	>0.05	>0.05
		p2-p4	>0.05	>0.05
		p3-p4	>0.05	>0.05

Table V. Indicators of visual memory function in 13-16-year-old high schoolers with different blood groups who were not engaged in sports, $X \pm m$, (n = 106)

No	Blood groups	n	Visual memory	
			Number of errors, pcs.	Score, points
1	O(I)	28	2.8±0.34	7.4±0.30
2	A(II)	30	3.2±0.34	7.1±0.26
3	B(III)	26	3.2±0.28	7.0±0.24
4	AB(IV)	22	3.0±0.28	7.1±0.25
Reliability of the difference		p1-p2	>0.05	>0.05
		p1-p3	>0.05	>0.05
		p1-p4	>0.05	>0.05
		p2-p3	>0.05	>0.05
		p2-p4	>0.05	>0.05
		p3-p4	>0.05	>0.05

Table VI. Indicators of visual memory function in 17-20-year-old students with different blood groups who were not engaged in sports, $X \pm m$, (n = 212)

No	Blood groups	n	Visual memory	
			Number of errors, pcs.	Score, points
1	O(I)	67	2.0±0.19	8.1±0.16
2	A(II)	65	2.6±0.23	7.6±0.19
3	B(III)	45	2.5±0.30	7.7±0.26
4	AB(IV)	35	2.6±0.41	7.6±0.32
Reliability of the difference		p1-p2	<0.05	<0.05
		p1-p3	>0.05	>0.05
		p1-p4	>0.05	>0.05
		p2-p3	>0.05	>0.05
		p2-p4	>0.05	>0.05
		p3-p4	>0.05	>0.05

geometric shapes. The subject had to memorize their location within 30 seconds, and then reproduce the given figures on the registration form within 45 seconds. The test task was performed twice using similar forms.

We counted the number of shapes correctly drawn and placed in the registration form (correct answers) and the number of errors made by the subject of interest. Based on the results of the two tasks, the state of the

individual's "visual memory" was assessed in terms of conditional points (Table I).

The tests were conducted in an isolated room in the morning (from 9 to 12 o'clock, no earlier than 2 hours after eating). One or two days before the examination, high schoolers and students were asked to reduce physical activity by 50 % in volume and intensity, not to take tonic and sedative pharmaceuticals, and not to drink strong tea or coffee on the day of testing. Blood group data was taken from the subjects' medical records. This research followed the regulations of the World Medical Association Declaration of Helsinki. Each subject voluntarily participated in the research. All high schoolers and students were healthy during the survey period. In the course of the research, the reliability of the difference between the studied high schoolers and students with different ABO blood groups was determined using the parametric Student's t-test. The difference was considered statistically significant at the 95 % significance level ($p < 0.05$).

RESULTS

The results of associative coupling of blood groups with properties of visual memory function of 13-16-year-old high schooler athletes without taking into account specifics of their sports are presented in Table II.

It was found that the number of errors made by high schooler athletes (not taking into account the specifics of sports) when performing the "Memory for geometric shapes" test remains practically the same for most of them, and therefore no statistically significant differences ($p > 0.05$) were found among persons of four blood groups. There were also no significant differences ($p > 0.05$) in the number of points in the assessment of visual memory in high schooler athletes.

The data of the comparative analysis of indicators of the function of short-term visual memory in high schooler athletes who specialized in sports with different training orientations (group A – speed and strength sports, group B – endurance sports) are presented in Tables III and IV.

As can be seen from Tables III and IV, we did not find a statistically significant difference ($p > 0.05$) between the indicators of visual memory function (number of errors and total score) in 13-16-year-old high schoolers who were engaged in various sports.

Table V presents the results of the research on visual memory function in 13-16-year-old high schoolers who did not play sports. The data of this table show that there is no significant difference in the values of the registered indicators characterizing the function of short-term visual memory between high schoolers of all four blood groups ($p > 0.05$).

From our previous studies [10-13] it is known that stability, the concentration of attention, perception of time, and logical thinking in young people improve over the years, and therefore, in our case, we can assume that the function of visual memory will also be more pronounced in juvenility than in adolescence. In this regard, we conducted the research on the influence of serological markers of blood groups upon the development of short-term visual memory function in 17-20-year-old students of higher educational institutions who were not engaged in sports (Table VI). The data in this table show that students with the O(I) blood group had significantly better values in terms of the number of errors and the overall score in the development of their visual memory compared to students with the A(II) blood group ($p < 0.05$). While no statistically significant difference was found between students belonging to the B(III) and AB(IV) blood groups ($p > 0.05$). Therefore, it can be assumed that students with the O(I) blood group had the best associative coupling with visual memory function.

DISCUSSION

Studies [14] have found that there is a close correlation relationship between the academic performance of high schoolers and university students and the volume (efficiency) of short-term visual memory, which ranges from $r = 0.26$ to 0.39 . Similarly, researchers [1, 15] found a positive relationship between the development of the working memory of young children and their academic performance in primary school and the research [16], respectively, established a high associative coupling between memory function and mathematical performance of primary schoolers. Studies [17, 18] have shown associative coupling between serological markers of blood groups of the ABO system and the possibilities of developing motor skills in athletes, which allows for the orientation of gifted children and adolescents to certain types of sports activities, and adults (men and women), respectively, to the development of certain motor skills. Research [13] shows that blood group markers can be used in the genetic prediction of mental properties of attention and logical thinking in adults. Our previous studies analyze the influence of serological blood group markers upon the development of logical thinking, attention, and time perception in young athletes (boys and girls) of adolescent age [10-12].

The generalized conclusions of the above works are as follows: 1) the use of serological markers of blood groups of the ABO system is possible in the genetic prediction of the development of mental properties of thinking, attention, and perception; 2) the best associa-

tive coupling with various properties of logical thinking is observed in individuals with the A(II) and O(I) blood groups, and the worst – in the AB(IV) and B(III) groups; 3) adolescent athletes with the O(I) blood group have the best associative coupling with different properties of attention, and respectively, the worst – with the A(II) group; 4) and finally, young athletes with the B(III) blood group have the best associative coupling with the properties of time perception, while the worst associative coupling cannot be established.

The conducted analysis of visual memory function indicators depending on serological markers of blood groups of the ABO system of 13-16-year-old high schooler athletes (with and without taking into account the orientation of the sport) shows the absence of significant differences between individuals with the O(I), A(II), B(III) and AB(IV) blood groups ($p > 0.05$). We also found no significant difference between the indicators of short-term visual memory function ($p > 0.05$) when studying the peculiarities of visual memory development in high schoolers with different blood groups who were not engaged in sports. The results of the study of students who were not engaged in sports indicate that the best associative coupling with visual memory properties was found in individuals with the O(I) blood group,

while the worst one remains unclear. It can be assumed that the properties of visual memory, similar to other mental functions (attention, perception, thinking), are more pronounced in juvenility than in adolescence.

CONCLUSIONS

The use of serological markers of blood groups according to the ABO system is possible in the genetic prediction of the development of visual memory in high schoolers and students, regardless of their social employment. It is worth noting that the associative coupling in the subjects of interest is more pronounced in juvenility than in adolescence. In general, based on the results of the research, we conclude that individuals with the O(I) blood group have the best associative coupling with the properties of short-term visual memory, while the worst coupling cannot be determined.

PROSPECTS FOR FURTHER RESEARCH

It is planned to study in more depth the possibilities of using serological blood group markers in the genetic prediction of the development of human mental functions (attention, memory, perception).

REFERENCES

1. Bidzan-Bluma I, Lipowska M. Physical Activity and Cognitive Functioning of Children: A Systematic Review. *Int J Environ Res Public Health*. 2018;15(4):800. doi:10.3390/ijerph15040800.
2. Castellà J, Boned J, Méndez-Ulrich JL, Sanz A. Jump and free fall! Memory, attention, and decision-making processes in an extreme sport. *Cogn Emot*. 2020;34(2):262-272. doi:10.1080/02699931.2019.1617675.
3. Engeroff T, Ingmann T, Banzer W. Physical Activity Throughout the Adult Life Span and Domain-Specific Cognitive Function in Old Age: A Systematic Review of Cross-Sectional and Longitudinal Data. *Sports Med*. 2018;48(6):1405-1436. doi:10.1007/s40279-018-0920-6.
4. Tomporowski PD, Pesce C. Exercise, sports, and performance arts benefit cognition via a common process. *Psychol Bull*. 2019;145(9):929-951. doi:10.1037/bul0000200.
5. Conejero Suárez M, Prado Serenini AL, Fernández-Echeverría C et al. The Effect of Decision Training, from a Cognitive Perspective, on Decision-Making in Volleyball: A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health*. 2020;17(10):3628. doi:10.3390/ijerph17103628.
6. Kang C, Wang Z, Surina A, Lü W. Immediate emotion-enhanced memory dependent on arousal and valence: the role of automatic and controlled processing. *Acta Psychol (Amst)*. 2014;150:153-160. doi:10.1016/j.actpsy.2014.05.008.
7. Khoroshukha M, Lopatenko G, Prysyazhnyuk S et al. The impact of training efforts of various focuses on the development of the function of the visual memory of student-athletes of 17-20 years old of high schools of physical culture. *Inter J Appl Exer Physiol*. 2019; 8(3.1): 225-231.
8. Weinberg RS, Gould D. *Foundations of Sport and Exercise Psychology* (6th ed.). Champaign, IL: Human Kinetics. 2015, 63p.
9. Korolchuk MS, Kraynyuk VM. *Socialjno-psykhologichne zabezpechennja dijajnosti v zvyhajnykh ta ekstremalijnykh umovakh [Socio-psychological support of activities in normal and extreme conditions]*. Kyiv: Nika-centr. 2006, 124p. (In Ukrainian).
10. Khoroshukha M, Putrov S, Sushchenko L et al. Influence of blood types serologic markers on development of concentration function of young 13-16 year old athletes. *J Phys Educ Sport*. 2018;18(4):1890-1895. doi:10.7752/jpes.2018.s4278.
11. Khoroshukha M, Ivashchenko S, Bosenko A et al. Gender features of the effects of serological markers of blood groups on the development of attention function of young adolescent athletes. *Georgian Medical News*. 2020;7-8(304-305):103-111.
12. Khoroshukha M, Putrov S, Sushchenko L et al. Peculiarities of using blood types serologic markers for the development of time perception function of young athletes aged 13-16. *J Phys Educ Sport*. 2019;19:567-72. doi:10.7752/jpes.2019.01083.

13. Khoroshukha M, Bosenko A, Tymchyk O et al. Research of peculiarities of development of time perception function in 13-15 year-old athletes with different blood groups. *Georgian Medical News*. 2020;10(307):142-149.
14. Mayers LB, Redick TS, Chiffrieller SH et al. Working memory capacity among collegiate student athletes: effects of sport-related head contacts, concussions, and working memory demands. *J Clin Exp Neuropsychol*. 2011;33(5):532-537. doi:10.1080/13803395.2010.535506.
15. Vaughan RS, Laborde S. Attention, working-memory control, working-memory capacity, and sport performance: The moderating role of athletic expertise. *Eur J Sport Sci*. 2021;21(2):240-249. doi:10.1080/17461391.2020.1739143.
16. Caamaño-Navarrete F, Latorre-Román PÁ, Párraga-Montilla JA et al. Association between Creativity and Memory with Cardiorespiratory Fitness and Lifestyle among Chilean Schoolchildren. *Nutrients*. 2021;13(6):1799. doi:10.3390/nu13061799.
17. Strikalenko EA, Serhiynko LP, Serhiynko LI. Blood groups and physical development of a person. *New Ideas in Sport Sciences*. 2003, p.229-231.
18. Teng Y, Yu Q, Yu X et al. Neuropsychological Study on the Effects of Boxing Upon Athletes' Memory. *J Strength Cond Res*. 2022;36(12):3462-3467. doi:10.1519/JSC.0000000000003909.

This study was carried out according to the research work of the Department of Physical Therapy and Biokinesiology of Boris Grinchenko Kyiv University for 2018-2022 on the theme of "Criteria for assessing the functional status and effectiveness of physical therapy of persons with diseases and injuries of the musculoskeletal and nervous systems" (state registration number 0118U001228).

ORCID and contributionship:

Mykhailo F. Khoroshukha: 0000-0001-5024-5792^{A,B}

Grygoriy P. Griban: 0000-0002-9049-1485^D

Anatolii I. Bosenko: 0000-0003-3472-0412^C

Natalia A. Lyakhova: 0000-0003-0503-9935^E

Alla M. Harlinska: 0000-0001-7859-8637^D

Pavlo P. Tkachenko: 0000-0003-4407-8611^F

Anna A. Bondar: 0000-0001-6051-1898^{B,C}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Grygoriy P. Griban

Zhytomyr Ivan Franko State University

40 Velyka Berdychivska st., 10002 Zhytomyr, Ukraine

tel: +380973341092

e-mail: gribang@ukr.net

Received: 17.12.2022

Accepted: 27.05.2023

A - Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

ORIGINAL ARTICLE

EMOTIONAL INTELLIGENCE AS A FACTOR IN STRENGTHENING THE STUDENTS' MENTAL HEALTH DURING THE COVID-19 PANDEMIC

DOI: 10.36740/WLek202306121

Borys P. Savchuk¹, Inga V. Yehorova¹, Oksana V. Vintoniak², Ruslan M. Kotenko¹, Nadiya O. Fedchyshyn³, Svitlana Yu. Nesterova⁴, Halyna V. Bilavych¹

¹VASYL STEFANYK PRECARPATHIANNATIONAL UNIVERSITY, IVANO-FRANKIVSK, UKRAINE

²KOLOMYIA PEDAGOGICAL PROFESSIONAL COLLEGE, KOLOMYIA, UKRAINE

³I. HORBACHEVSKY TERNOPIL NATIONAL MEDICAL UNIVERSITY, TERNOPIL, UKRAINE

⁴VINNYTSIA MYKHAILO KOTSIUBYNSKYI STATE PEDAGOGICAL UNIVERSITY, VINNYTSIA, UKRAINE

ABSTRACT

The aim of the article is to reveal the potential of Emotional Intelligence (EI) as a factor in strengthening the students' mental health (MH) during and after the COVID-19 pandemic.

Materials and methods: The experimental work was carried out in four stages: 1) preparation - substantiation of its scientific and theoretical principles; 2) ascertaining - development of prognostic tools, conducting an on-line survey of students, an analysis of its results; 3) formative - training with the experimental group participants following the author's methodology; 4) control - survey of experimental group members, determination of experimental results. About 230 students of Ukraine took part in the survey. The statistical processing of the survey results was performed by formal mathematical calculations and calculating Student's t-criterion in order to verify the equality of the mean dependent values in different samples.

Results: The presented results of the research and experiment prove that Emotional Intelligence, in particular its four identified components (information, adaptive behaviour, self-control, empathy), can be an effective factor not only in maintaining university students' mental health during the COVID-19 pandemic, but also in their adaptation to other adverse conditions. A comparison of the results of our research with similar sociological research shows the similarity of problems and changes in the students' mental health all over the world during the pandemic. The materials tested during the development of prognostic tools and training methods can be taken into account for the organization of such research and training activities.

Conclusions: The presented results of the research and experiment prove that EI, in particular its four identified components, can be an effective factor not only in maintaining university students' MH during the COVID-19 pandemic, but also in their adaptation to other adverse conditions. A comparison of the results of our research with similar sociological research shows the similarity of problems and changes in the students' MH all over the world during the pandemic. The materials tested during the development of prognostic tools and training methods are publicly available on the Internet, so they can be taken into account for the organization of such research and training activities. At the same time, we insist that the pandemic should not only intensify the study of changes in MH, but also stimulate the search for effective means to strengthen it. Sir Winston Churchill's eloquent appeal "Never let a good crisis go to waste" should be a guideline in solving this problem.

KEY WORDS: Emotional Intelligence, mental health, COVID-19, higher education, university students

Wiad Lek. 2023;76(6):1470-1477

*"Never let a good crisis go to waste".
Sir Winston Churchill's*

INTRODUCTION

Sir Winston Churchill's statement in the epigraph to the article should be taken as a guide to action in the context of the mankind's struggle against the COVID-19 pandemic. The latter has caused a global chaos, as it quickly escalated from a public health emergency in early 2020 into a pandemic that brought the normal life to a halt [1].

Every crisis, however, is an opportunity to re-evaluate the past and the present, in order to get rid of stereotypes and stigmas and intensify a further progress.

This approach defines the conceptual line of re-research, which involves not only describing the impact of COVID-19 on students' mental health (MH), but also finding effective tools for its preservation and mobilization of their social activity.

The new situation in the higher education system as a result of the COVID-19 pandemic has become the subject of a systematic analysis by international organizations, na-

tional governments and scientists. Their reports [2-4 etc.], a series of articles "In the COVID-19 and Higher Education series, United Nations Academic Impact", accessible on the Internet, and other documents certify unprecedented measures by universities to reform the educational process and ensure its continuity. The studies by scholars from different countries show that COVID-19 caused lifestyle changes, limited mobility, distance learning, social exclusion, etc., which affected the MH of students [5-15].

The conclusion of scientists who, after analyzing a study by the Indian Psychiatric Society, showed that the ongoing COVID-19 crisis emphasised the necessity of a holistic understanding of human mental disorders and strategies for MH preservation during and after the pandemic [16]. This statement is in agreement with the data of US scientists, who prove that MH problems have been and remain one of the main obstacles to successful learning, because they negatively affect the students' motivation, social interaction, concentration, etc. In addition, COVID-19 has caused a significant increase in various mental illnesses [7].

Based on the materials of the above-mentioned and other studies [8], MH is considered as an interdisciplinary category, which denotes: the state of a person who functions at a satisfactory level of emotional and behavioural adaptation; the ability of individuals to realize themselves as subjects of interaction with the outside world; mental mechanisms that determine a person's social activity. MH determines a person's mental life and their individual reactions to ordinary and extreme life situations.

Important for our study is the statement that MH plays a key role in overcoming "normal life stresses", coping with life stresses and ensuring productive social and professional work [17]. Fear, anxiety, stress - these are the usual reactions to the perception of real and imagined threats, however, under the influence of the epidemic COVID-19, they have increased significantly, because the person is faced with uncertainty due to new realities [1].

From the standpoint of the Emotional Intelligence (EI) impact on the students' MH, the former is considered as: (1) the ability of a person to recognize and understand their own emotions, intentions, desires and those of others and control them to solve practical problems [18]; (2) the unity of intellectual and affective processes and a tool for effective interaction with the social environment, which can help to avoid stress [19].

When structuring EI we rely on the "Bar-On model", which determines the EI/EQ (emotional quotient) formation level based on the level of controlling oneself which includes 15 abilities: 1) assessment of one's own abilities and limitations; 2) awareness of one's emotional state and the reasons for its occurrence; 3) expression of one's feelings, thoughts, the ability to mobilize the emotional energy; 4) emotional stability; 5) empathy; 6)

self-identification of a member; 7) social contacts based on emotional intimacy; 8) resistance to stress, effective control of emotions; 9) control of impulses, restraint of emotions; 10) a balanced assessment of the reality, external influences and their comparison with reality; 11) flexible adjustment of feelings, thoughts, ideas, and behavior in accordance with changing circumstances; 12) effective problem solving; 13) self-actualization; 14) optimism and emotional balance in any situation; 15) satisfaction with oneself, others, life in general [20].

When determining the EI potential as a tool to strengthen the mental health of an individual in the extreme conditions of COVID-19, we emphasise two important aspects. The first one (according to Goleman, 1998[19]) is an organic combination in the EI structure of personal and interpersonal components that focus on their own emotions and the emotions of others. The second one (according to Piaget, 1966 [21]) is a clear fixation of the influence of intelligence on adaptation, which includes assimilation, i.e. reproduction in the subject's (student's) cognitive activity of the basic characteristics of the object of cognition (threats and consequences of COVID-19) and accommodation, i.e. adaptation of the subject to the requirements of the new real world.

The presented provisions allow us to identify the four basic components that outline the EI potential as a factor in the adaptation and impact on students' MH during the pandemic. Their essence and indicators for determining the EI level are presented in table I.

THE AIM

The purpose of the article is to reveal the potential of Emotional Intelligence (EI) as a factor in strengthening the students' MH during and after the COVID-19 pandemic.

The main concept, structure and logic of the research have been determined by three considerations. First, the COVID-19 pandemic caused drastic changes in the higher education system, which affected the students' MH. Second, this problem requires a thorough interdisciplinary study to identify changes in the students' MH and find effective ways to correct it and increase their social activity. Third, EI as one of the leading skills of the 21st century specialists can be such an effective tool.

On this basis, the assumption of the experimental study was determined: increasing the EI level can stabilize and improve the students' MH during the pandemic and in other stressful situations.

MATERIALS AND METHODS

The experimental was carried out in four stages: 1) preparatory - substantiation of its scientific and theoretical principles; 2) ascertaining - development of

Table I. Indicators of the of EI levels as a factor in strengthening the MH during the COVID-19 pandemic

EI component	Indicators of EI components *
<i>Information</i> - psycho-emotional perception of COVID-19	Information channels, subjects of informing; the character of information perception; its effect on the psyche
<i>Adaptive behavior</i> - adaptation to new living conditions	Adaptability - absolute / relative conformity between goals and results of life, determined by a person's attitude to oneself and the environment; maladaptability - a conscious discrepancy between goals and results of life; disadaptability - disharmony between goals and results of activities that cause mental stress, and negative emotional background
<i>Self-control</i> – a conscious control of behavior, emotions, mental state, reactions to events	The ability to perceive and control feelings and emotions; tolerance; positive thinking; optimism; ability to psychological adaptation
<i>Empathy</i> - perception of the feelings of others	The ability to understand the feelings and emotional state of another person; adequate perception of the social environment; development of social compassion; ability to sincere emotional relationships; willingness to help others

* In a broader sense, these indicators are specified in our questionnaire

prognostic tools, on-line survey, analysis of its results; 3) formative - training with the experimental group (EG) participants according to the author's methodology; 4) control - on-line survey of EG members, determination of experimental results and recommendations.

At the ascertaining stage the questionnaire "Self-assessment of mental health during COVID-19" was developed by combining two groups of diagnostic techniques and scientific researches. The first group consisted of tools for identifying the links between EI and indicators of adaptive behavior in stressful situations: the method of measuring EI according to the Emin questionnaire [22]; methodology for diagnosing the level of social frustration L. Wasserman (modification by V. Boyko); V. Zunge's method of differential diagnostics of depressive states (adapted by T. Balashova); depression scale (adapted by T. Balashova); diagnostics of empathy by A. Mehrabyan and N. Epstein; self-monitoring questionnaire [13]. The research of EI as a factor of social and psychological adaptation of students to changing living conditions was used [23].

The second group consisted of diagnostic methods (Mental health, 2020) and studies on changes in the university students' mental health during the COVID-19 epidemic [5-7, 9, 10, 12, 14, 15].

The questionnaires formulated in a closed form were divided into four groups according to the indicated EI components. Questions and answer options were presented in a concise wording and affirmative form. Questions for which respondents could choose several answers were marked with "***".

I. Informative component:

1. *Sources of information* about COVID-19*: a) mass media (14%); b) social networks (54%); c) video hosting (46%); d) Internet sites (36%); e) friends, acquaintances, family members (74%);

2. *Frequency, nature and method of obtaining information* about COVID-19: a) constant and purposeful (8%);

b) periodical, but purposeful and systematical (12%); c) periodical / accidental (62%); d) did not receive information because they were not interested (12%); e) deliberately avoided any information (6%);

3. *Interest in the character of information* about the nature and clinical consequences of COVID-19*: a) any information (38%); b) symptoms of the disease and precautions (54%); c) statistics on the number of affected in Ukraine (54%), other countries (22%); d) measures and experience in combating the pandemic in Ukraine (32), other countries (16%); e) did not receive (avoided) information about COVID-19 (12%);

4. *Attitude to various sources of information*: a) complete trust (36%); b) no trust at all (18%); c) partial trust (26%); d) independent analysis and comparison of different sources (16%); e) difficult to answer (4%);

5. *Reaction to information* about COVID-19: a) makes a strong impression, experience, distracts from classes (26%); b) forms an understanding of the essence of the pandemic and the need to comply with the requirements of personal and social hygiene (46%); c) gives an understanding of the nature and danger of COVID-19, but does not encourage compliance with the requirements of personal and social hygiene (24%); e) has no effect (4%).

II. Changes in adaptive behavior:

1) *Attitude towards restrictive measures* (quarantine, freedom of movement, social communication): a) full approval, strict compliance (32%); b) perception as a formalism, feigned observance (52%); c) complete disregard (16%);

2) *Compliance with the requirements* of personal and social hygiene: a) strict, conscious compliance under any circumstances (22%); b) compliance only under certain circumstances (in public transport, supermarket, etc.) (68%); complete disregard (10%);

3) *Changes in the exponential curve* of anxiety and worry, compared with the initial stage of the pandemic:

a) increased (18%); b) decreased (38%); d) unchanged (22%); e) no worries (12%);

4) *Changes in the mental health*: a) sleep disorders - yes (18%), no (82%); b) manifestations of depression - constantly (yes - 18%, no - 82%); periodically (yes - 42%; no - 58%); increased (yes - 46%, no - 54%); manifestations of aggression: increased (26%); b) unchanged (52%); c) difficult to answer (22%);

5) *Changes in physical activity*: a) increased (6%); b) decreased (68%); c) no changes (26%);

6) *Changes in mental health due to fears that* *: a) I will get sick myself (82%); b) family members may get sick (86%); c) negative diseases will affect my health (84%) and that of my family members (92%); d) no fears (8%);

III. Self-control during the pandemic:

1) Belief in one's own abilities: a) greatly changed (2%); b) slightly changed (26%); not change at all (72%);

2) Learning activity: a) increased (42%); b) no change (26%); d) decreased (32%);

3) Passivity, apathy: a) increased (18%); b) decreased (8%); c) no change (64%); d) difficult to answer (10%);

4) Life goal: a) changed (6%); b) no changed (74%); c) difficult to answer (20%);

5) The meaning of life: a) changed (8%); b) no changed (72%); c) difficult to answer (20%);

6) Cheerfulness: a) increased (16%); b) no changed (52%); c) decreased (24%); c) difficult to answer (8%);

7) Optimism: a) increased (34%); b) no change (52%); c) decreased (10%); d) difficult to answer (4%);

8) Self-confidence: a) increased (22%); b) no change (54%); c) decreased (12%); d) difficult to answer (6%);

9) Perseverance: a) increased (22%); b) no change (46%); c) decreased (18%); d) difficult to answer (4%);

10) Adaptability to stress: a) increased (44%); b) no change (36%); c) decreased (4%); d) difficult to answer (16%);

11) Nervous tension: a) increased (48%); b) no change (44%); c) decreased (4%); d) difficult to answer (6%);

12) Activity in overcoming pregnancy: a) increased (56%); b) no change (32%); c) decreased (8%); d) difficult to answer (4%);

13) Lack of emotional restraint: a) increased (34%); b) not change (42%); c) decreased (6%); d) difficult to answer (8%);

14) Impulsive behavior: a) increased (28%); b) not change (46%); c) decreased (10%); d) difficult to answer (16%);

15) Consumption: regular food - decreased (18%), increased (82%); cigarettes, alcohol - increased (34%), decreased (4%), little / no use (58%); coffee, tea - increased (68%), decreased (4%), little / no use (28%); psychotropic / sedative drugs - increased (12%), decreased (6%), little / no use (82%);

IV. Manifestations of empathy during the COVID-19 pandemic:

1) Social openness: a) increased (48%); c) decreased (38%); d) no change (14%);

2) Openness has changed due to: a) contacts in social networks (84%); b) live personal contacts (10%); c) other ways and means (6%);

3) Feelings of discomfort due to changes in openness, lack of communication: a) increased (16%); b) no change (72%); d) difficult to answer (12%);

4) Reaction to the nervousness of another person: a) increase of my own nervousness (32%); b) physical and mental alienation (12%); c) finding out the reason, sympathy (24%); d) finding out the reason, trying to help (8%); e) compassion and preservation of one's own peace (10%); f) indifference (4%); g) contempt for "milkshakes" (4%);

5) Response to reports of COVID-19 rate increase in the country: a) strong feelings (28%); b) compassion, willingness to help, if it does not threaten my own safety (32%); c) experience, willingness to help despite the threat to my own safety (18%); d) alienation, concentration on my own affairs (22%);

6) Social empathy during COVID-19: a) significantly changed (32%) b) slightly changed (16%); c) no change (36%); difficult to answer (16%).

About 230 students of Ukraine took part in the survey. After the initial processing, 50 questionnaires were selected for subject analysis, those with complete answers and presenting a common reflection of the research problem. The selected respondents majored in pedagogical (68%) and other specialties, having the average age of 20.8 years, women (74%) prevailing over men (26%).

The statistical processing of the survey results was performed by formal mathematical calculations and calculating Student's t-criterion in order to verify the equality of the mean dependent values in different samples.

RESULTS

Based on the cluster analysis according to the EI measuring method by Emin Lyusin 2006), three cluster groups with high (14.5%), medium (51.5%) and low (34%) EI levels were identified among the selected respondents (n = 50).

The results of the study show that the level of students' possession of the four identified components of EI does not correspond to its potential as a factor in strengthening the MP in the COVID-19 pandemic. This determined the feasibility and direction of the formative stage of the experiment. While determining the content and methods of experimental learning we sought to make them interesting and suitable for organizing sim-

ilar practices with students from different countries. In order to do this, the results of the above studies on the nature of changes in their MH were taken into account.

The formative experiment took place in the form of the workshop "Mental health during the COVID-19 pandemic" (four days of three lessons (120 minutes) with 25 members of the experimental group, which consisted of 3rd and 4th year students of pedagogical specialties of Precarpathian National University (Ivano-Frankivsk, Ukraine). At the workshop a wide arsenal of methods and forms of learning (role-playing games, mini-training, coaching techniques, project method, "brainstorming", "case study", etc.) and tasks, tests and exercises were tested.

Let us present the content of the experimental training in terms of the development of the four EI components as a factor of strengthening the students' MH.

1. First of all, attention was paid to: a) the development of skills and abilities to critically analyze various (negative, positive, objective, fake) information about COVID-19 and its impact on human life; b) developing the ability to avoid / displace the emotional experiences that arise under the influence of the information and psychological pressure and lead to stressful situations and unfounded worries.

To do this, the participants analyzed and discussed the following problems and phenomena:

- "Infodemia" (misinformation, incitement, intimidation), which has spread over the modern world and complicated the struggle against the COVID-19 pandemic, causing concern among psychologists, doctors, scientists [24];

- Global information inroad in the form of various apocalyptic scenarios. In particular, analyzing the genre of post-apocalyptic fiction, students understood how due to the impact on a person's basal emotions (anxiety, fear, horror) and due to the lack of reliable information or its excessive amount, people are overwhelmed by panic and hysteria. They discussed the film "Infection" (2011), whose events are reminiscent of the situation of the COVID-19 pandemic, etc.; - The impact of the viral pandemic on the rise of a "parallel epidemic of anxiety" (according to the above and other materials of international organizations and research);

- Dissemination of fake news, which distort the reality by exaggerating various threats and negatively affecting human consciousness and psyche (studying their essence and analysis techniques, performing practical tasks based on materials: COVID-19: Fake News: www.europol.europa.eu/cov...; Fake News... COVID-19: fi-admin.bvsalud.org/document/view; Fake news agenda in the era of COVID-19: Identifying trends through fact-checking content, etc.).

Thus, EG members developed the ability to self-correlate the perception of information on COVID-19.

2. In order to develop the ability to flexibly change and correlate the adaptive behavior, the EG members analyzed relevant information from international organizations and research and learned about global societal changes in public life and modern education as a result of the pandemic; they did research projects on ethnic and sociocultural responses to critical situations in various countries, etc.

3. The development of skills and abilities of self-control is based on the manual "Psychodiagnostics of personality in critical situations", which reveals the theoretical aspects of this problem and provides relevant practical materials (methods of diagnosing the coping strategies; tests, tasks, meditative exercises, etc.) [25].

4. With the development of the ability to empathize, the emphasis shifted from the formation of the ability of "passive empathy" to the willingness to provide active real psychological and other assistance to those who need it. This was reflected in the preparation and discussion by EG members of the research projects that offered theoretical justifications and practical solutions to specific problems. For example: "Media psychological phenomena of infodemia" (an analysis of oversaturation with disturbing information, development of measures for the rise of media culture and strengthening the media immunity of individuals); "Psychohygiene during the pandemic" (the theoretical and practical aspects of strengthening MH through a balanced diet, abandonment of bad habits, yoga, Qigong and Tai Chi Xuan; meditation practices); "Social optimism during quarantine" (theory and practice of changing behavioral patterns, formation of positive expectations, rise of social activity), etc.

After the workshop in the EG, a check experiment was made based on the same prognostic tools used during the ascertainment experiment. The indicators of the EG members' (25 people) levels of the four IE components determined at these stages of the experiment actually differed from the total number of respondents (50 people). Therefore, we consider the results of the diagnosis presented in table II to be quite plausible.

The presented data are to some extent conditional, because changes in MH are a complex process caused by various factors, so one educational event a priori can not radically improve its quality. However, a comparison of the results of the observational and control stages of the experiment shows that the defined EI components have a significant potential to solve this problem. Their overall performance at the high level increased from 14.5 to 30% (2 times), at the average level decreased from 51.5 to 47% (1.1 times), and at the low level - from 34 to 23% (1.5 times)).

Table II. The results of the diagnosis of changes in the levels of the 4 EI components as a factor in strengthening the students; MH during COVID-19 pandemic (%)

EI possession levels	Main EI components							
	Information		Adaptive Behavior		Self-Control		Empathy	
	1*	2**	1*	2**	1*	2**	1*	2**
High	6 %	32 %	16 %	24 %	22%	38 %	14 %	26 %
Average	48 %	44 %	52 %	48 %	54 %	44 %	52 %	52 %
Low	46 %	24 %	32 %	28 %	24 %	18 %	34 %;	22 %

* The ascertaining experiment data with 50 respondents.

** Check experiment data with 25 EG members.

DISCUSSION

The new interesting aspects of study of students' mental health under the conditions of the COVID-19 pandemic received as a result of research work are characterized through comparison with data of other researches and in a section of four components of emotional intelligence defined by us.

1. Compared to official sources of information, the informal channels (friends, acquaintances, family members, social networks, video hosting) telling the students of COVID-19 prevailed (3-4 times higher). This "secondary" (processed in other persons' mind) information was more subjective, emotional, and affected the students' perception and understanding of the pandemic issues. They did not have clear guidelines for its systematic targeted reception, and almost one in five was not interested in or deliberately avoided any information on COVID-19. The interest in it was mostly utilitarian and concerned Ukraine, which indicates a lack of understanding of the global scale of the pandemic. Underdeveloped skills of critical attitude to information exacerbated the inadequacy of its perception and caused mental discomfort and stress due to the COVID-19 threat.

2. Practically two thirds of respondents did not understand the appropriateness of the restrictive measures imposed because of COVID-19 and demonstrated a relatively low level of compliance. This is also explained by the inherent security of young people, ignoring the social requirements, low level of civic and moral culture and responsibility. These circumstances, however paradoxical (!), on the one hand, led to a relatively stable MH level, which manifested itself in minor changes in the exponential curve of anxiety, worry, sleep disorders, manifestations of aggression and so on. On the other hand, there was a cognitive dissonance in the form of collision in the minds of respondents, when misunderstanding/denial of the requirements for restrictive measures clearly contradicted the high fear of COVID-19 and awareness of its negative consequences for their own health and that of their families.

3. The level of self-control among the students' identified EI components was the highest. During the

COVID-19 pandemic and being in forced isolation, their basic goals and values (life goal, meaning of life, belief in one's own abilities) have not actually changed, and optimism, self-confidence, perseverance have even somewhat increased. Their polar personality traits (passivity, apathy, cheerfulness and optimism) have undergone slight correlations, which is quite natural for the development of a young person. The growing trend of learning activity is due to the new requirements associated with the transition to online and mixed classes.

Students showed a fairly high level of stress resistance. Half of the respondents acknowledged the increase of nervous tension and demonstrated the ability to adapt to stress. The rate of "growth of activity in overcoming difficulties" was 1.8 times higher than the rate of growth of the lack of emotional restraint and 2 times higher than the rate of "increase in impulsive behaviour". The increase in the consumption of ordinary food and coffee and tea is explained not so much by the psychological phenomenon of overcoming stress by eating, but by "closeness to the kitchen", because the usual mobile lifestyle had not allowed eating at any moment. This circumstance explains some increase in the consumption of cigarettes and alcohol, despite the fact that most respondents never/almost never consumed them.

4. The results of our survey do not agree with the dominant position in the modern information environment, according to which the social isolation caused by COVID-19 significantly reduced interpersonal contacts, which in turn increased mental stress. Half of the respondents indicated an increase in openness during the pandemic due to increased communication, and 2/3 did not feel discomfort due to changes in its nature, because the decrease in live communication intensified the contacts in social networks, which is the main communication channel of the modern youth.

The relatively high level of emotional and cognitive empathy of the respondents was manifested in the reactions of empathy, sympathy for the growing number of the pandemic victims in Ukraine and in the whole world. For half of the respondents, such emotional identification involved

altruistic behavioral action (willingness to help if it does not threaten or even if threatens their own safety). However, a quarter of respondents demonstrated individualism and egocentrism (alienation from external challenges, focusing on their own affairs). Almost half of them indicated an increase in social empathy during COVID-19.

The global COVID-19 pandemic has been going on for more than a year now. During this time, scientists from different countries working in the fields of psychology, medicine, sociology, etc., have accumulated considerable empirical material, which indicates significant changes in the mental health of students and other categories of the population. However, the vast majority of them are limited to stating the changes and, at best, offer some general recommendations to improve the situation. This updates the need to develop and test special tools and techniques that would contribute to the preservation and improvement of people's mental health. We consider that our study can be one of such examples.

CONCLUSIONS

The presented results of the research and experiment prove that EI, in particular its four identified components, can be an effective factor not only in maintaining university students' MH during the COVID-19 pandemic, but also in their adaptation to other adverse conditions. A comparison of the results of our research with similar sociological research shows the similarity of problems and changes in the students' MH all over the world during the pandemic. The materials tested during the development of prognostic tools and training methods are publicly available on the Internet, so they can be taken into account for the organization of such research and training activities. At the same time, we insist that the pandemic should not only intensify the study of changes in MH, but also stimulate the search for effective means to strengthen it. Sir Winston Churchill's eloquent appeal "Never let a good crisis go to waste" should be a guideline in solving this problem.

REFERENCES

1. World Health Organization. Coronavirus disease 2019 (COVID-19): situation report, 51. World Health Organization. 2020. <https://apps.who.int/iris/handle/10665/331475> [12.12.2022].
2. COVID-19 and Higher Education. Learning to Unlearn to Create Education for the Future. 4 May 2020. <https://www.un.org/en/academic-impact/covid-19-and-higher-education-learning-unlearn-create-education-future>. [12.12.2022].
3. Regional National Perspectives on the Impact of Higher Education. Published by the International Association of Universities. 2020; August: www.iau-aiu.net > IMG > pdf > iau_covid-19_regional. [10.01.2023].
4. Policy Brief. Education during COVID-19 and beyond. United Nations. 2020, p.26. <https://unsdg.un.org/resources/policy-brief-education-during-covid-19-and-beyond>. [05.01.2023].
5. Aqeel M, Abbas J, Shuja KH et al. The influence of illness perception, anxiety and depression disorders on students mental health during COVID-19 outbreak in Pakistan: a Web-based cross-sectional survey, *International Journal of Human Rights in Healthcare*, 2022;15(1):17-30. doi: <https://doi.org/10.1108/IJHRH-10-2020-0095>.
6. Cao W, Fang Z, Hou G et al. The psychological impact of the COVID-19 epidemic on college students in China. *Psychiatry Res. Psychiatry Res.* 2020 May;287:112934. doi: <https://doi.org/10.1016/j.psychres.2020.112934>.
7. Centers for Disease Control and Prevention. Cases in the U.S. 2020: <https://www.cdc.gov/coronavirus/2019-ncov/>. [05.01.2023].
8. Chaban OS, Khaustova OO. Psykhichne zdorovia pid chas pandemii COVID-19 (osoblyvosti psykholohichnoi kryzy, tryvohy, strakhu ta tryvoznykh rozladiv) [Mental health during the COVID 19 pandemic (features of psychological crisis, anxiety, fear and anxiety disorders)]. *Neuro NEWS*. 2021;1:26-36. (In Ukrainian).
9. Eysenbach G, Fagherazzi G, Torous J. Effects of COVID-19 on College Students' Mental Health in the United States: Interview Survey Study. *J Med Internet Res.* 2020;22(9):e21279. doi:10.2196/21279
10. Liu X, Liu J, Zhong X. Psychological state of college students during COVID-19 epidemic. *SSRN J.* 2020. <https://ssrn.com/abstract=3552814> or <http://dx.doi.org/10.2139/ssrn.3552814>. [05.01.2023].
11. Mental health the most impacted during Covid-19, say students: Survey. 2021. <https://www.thehindubusinessline.com/news/science/mental-health-the-most-impacted-during-covid-19-say-students-survey/article33939481.ece>. [05.01.2023].
12. Mukherjee A, Bandopadhyay G, Chatterjee SS. COVID-19 pandemic: mental health and beyond – the Indian perspective. *Irish Journal of Psychological Medicine*. 2021;38(2):140-144. doi: <https://doi.org/10.1017/ipm.2020.63>
13. Tangney JP, Baumeister RF, Boone AL. High Self-Control Predicts Good Adjustment, Less Pathology, Better Grades, and Interpersonal Success. *Journal of Personality*. 2004;72(2):271-324. doi: 10.1111/j.0022-3506.2004.00263.x
14. Taneva SY. Behavioral model during pandemic (Covid-19) based on a student survey from Sofia Medical University. *Health, Physical Culture and Sports*. 2020; 3(19). doi: [https://doi.org/10.14258/zosh\(2020\)3.1](https://doi.org/10.14258/zosh(2020)3.1).
15. Wang C, Zhao H. The impact of COVID-19 on anxiety in Chinese university students. *Front Psychol.* 2020;11:1168. doi: 10.3389/fpsyg.2020.01168.

16. Banerjee D, Vaishnav M, Rao TS et al. Impact of the COVID-19 pandemic on psychosocial health and well-being in South-Asian (World Psychiatric Association zone 16) countries: A systematic and advocacy review from the Indian Psychiatric Society. *Indian J Psychiatry*. 2020;62(3):343–353. doi: 10.4103/psychiatry.IndianJPsychiatry_1002_20.
17. Sayers J. The world health report 2001 - Mental health: new understanding, new hope. *Bulletin of the World Health Organization*. 2002;79(11):1085. <https://apps.who.int/iris/handle/10665/268478> [12.12.2022].
18. Smith MK. Howard Gardner and multiple intelligences, *The encyclopedia of pedagogy and informal education*. 2008: <https://www.infed.org/mobi/howard-Stiven>. [12.12.2022].
19. Goleman D. Working with emotional intelligence. New York: Bantam Books. 1998. Chapter one. <https://archive.nytimes.com/www.nytimes.com/books/first/g/goleman-working.html>. [12.12.2022].
20. Bar-On R. The Bar-On Model of Emotional-Social Intelligence (ESI). *Psicothema*. 2006;18 Suppl:13-25. PMID: 17295953.
21. Piaget J. The Psychology of Intelligence and Education. *Childhood Education*. 1966;42(9):528. Published online: 10 Sep 2013. <https://doi.org/10.1080/00094056.1966.10727991>.
22. Lyusin DV. A new technique for measuring emotional intelligence: Emin's questionnaire. *Psychological diagnostics*. 2006;4:3-22.
23. Derevyanko SP. Emotional intelligence as a factor of socio-psychological adaptation of the individual to the student environment [Emotsiyni intelekt yak chynnyk sotsialno-psykholohichnoi adaptatsii osobystosti do studentskoho seredovyscha]. The dissertation of the candidate of psychological sciences. Kyiv. 2020, p.254. (In Ukrainian).
24. Zarocostas J. How to fight an infodemic. *The Lancet. World Report*. 2020;396(10225):676. doi: [https://doi.org/10.1016/S0140-6736\(20\)30461-X](https://doi.org/10.1016/S0140-6736(20)30461-X).
25. Zlivkov VL, Lukomskaya SO, Fedan OV. Psykhodiagnostyka osobystosti v kryzovykh zhyttievykh sytuatsiiakh [Psychodiagnostics of personality in crisis life situations]. Kyiv: Pedahohichna dumka. 2016, p.219. (In Ukrainian).

ORCID and contributionship:

Borys P. Savchuk: 0000-0003-2256-0845^{A, D, F}

Inga V. Yehorova: 0000-0001-8070-9455^{B, D}

Oksana V. Vintoniak: 0000-0003-0040-3582^{E, D}

Ruslan M. Kotenko: 0000-0003-3539-6159^{E, F}

Nadiya O. Fedchyshyn: 0000-0002-0909-4424^{B, F}

Svitlana Yu. Nesterova: 0000-0002-9621-0218^{B, D}

Halyna V. Bilavych: 0000-0002-1555-0932^{C, F}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Nadiya O. Fedchyshyn

Horbachevsky Ternopil National Medical University

Maidan Voli, 1, 46001 Ternopil, Ukraine

tel: +380977008085

e-mail: feddushunno@tdmu.edu.ua

Received: 10.09.2022

Accepted: 17.05.2023

A - Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

ORIGINAL ARTICLE

COMPARATIVE HYGIENIC ASSESSMENT OF THE POTENTIAL DIQUAT HAZARD TO THE POPULATION WHEN CONSUMING AGRICULTURAL CROPS TREATED WITH THE REGLONE AIR 200 SL FORMULATION USING DIFFERENT APPLICATION TECHNOLOGIES (UAV, AERIAL, HIGH-CLEARANCE ROD SPRAYER TREATMENT)

DOI: 10.36740/WLek202306122

Andrii A. Borysenko, Anna M. Antonenko, Vasyl Aleksiihuk, Mykola Kondratiuk, Igor Pelo

BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE

ABSTRACT

The aim: Assessment of the hazard to the population when consuming treated crops by using different technologies.**Materials and methods:** Unmanned aerial vehicle XAG XPlanet 2020 equipped with four rotating rotors, which allows to keep in the air a 20-liter tank was used for spraying field; a manned aircraft AN-2 aggregated with a serial sprayer. High-clearance rod treatment of sunflower and rapeseed crops was carried out by using a PLA MAP II 2010 tractor.**Results:** When the herbicide was applied by aerial application with UAV, the initial content of diquat dibromide in treated rapeseed and sunflower plants on the day of treatment was significantly higher than in the soil under crops ($p \leq 0.05$). The analysis of the diquat content dynamics in sunflower also showed a similar behavior of the a.i. in the plant after processing by another application methods: UAV, aerial and high-clearance rod treatment. The integral index of hazard when using pesticide-contaminated products (IIHPCPC) = $ADD + C + DT50 = 4 + 1 + 1 = 6$ points. That is why, diquat dibromide can be classified according to this index can be classified as compound of 3rd hazard class.**Conclusions:** As a result of the conducted researches, it was established that the content of diquat in rapeseed and sunflower samples grown with the Reglone Air 200 SL application (after treatment and before harvesting) was below the maximum residue levels in those crops. There are no statistically significant differences in the behavior of diquat dibromide when applying by different methods of application (UAV, aerial, high-clearance rod treatment) in different agro-climatic zones of Ukraine.**KEY WORDS:** plant protection, risk assessment, human health, environment

Wiad Lek. 2023;76(6):1478-1484

INTRODUCTION

Plants occupy a special place in the migration chains of chemical plant protection products (CPPs). Since plants are an integral part of biota, they are closely related to other elements of the environment (water, soil, air). Plants are also capable of accumulation, especially perennial crops, and enzymatic degradation of pesticides [1, 2].

The integral principle of choosing plant protection methods in itself regulates the degree of negative impact of chemical agents on the ecosystem. When substantiating the chemical method, not only the biological and economic efficiency of the measures should be taken into account, but also the possibility of negative environmental consequences, which also have an economic price [2-4].

The study of the dynamics of the pesticides residue amounts in plants makes it possible to obtain a reliable quantitative and qualitative characteristic of the process using all experimental points of the dynamics; to quantitatively assess the influence of aggregate factors on the behavior of pesticides in the studied objects; to compare the results of research carried out in different conditions and with different objects, to predict the behavior of pesticides in plants.

Mechanization of the desiccation process is one of the key factors in increasing yield, work efficiency, and saving time and working forces [5, 6] in rapeseed and sunflower cultivation. Desiccation is a process of pre-harvest drying of plants with chemical formulations, which allows to speed up crop ripening by at least 5–10 days, partially destroy weeds, ensure uniform

ripening, stop the spread of diseases and improve the quality of the grown crop [7].

However, in high density of crops such as cotton, the leaves usually overlap, so it is difficult to spray chemicals with traditional sprayers to ensure sufficient penetration of chemicals into the lower layers of cotton plants [8, 9]. It has been proven that aerial spraying is one of the most effective approaches to the chemicals application in plant protection [9, 10]. It provides rapid delivery of chemicals while reducing crop damage [11]. Unmanned aerial system (UAV) has great advantages of simple operation and good adaptation to the spraying environment, it has great potential for optimal spraying of pesticides according to the actual needs of the crop [12].

THE AIM

The aim was to comparative hygienic assessment of the potential diquat hazard to the population when consuming agricultural crops treated with the Reglone Air 200 SL formulation using different application technologies (UAV, aerial, high-clearance rod sprayer treatment).

MATERIALS AND METHODS

Reglone Air 200 SL – one-component herbicide-desiccant of contact action. The active ingredient (a.i.) belongs to the dipyrindylum derivatives. According to [13], diquat dibromide is characterized by rapid adsorption by green parts of plants and turning into hydrogen peroxide, which destroys cell membrane walls. This leads to rapid drying of the plant on which the formulation has fallen, too fast to ensure transfer to other parts of the plant. The herbicide interferes with cellular respiration, the process by which plants produce energy. Diquat dibromide decomposes on the surface of plants by photochemical degradation (Table I).

UAV. Field studies using the Reglone Air 200 SL were conducted in 2021. Processing of rapeseed and sunflower crops was carried out in the Kyiv region in accor-

dance with the formulation consumption rate – 2.3 l/ha, working solution – 8 l/ha, spraying speed – 5.0 l/min. The total cultivated area was 5 hectares of sunflower and 2 hectares of rapeseed. Unmanned aerial vehicle (drone) XAG XPlanet 2020 equipped with four rotating rotors, which allows to keep in the air a 20-liter tank was used for spraying fields.

Aerial treatment. The introduction of the Reglone Air 200 SL formulation was carried out using a manned aircraft AN-2 aggregated with a serial sprayer in the Kherson region in 2012. Consumption rate – 2.3 l/ha, working solution – 25 l/ha, processing height 2-3 m above the crop. The total cultivated area: 2 hectares of sunflower and 2 hectares of rapeseed.

High-clearance rod treatment of sunflower and rapeseed crops was carried out in 2013 in the Kyiv region using a PLA MAP II 2010 tractor. Consumption rate – 2.3 l/ha, working solution – 300 l/ha, processing height 10-15 cm above the crop. The total cultivated area: 2 hectares of sunflower and 2 hectares of rapeseed.

Phase of rapeseed plants development at the treatment time: 87 BBCH, plant height – 70-80 cm. Phase sunflower plants of development at the time of processing: 87 BBCH, plant height – 180 cm. Soil-climatic zone: forest-steppe, soils – gray podzolic.

All pesticide application procedures were carried out in the evening hours (after 7 PM) with minimal upward air currents, with air velocity not exceeding 2 m/sec, air temperature not higher than + 20°C, relative humidity was in the range of 30-70%.

The study of the investigated chemical compound behavior was carried out using a specific hygienic method of natural experiment, sampling of plants – according to [14], starting from the first day of treatment and thereafter at equal intervals during the crop growing season until harvest. The study of the diquat dibromide residual amounts dynamics in the green mass of plants, rapeseed and sunflower seeds was carried out by chromatographic methods. Control samples were taken from plots where untreated crops of rapeseed and sunflower were grown.

Table I. Basic physical and chemical properties of diquat

Physical and chemical properties	Diquat dibromide
CAS RN	34417-68-0
IUPAC Name	7,10-diazoniatricyclo[8.4.0.0 ^{2,7}]tetradeca-1(14),2,4,6,10,12-hexaene;dibromide
Empirical formula	C ₁₂ H ₁₂ Br ₂ N ₂
Solubility in water, g/dm ³	700
Solubility in organic solvents, g/dm ³	in acetone, toluene, hexane – 0,1, in methanol – 25
Relative molecular weight	344.04
Coefficient n-octanol/water (20°C)	log K _{ow} = - 4.60

Table II. Diquat content in rapeseed and sunflower

Day after treatment	Diquat content (mg/kg)					
	UAV treatment		Aerial		High-clearance rod sprayer treatment	
	rapeseed	sunflower	rapeseed	sunflower	rapeseed	sunflower
Day of treatment	4,0±0,5 – pods	4,1±0,6 – baskets 0,73±0,01 – seed	3,2±0,5 – pods	2,9±0,5 – baskets 0,65±0,01 – seed	3,8±0,3 – pods	3,6±0,2 – baskets 0,7±0,01 – seed
2	1,1±0,1 – pods	1,94±0,05 – baskets 0,66±0,02 – seed	0,95±0,2 – pods	1,3±0,2 – baskets 0,48±0,02 – seed	1,2±0,15 pods	2,1±0,05 – baskets 0,42±0,02 – seed
4	0,53±0,1 – pods	0,79±0,05 – baskets 0,50±0,01 – seed	0,4±0,1 – pods	0,26±0,05 – baskets 0,1±0,01 – seed	0,45±0,15 – pods	0,32±0,1 – baskets 0,23±0,01 – seed
7 (harvest)	<0,4* – seed <0,5* – oil	0,28±0,01 – seed <0,05* – oil	<0,4* – seed <0,5* – oil	0,2±0,01 – seed <0,05* – oil	<0,4* – seed <0,05* – oil	0,25±0,01 – seed <0,05* – oil
k, day ⁻¹	0,34±0,007	0,39±0,008	0,38±0,01	0,4±0,03	0,43±0,03	0,45±0,04
τ ₅₀ , day	2,04±0,04	1,78±0,04	1,75±0,13	1,67±0,1	1,59±0,14	1,69±0,1
τ ₉₅ , day	8,83±0,2	7,7±0,15	7,63±0,16	7,43±0,26	7,15±0,23	6,89±0,17

Notes: 1. "*" - below the limit of quantification of diquat in rapeseed – 0.4 mg/kg, oil – 0.5 mg/kg; in sunflower – 0.05 mg/kg, oil – 0.05 mg/kg; 2. in the control samples, diquat is below the limit of quantification of the method.

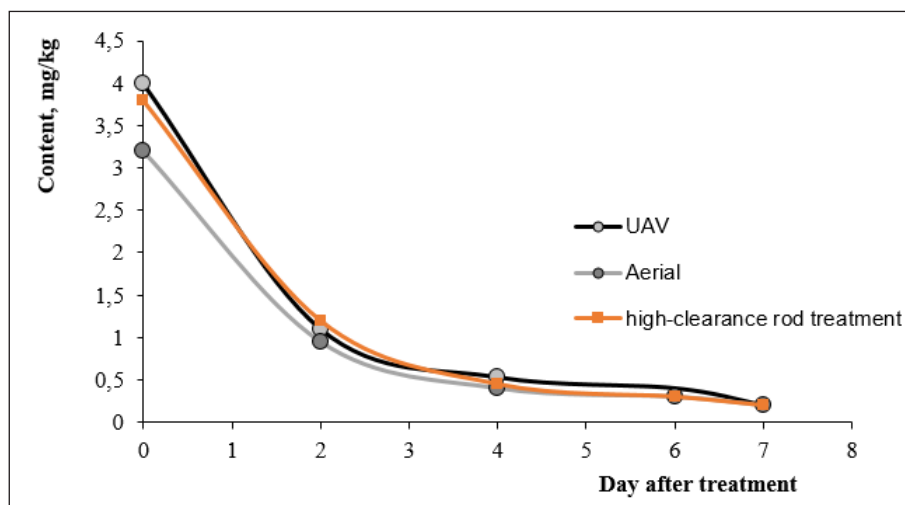


Fig. 1. Dynamics of diquat dibromide residual amounts in rapeseed after different types of treatment (UAV, aerial, high-clearance rod treatment)

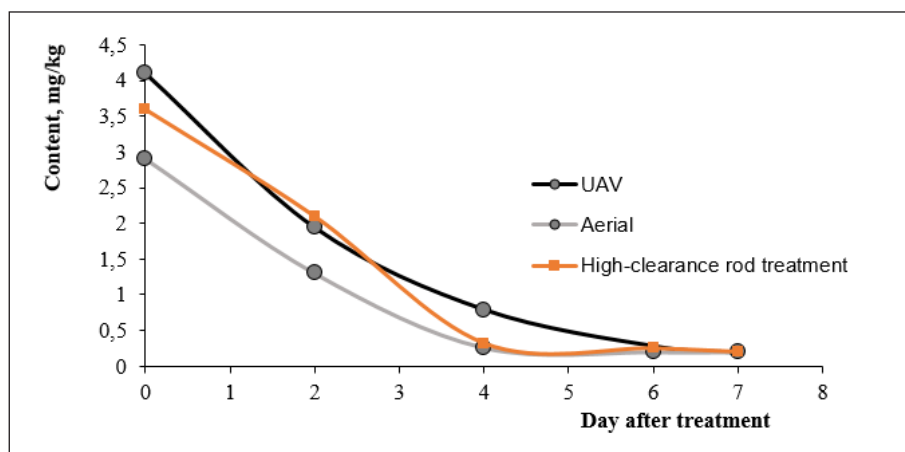


Fig. 2. Dynamics of diquat dibromide residual amounts in sunflower after different types of treatment (UAV, aerial, high-clearance rod treatment)

The obtained results of the actual content of the studied a.i. in the soil, green mass of plants, rapeseed and sunflower seeds made it possible to calculate the constant of decomposition rate (k), half-life periods (DT_{50}) and almost complete decay (DT_{95}) in these objects using regression analysis methods. According to stability in plants, the substances were classified by [15].

The risk assessment for the population when using agricultural products grown in chemical protection systems (non-professional contingents) was carried out according to, which involve the evaluation of the half-life (DT_{50}) in plants, the value of the acceptable daily dose (ADD) and the average daily consumption of the product on a four-gradation scale [16-19].

Statistical processing of the results was performed using the licensed statistical software package IBM SPSS Statistics Base v.22.

RESULTS

The organoleptic properties of rapeseed and sunflower seeds (smell, color, appearance) at harvest in the treated samples did not differ from the control samples.

When the herbicide was applied from the air using a UAV, the initial content of diquat dibromide in treated rapeseed and sunflower plants on the day of treatment was significantly higher than in the soil under them ($p \leq 0.05$). This indicates the high efficiency of this type of processing and the relatively low level of environmental contamination. The concentration in the soil in all the studied samples was below the limit of quantitative determination of the method.

The analysis of the data presented in Table II shows that with all types of processing during the crop growing season, the content of diquat in rapeseed gradually decreased and after 7 days in the seeds was below the limits of quantification (LOQ) of the method. When harvesting the rapeseed crop, the content of diquat in the seeds was also below the LOQ of the corresponding method and did not exceed the maximum residue level (MRL) established for diquat in rapeseed – 0.4 mg/kg (the LOQ by the spectrophotometric method (SP) – 0.4 mg/kg), in rapeseed oil – 0.5 mg/kg (the LOQ of SF – 0.5 mg/kg).

The analysis of the diquat content dynamics in sunflower also showed a similar behavior of the a.i. in the plant during processing from a drone, aerial and high-clearance rod treatment. The concentration of diquat gradually decreased and after 6 days in the seeds was below the MRL. When harvesting the sunflower crop, the content of diquat in the seeds was below the LOQ of the corresponding method and did not exceed the MRL established for diquat in sunflower (seeds) – 0.5 mg/kg (LOQ of SF – 0.05 mg/kg), in sunflower oil – 0.1 mg/kg (LOQ of SF – 0.05 mg/kg).

The obtained results made it possible to substantiate the pre-harvest interval for sunflower – 6 days, rapeseed – 7 days.

The a.i. residual amounts in rapeseed and sunflower plants decreased at different rates. On average, on the 2nd day after treatment, the content of diquat dibromide in rapeseed was 3.4 times decreased ($p < 0.01$), 8 times ($p < 0.01$) on the 4th day and 9.3 ($p < 0.01$) times per 7 days compared to the initial concentration and was determined at or below the LOQ (Fig. 1). The concentration of diquat dibromide in sunflower during a similar time period decreased in plants more slowly (by 2 times on the second day compared to the initial content), and on the 4th day, significantly faster, by 9.4 times ($p < 0.01$) and by 14.5 ($p < 0.01$) times on the 7th day compared to the initial concentration and was determined at the LOQ or below it (Fig. 2).

Mathematical processing of the results we obtained proved that the process of destruction of diquat dibromide obeys an exponential dependence. Based on the actual data of field experiment, we calculated the constant of decomposition rate (k), obtained equations describing the dependence of the concentration of the studied herbicide in rapeseed and sunflower plants from the moment of treatment. Since the differences in the k , DT_{50} and DT_{95} values are not reliable ($p > 0.05$), we calculated their averaged values (Table II).

The next stage of this study was a comparative assessment of the risk to human health when consuming products grown after application of diquat dibromide in different ways.

Three main indices were evaluated on a 4-point scale:

1. the acceptable daily dose (ADD) of diquat dibromide is approved in Ukraine at the level of 0.002 mg/kg [20] that according to [16] gives 4 points;
2. DT_{50} in plants (for both sunflower and rapeseed) with different types of treatment did not differ reliably and in all cases did not exceed 5 days, i.e. it is estimated at 1 point;
3. there are no separate consumption norms (C) for sunflower seeds or sunflower oil, and rapeseed in Ukraine is mainly used as a technical crop and, quite a bit, is consumed in the form of oil, so we estimated the overall rate of oil consumption by the population of our country at 1 point (7,1 kg/person/year = 19.5 g/person/day).

Therefore, the integral index of hazard when using pesticide-contaminated products (IIHPCPC) = $ADD + C + DT_{50} = 4 + 1 + 1 = 6$ points. That is, diquat dibromide can be classified according to this index as compound of 3rd hazard class (moderately hazardous compounds). In this case, the rather high toxicity of the pesticide (low value of ADD) is compensated by its low persistency in agri-

cultural crops and the insignificant share of processed crops in the diet of Ukrainians. In addition, both studied crops undergo mechanical and often heat treatment before use, which leads to even greater destruction of diquat residues in them after processing.

DISCUSSION

The data represented in Table II show that diquat dibromide quickly disappears from plant leaves in soil and climatic conditions of South-East Europe. According to the hygienic classification of pesticides by degree of hazard, according to persistency in vegetative agricultural plants diquat pertains to the 3rd class – moderately persistent.

It should also be noted that there are no statistically significant differences in the behavior of diquat dibromide after treatment with different application methods (UAV, aerial, high-clearance rod treatment) in agro-climatic zones of South-East Europe. And therefore, carrying out desiccation using a new method using a drone does not lead to a deterioration of the ecological situation in the region and does not increase the risk of a negative impact of diquat on non-professional contingents (consumers of agricultural products) and biocenoses. Considering the significant technological and economic advantages, convenience and efficiency of processing by this method, there is less risk of negative impact on agricultural workers (professional contingents) [8, 18, 19], the use of UAVs is very promising and will be actively and widely implemented in agricultural practice in the future.

It is important to note that the results of a comparative assessment of the risk to human health when consuming products grown after the pesticides application can vary depending on a set of factors, such as the dosage, application method, type of crop, and consumption rate [1, 4, 12].

Therefore, it is crucial to evaluate the specific context in which the pesticide is being used and its potential impact on human health and the environment. It is also important to consider the reliability and validity of the methods used to assess the risk and compare the results with other studies conducted in similar contexts [16, 17].

In this particular study, the risk associated with the application of diquat dibromide was evaluated using

three main indices and was found to be moderate. The results suggest that the risk to human health when consuming products grown after the application of diquat dibromide in agro-climatic conditions of South-East Europe is relatively low due to the low persistence of the pesticide in agricultural crops and the small amount of processed crops in the diet of this region population [16, 17]. There are no statistically significant differences in the risk of products consumption grown after the application of a diquat dibromide after treatment with different application methods (UAV, aerial, high-clearance rod treatment). However, the use in different application technics of this pesticide and others should be monitored and evaluated to ensure safety and minimize any potential risks for population [2, 18, 19].

CONCLUSIONS

1. As a result of the conducted researches, it was established that the content of diquat in rapeseed and sunflower samples grown with the Reglone Air 200 SL application for 7 and 6 days, respectively, after treatment and before harvesting, was below the maximum residue levels in those crops. There are no statistically significant differences in the behavior of diquat dibromide when applying by different methods of application (UAV, aerial, high-clearance rod treatment) in different agro-climatic zones of Ukraine.
2. It was established that according to State Standard 8.8.1.002-98, diquat belongs to the 3rd hazard class – moderately stable compounds; by the value of the integral index of hazard when using pesticide-contaminated products, diquat dibromide can be classified as 3rd class (moderately hazardous compounds).
3. It is shown that treatment using UAVs does not lead to a deterioration of the ecological situation in the region and does not increase the risk of a negative impact of diquat on the population and environmental objects. Taking into account the above, as well as significant agro-economic advantages and greater safety for agricultural workers, the use of UAVs is very promising and will be actively and widely implemented in agricultural practice in the future, therefore this technology needs a comprehensive and detailed study from a hygienic point of view.

REFERENCES

1. Antonenko AM, Shpak BI et al. Forecasting of the hazard for human health of the consumption of vegetables grown with the application of abamectin-based insecticide formulations. Medical sciences: history, the present time, the future, EU experience: international scientific and practical conference. Włocławek, Poland. 2019, p.224–226.

2. Kalogiannidis S, Kalfas D, Chatzitheodoridis F et al. Role of crop-protection technologies in sustainable agricultural productivity and management. *Land*. 2022; 11(10): 1680.
3. Alix A, Capri E. Modern agriculture in Europe and the role of pesticides. *Advances in Chemical Pollution, Environmental Management and Protection*. Elsevier. 2018; 2: 1-22.
4. Special Report 05/2020: Sustainable use of plant protection products: limited progress in measuring and reducing risks. European Union. 2020.
5. Depenbusch L, Farnworth CR, Schreinemachers P et al. When Machines Take the Beans: Ex-Ante Socioeconomic Impact Evaluation of Mechanized Harvesting of Mungbean in Bangladesh and Myanmar. *Agronomy*. 2021; 11(5): 925.
6. Sims B, Corsi S, Gbehounou G et al. Sustainable weed management for conservation agriculture: Options for smallholder farmers. *Agriculture*. 2018; 8(8):118.
7. Desykatsiia posiviv soniashnyka ta soi [Desiccation of sunflower and soybean crops]. <https://superagronom.com/articles/534-desikatsiya-posiviv-sonyashnika-ta-soyi> [date access 25.12.2022] (In Ukrainian).
8. Xin F, Zhao J, Zhou Y et al. Effects of dosage and spraying volume on cotton defoliants efficacy: a case study based on application of unmanned aerial vehicles. *Agronomy*. 2018; 8(6):85.
9. Yu K, Liu Y, Gong Z et al. Chemical topping improves the efficiency of spraying harvest aids using unmanned aerial vehicles in high-density cotton. *Field Crops Research*. 2022; 283:108546.
10. Omar Z, Idris N, Rahim MZ. Preliminary design of aerial spraying system for microlight aircraft. *IOP Conf. Series: J. Phys.: Conf. Series*. 2017; 914: 1–10.
11. Zhang Y, Li Y, He Y et al. Near ground platform development to simulate UAV aerial spraying and its spraying test under different conditions. *Comput. Electron. Agric*. 2018; 148: 8–18.
12. Liao J, Zang Y, Luo X et al. The relations of leaf area index with the spray quality and efficacy of cotton defoliant spraying using unmanned aerial systems (UASs). *Computers and Electronics in Agriculture*. 2020; 169: 105228.
13. National Library of Medicine. Diquat dibromide. <https://pubchem.ncbi.nlm.nih.gov/compound/Diquat-dibromide> [date access 25.12.2022]
14. Unyfytsyrovannyye pravyla otbora prob selskokhoziaistvennoi produktsyy, produktov pytanyia y ob'ektov okruzhaiushchei sredy dlia opredeleniia mykrokolychestv pestytsydiv: Metod. Ukazaniia [Unified rules for sampling agricultural products, foodstuffs and environmental objects for the determination of microquantities of pesticides: Method. guidelines] № 2051-79. – M.: MZ SSSR. 1980. (In Russian).
15. StateSatndard 8.8.1.002-98. State sanitary norms and rules. «Hygienic classification of pesticides by degree of danger» . 1998;2:20. (In Ukrainian).
16. Antonenko AM, Vavrinevych OP, Korshun MM et al. Gigiyenichne obg`runtuvannya modeli prognozuvannya nebezpeky` dlya lyudy`ny` pry`vzhy`vanni sil` s`kogospodars`ky`x produktiv kontaminovany`x pesty`cy`div (na pry`kladi fungicy`div klasu pirazolokarboksamidiv) [Hygienic justification of the model for predicting the danger to humans when using agricultural products contaminated with pesticides]. Information letter about innovations in the field of health care # 29. Ky`yiv. 2018, p.4. (In Ukrainian).
17. Vavrinevych O, Antonenko A. Forecasting of triazole, amid, piperdinyly thiazol isoxazoline, oxazole fungicides hazardous effect on human health in consumption of vegetables growed in their application. Proceedings of the 2nd Annual Conference 30 October 2018 Tallinn, Estonia "Technology transfer: innovative solution in medicine". 2018, p.3-5.
18. Borysenko AA, Antonenko AN, Omelchuk ST et al. Professional risks when applying pesticides using unmanned aircraft: features and comparative hygienic assessment. *Medical Science of Ukraine (MSU)*. 2021; 17(4):102-107. doi: 17. 10.32345/2664-4738.4.2021.15.
19. Borysenko A, Antonenko A, Omelchuk S et al. Ecological and hygienic assessment and regulation of innovative technology of pesticide application using unmanned aerial vehicles. *Ecological and hygienic assessment and regulation of innovative technology of pesticide application using unmanned aerial vehicles*. *RMJ*. 2022; 47(1): 213-216.
20. StateSatndard 8.8.1.2.3.4-000-2001. State sanitary norms and rules. Derzhavni sanitarni pravyla ta normy «Dopustymi dozy, kontsentratsii, kilkosti ta rivni vmistu pestytsydiv u silskohospodarskii syrovyni, kharchovykh produktakh, povitri robochoi zony, atmosfernomu povitri, vodi vodoimyshch, hrunti» [State sanitary rules and norms «Permissible doses, concentrations, quantities and levels of pesticide content in agricultural raw materials, food products, air of the working area, atmospheric air, water of reservoirs, soil»]. 2001;137:20. (In Ukrainian).

ORCID and contributionship:

Andrii A. Borysenko: 0000-0002-0211-607X^{B-D}

Anna M. Antonenko: 0000-0001-9665-0646^{E,F}

Vasyl Aleksiiichuk: 0000-0002-1700-6391^{A,D}

Mykola Kondratiuk: 0000-0001-5500-6352^{C,E}

Igor Pelo: 0000-0002-4764-102X^{A,F}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Andrii A. Borysenko

Bogomolets National Medical University

34 Peremohy av., 03057 Kyiv, Ukraine

tel. +380932232377

e-mail: Andrey-b.07@ukr.net

Received: 02.10.2022

Accepted: 29.05.2023

A - Work concept and design, **B** - Data collection and analysis, **C** - Responsibility for statistical analysis, **D** - Writing the article, **E** - Critical review, **F** - Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

MINE-BLAST TRAUMA AS A FACTOR IN THE EARLY DEVELOPMENT OF VASCULAR DISEASES OF THE BRAIN

DOI: 10.36740/WLek202306123

Volodymyr O. Korshnyak¹, Julia V. Bovt¹, Oleksandr R. Pulyk², Oleksandr M. Stoyanov³¹STATE INSTITUTION "INSTITUTE OF NEUROLOGY, PSYCHIATRY AND NARCOLOGY OF THE NATIONAL ACADEMY OF MEDICAL SCIENCES OF UKRAINE", KHARKIV, UKRAINE²UZHGOROD NATIONAL UNIVERSITY, DEPARTMENT OF NEUROREHABILITATION, UZHGOROD, UKRAINE³ODESA NATIONAL MEDICAL UNIVERSITY OF THE MINISTRY OF HEALTH OF UKRAINE, ODESA, UKRAINE

ABSTRACT

The aim of this study is to investigate the state of bulbar conjunctival vessels, rheological properties of blood, catecholamines (adrenaline, norepinephrine), lipid metabolism, alkaline proteins of blood serum in patients with consequences of mild combat traumatic brain injury.

Materials and methods: 76 individuals aged 28 to 41 years were examined. The duration of the injury lasted from 2 to 4 years. The control group consisted of 28 individuals aged 45 to 49 years with primary cerebral atherosclerosis and manifestations of cerebral circulation disorders. The state of the bulbar conjunctiva vessels and blood circulation was studied using a slit lamp SHCHL-2B at 40-fold magnification. Rheological parameters, lipid metabolism, serum alkaline proteins, total catecholamines were studied according to generally accepted methods.

Results: Changes in the vessels of the bulbar conjunctiva (stage II-III) were detected in 76% of the subjects, indicating the formation of cerebral vascular pathology, and in 87% of patients with initial cerebral atherosclerosis. The analysis of lipid metabolism showed significantly ($p < 0.05$) increased data on all studied parameters (cholesterol, high-density lipoprotein, β -lipoprotein, atherogenic index), both in patients with aftereffects of mild combat traumatic brain injury and in patients with initial cerebral atherosclerosis. An increase in alkaline proteins indices we detected in 62% of patients with aftereffects of mild combat cerebral trauma and in 55% of patients with initial cerebral atherosclerosis. At the same time, there was an increase in total catecholamines in the erythrocytes of patients with combat head injury. An increase in fibrinogen was noted in both groups, but in the group with initial cerebral atherosclerosis it was more pronounced.

Conclusions: Combat traumatic brain injury contributes to the early formation of cerebral atherosclerosis and cerebral circulation disorders in this category of patients. The examination methods we have studied should be included in the survey plan for these patients. They are important not only for diagnosis, but also for improving treatment and preventing vascular disasters.

KEY WORDS: mild combat traumatic brain injury, cerebral atherosclerosis, cerebral circulation disorders, biomicroscopy of bulbar conjunctiva vessels

Wiad Lek. 2023;76(6):1485-1490

INTRODUCTION

The number of victims with aftereffects of mild combat traumatic brain injury is growing exponentially as the war in Ukraine continues. Accordingly, the number of victims with aftereffects of cerebral trauma, the course of which is much more severe than that of civilian traumatic brain injury (TBI), is also increasing over time.

Combat injuries are complex combined injuries that include concussions, acoustic and vibration injuries, additional head contusion, spine, lungs, heart, and other organs and body parts [1, 2].

At the same time, in the available literature, we have not found a consensus on the correlation between vascular disorders of traumatic origin and vascular diseases of the brain after combat TBI. Along with this, it has been suggested that traumatic encephalopathy in

many patients, including those with mild TBI, is formed with signs of atherosclerotic type [3].

Vasospasms are of great importance in the formation of cerebrovascular pathology in patients with combat traumatic brain injury. Cerebral arteries respond to mechanical stimuli by contracting smooth muscle, which can be either short-term or long-term. Vasospasms of traumatic origin inevitably affect cerebral blood flow. Intracranial vessels spasm in the long-term aftereffects of TBI can cause ischemia of diencephalic structures, which in most cases determine the clinical manifestations of closed traumatic brain injury (TBI) and its long-term aftereffects.

Under the influence of a traumatic agent, the mechanical properties of blood vessels can change: their strength is impaired, deformations and occlusions occur due to damage to the arterial wall.

Clinical observations have shown that a significant role in the formation of cerebral vasospasm, vasomotor lability, blood flow disorders with subsequent neurotrophic changes in the remote period of mild combat TBI belongs to brainstem pathology [4,5], which in turn is associated with transient circulatory disorders in the vertebrobasilar basin, which supplies blood to the stem parts. The trauma of vertebral arteries with perivascular vegetative plexuses aggravates stem hemodynamic disorders. One of the causes of posttraumatic angiospasm is the increase in the serotonin content in the CSF both in the acute period and in the long term of TBI. It is believed that the severity of TBI and its aftereffects correlate with the serotonin content (as well as adrenaline and norepinephrine). The long-lasting angiospasm can lead to changes in the mechanical properties of blood vessels, which also affects cerebral blood flow, contributing to its slowing.

Traumatic brain injury worsens the blood supply to the brain, which leads to metabolic disorders that are typical for vascular diseases of the brain. Young and middle-aged people who have suffered mild combat cerebral traumatic brain injury often develop hypertension and early cerebral atherosclerosis. The latter is especially common, and it affects the vessels of the vertebrobasilar basin to a greater extent.

Thus, it can be said that in the long-term period of mild combat TBI, secondary vascular disorders occur that are not related to the direct vascular injury and changes in the vascular wall. Cerebral circulation is very sensitive to mechanical stress and its disruption can last for a very long time and manifest itself even in the remote period of combat cerebral injury.

It is well known that the state of the bulbar conjunctiva vessels is an identical reflection of the state of the brain vessels because the conjunctiva of the eyeball is supplied with blood from the internal carotid artery system. Biomicroscopic examination of the conjunctival vessels allows to identify the vascular disorders much earlier than they appear on the eye fundus.

THE AIM

To investigate the state of bulbar conjunctival vessels, lipid parameters and rheological parameters of blood in patients with aftereffects of mild combat traumatic brain injury and in patients with initial cerebral atherosclerosis.

MATERIALS AND METHODS

We have examined 76 individuals aged 28 to 41 years who stayed in the neurosurgical clinic of SI Institute of neurology, psychiatry and narcology of the National

Academy of medical sciences of Ukraine with a diagnosis of long-term aftereffects of mild mine-blast trauma. The duration of the injury was from 2 to 5 years. The presence of acute cerebral injury was confirmed by the relevant medical documents. We also examined 28 individuals aged 45 to 49 years with primary cerebral atherosclerosis and initial manifestations of cerebral circulatory failure.

The state of the bulbar conjunctiva vessels was studied using a slit lamp SHCHL-2B at 40 fold magnification. The outer (temporal) division of the bulbar conjunctiva, the limbus and the conjunctiva of the lower transitional fold are the most accessible for biomicroscopic study of the microvasculature of the eyeball.

It has been known that the state of the bulbar conjunctiva vessels reflects the state of the brain vessels. Therefore, in vivo biomicroscopic examination of conjunctival vessels allows detecting vascular disorders much earlier than they appear on the fundus.

Three stages are recognized while analyzing the vascular changes:

I stage - venules are evenly dilated, convoluted, in ratio a:b = 1:2 - 1:3, blood flow is somewhat slowed.

II stage - vessels of irregular caliber with microaneurysms, a:b = 1:3 - 1:4. The capillaries in the limbus area are deformed with microaneurysms. Blood flow is slowed.

III stage - a : b = 1:4, irregular caliber. Point hemorrhages under the conjunctiva. Blood flow is slow, push-like.

The factors that influence the presence of microangiopathies are: a) the severity of TBI; b) the severity of cerebrospinal fluid hypertension; c) the presence of comorbidities (diabetes) and the patient's age. Disorders of conjunctival microcirculation are characterized by full blood flow and mydriatic tortuosity of venules, changes in arteriolar/venule ratio, irregular vessel caliber, the appearance of single microaneurysms in the capillary net, and sludge-phenomenon.

In addition, we studied the indices of alkaline proteins, which we first studied in the aftereffects of mild TBI and initial cerebral atherosclerosis. Alkaline proteins have pathogenetic significance in the development of cerebral atherosclerosis, the formation of which is accompanied by decrease of their content. In healthy people, alkaline proteins (AP) are true to 21.0 ± 0.8 mg/ml. Method of determination: first, total serum proteins were precipitated with 20% trichloroacetic acid. 0.2 N sulphuric acid was added to the sediment and incubated for 30 minutes in the cold, stirring constantly and centrifuged. This procedure was repeated for 5 times. The acid extracts were then precipitated with a sixfold volume of acetone. The resulting sediment was separat-

ed by centrifugation, and then the amount of protein was determined by the Lowry method of protein assay in Miller modification.

Blood rheological properties were assessed by the results of the study of prothrombin, thrombin time, fibrinogen, and recalcification time. Regulation of vascular tone was assessed by the content of total catecholamines in erythrocytes and by the concentration of adrenaline and norepinephrine in urine.

The data obtained were statistically evaluated to determine the averages and Student's t-distribution correlation coefficient.

RESULTS

The state of the vascular bed was assessed by changes in the fundus vessels detected during ophthalmoscopy (the diameter of arteries, veins, tortuosity of vessels, the ratio of the caliber of arteries and veins, in which the diameter of the arteries was taken as a unit).

Biomicroscopy of the bulbar conjunctiva revealed abnormalities in 73 patients (96 %) ($p < 0.05$) with consequences of combat closed TBI.

The following results were obtained in the analysis of vascular changes in the conjunctiva: Stage I - there were 18 (24%) patients. The second stage was in 28 (37%) patients. In 30 (39%) patients, the examination revealed stage III. These patients subsequently had cerebral circulation disorders.

In the group of patients with the initial cerebral atherosclerosis, in the majority of subjects, circulatory disorders in the vessels of the bulbar conjunctiva corresponded to stages II and III (Table I).

Thus, according to biomicroscopy of bulbar conjunctival vessels, patients with mild combat TBI have cerebral vascular pathology and atherosclerosis, which requires further monitoring of this group of patients.

Indices of lipid metabolism in patients with consequences of mild TBI and initial cerebral atherosclerosis are presented in Table II.

As can be seen from the results of the examination (Table II), in the group of patients with aftereffects of mild combat traumatic brain injury, there was a significant increase in 4 out of 7 studied lipid metabolism parameters, which indicates the development of cerebral atherosclerosis in the given contingent. Comparison of these data in patients with initial cerebral atherosclerosis showed that there was an increase in 5 of the 7 studied parameters (cholesterol, triglycerides, high-density lipoprotein, β -lipoprotein and atherogenicity coefficient). The data obtained indicate that in patients with the aftereffects of mild combat traumatic brain injury, the atherosclerotic pro-

cess is potentiated by the traumatic one and confirms the importance of the vascular factor in the genesis of traumatic brain disease.

The content of alkaline proteins in these groups of patients was also determined. As a control group, we studied the content of alkaline proteins in practically healthy men aged 27 to 37 years, with no history of traumatic brain injury and other pathology of the nervous system, which corresponded to $26,4 \pm 1,17$ mg/ml. This indicator was used to assess the content of alkaline proteins in the subjects of the two groups.

As can be seen from the obtained data (Table III), the absence of significant differences in alkaline proteins between the groups with consequences of mild combat cerebral trauma and cerebral atherosclerosis indicates the similarity of the mechanisms of these metabolic functions in these groups of patients.

The rheological properties of the blood were assessed by the results of the study of prothrombin, thrombin time, fibrinogen, and recalcification time. Regulation of vascular tone was assessed by the content of total catecholamines in erythrocytes and by the concentration of adrenaline and norepinephrine in urine (Table IV).

According to the obtained data, the content of total protein in the blood of patients of both groups was within the physiological corridor. The level of prothrombin in patients of the IInd group was higher than in the control group. The same was true for the index of thrombin time. The level of fibrinogen was increased in patients of both groups, but this phenomenon was more pronounced in patients of the IInd group. Accordingly, a decrease in recalcification time was observed in these patients. Evaluating the rheological properties of blood by the state of the coagulation system, we can talk about a higher frequency (higher than normal) of these indicators in patients with initial cerebral atherosclerosis compared with those in patients of group I. This is especially evident in such indicators as prothrombin ($p < 0.05$) and thrombin time ($p < 0.05$), which may be associated with changes in lipid and protein metabolism in patients with this pathology.

Assessing the controllability of the vascular tone by the activity of catecholamine metabolism, it can be noted that both groups are characterized by an increase in the content of total catecholamines in erythrocytes. This increase is more pronounced among patients of group I. It should be noted that the increase in the content of catecholamines and the corresponding tendency to vasospasm in patients of both groups is most likely of a different nature. In group I, the increase in catecholamines is combined with a normal rate of urinary excretion of norepinephrine

Table I. Findings from the examination of the bulbar conjunctiva in patients with aftereffects of mild combat traumatic brain injury and initial cerebral atherosclerosis

Stages	Aftereffects of combat TBI (n=76)	Initial cerebral atherosclerosis (n=38)
I stage	18 (24%)	5 (13%)
II stage	28 (37%)	10 (53%)
III stage	30 (39%)	13 (34%)

Table II. Indices of lipid metabolism in patients with aftereffects of mild combat TBI and initial cerebral atherosclerosis

Indices	Normal range	Aftereffects of combat TBI (n=76)	Initial cerebral atherosclerosis (n=28)
Cholesterol	up to 5,2 mmol/l	>6,48 (59 ind.)*	>6,37 (28 ind.)*
Triglycerides	(0,56 - 1,85 mmol/l)	>1,96 (35 ind.)	>2,0 (23 ind.)*
High density lipoproteins	(0,9 - 1,94 mmol/l)	>2,1 (51 ind.)*	>2,2 (21 ind.)*
Low density lipoproteins	(1,68 - 4,53 mmol/l)	>4,88 (38 ind.)	>4,9 (12 ind.)
Very low density lipoproteins	(0,26 - 1,04 mmol/l)	>1,07 (32 ind.)	>1,07 (14 ind.)
β -lipoproteins	(35-55 conventional units)	>59 (68 ind.)*	>60 (23 ind.)*
Atherogenic index	(0 - 3)	>3,7 (72 ind.)*	>3,6 (27 ind.)*

Note: * - p < 0,05

Table III. Indices of alkaline proteins in patients with aftereffects of mild combat TBI and initial cerebral atherosclerosis

Alkaline proteins	Aftereffects of combat TBI (n=52)	Patients with initial cerebral atherosclerosis (n=22)
normal range 26,4 \pm 1,17 mg/ml	9 (17%)	7 (32%)
above normal range 29,8 \pm 1,1 mg/ml	32 (62%)*	12 (55%)*
below normal range 24,0 \pm 1,2 mg/ml	11 (21%)	3 (14%)

Note: p < 0,05

Table IV. Comparative evaluation of blood rheological properties in patients with aftereffects of mild combat TBI and initial cerebral atherosclerosis

Group Index	Control group	Aftereffects of traumatic brain injury (group I)	Initial stage of cerebral atherosclerosis (group II)
total protein, g/l	65 - 85	74,12 \pm 8,07	81,43 \pm 10,1
prothrombin, %	85 - 105	91,24 \pm 8,28	110,0 \pm 4,9*
thrombin time, sec.	14 - 16	15,8 \pm 1,4	19,1 \pm 1,6*
fibrinogen, g/l	2 - 4	4,4 \pm 0,9	4,8 \pm 0,6
recalcification time, sec.	50 - 70	58,0 \pm 4,9	47,3 \pm 4,4*
total catecholamines, conventional units of optical density	1,8 - 2,1	2,94 \pm 0,16	2,73 \pm 0,09
urinary adrenaline, ng/min.	6 - 14	6,46 \pm 0,72	4,35 \pm 0,14*
urinary norepinephrine, ng/min.	20 - 40	43,3 \pm 3,6	34,5 \pm 3,4*

Note: * validity of differences between the indicators of groups I and II (p < 0,05)

and epinephrine, i.e., it can be assumed that there is an increase in catecholamine synthesis associated with the level of functional activity of the central nervous system. In patients of group II, an increase in the content of catecholamines is associated with a significant

decrease in the amount of catecholamines excreted in the urine. That is, there is obviously an accumulation of catecholamines due to changes in the rate of their metabolism, and this is most likely associated with metabolic disorders.

DISCUSSION

The neuro-ophthalmological evaluation of the vessels of the bulbar conjunctiva allows judging the state of the vascular system of the brain to a large extent.

Among the 76 patients who were examined, 58 had abnormalities in vascular parameters (according to biomicroscopy): 28 patients had slowed blood flow and microaneurysms; 30 had dilated and tortuous veins, splinter hemorrhages under the conjunctiva, and slow and jerky blood flow.

In patients with initial cerebral atherosclerosis, abnormalities were detected in 23 patients: the arteries were narrowed, there was dilation and sharp tortuosity of the veins, and in 22 patients the arteries were sclerosed.

Thus, the results of our studies have shown that changes in cerebral hemodynamics in patients with long-term aftereffects of mild combat traumatic brain injury and atherosclerosis with initial manifestations of cerebral circulatory failure have a number of common features. On the part of the microcirculatory system, these are narrowing of the arteries, tortuosity and dilation of the veins, changes in the ratio of the caliber of the arteries and veins, and slowing of blood flow.

The humoral component of vascular tone regulation is an increase in the level of total catecholamines in red blood cells. On the part of blood rheology, it is a change in the level of blood coagulation proteins and related indicators.

At the same time, it is necessary to note a number of significant differences in the changes of the studied systems, which imply different mechanisms of formation of these changes. While both nosologies are characterized

by narrowing of small arteries, in atherosclerotic lesions it is complemented by sclerosis of the vascular wall. Elevation in the level of catecholamines in red blood cells in atherosclerosis is associated with a decrease in their secretion and, accordingly, is most likely associated with their deposition. In TBI, an increase in the concentration of catecholamines is associated with an increase in their secretion, and their synthesis is obviously enhanced.

The analysis of the obtained indicators of alkaline proteins between the two groups of survey sample revealed the similarity of the mechanisms of these metabolic functions in these groups of patients. Similar results were obtained for lipid metabolism: increased cholesterol, triglycerides, high-density lipoprotein, β -lipoprotein, and atherogenic index indicate potentiation of the atherosclerotic process by trauma and confirm the importance of the vascular factor in the genesis of traumatic brain injury.

CONCLUSIONS

Biomicroscopy of the eye conjunctiva allows to assess the degree of pathological changes in the vascular system of the brain in combatants, to clarify the stage of the pathological process and to monitor the effectiveness of treatment for vascular diseases of the nervous system and is an inexpensive and accessible method.

Impaired lipid metabolism, increased levels of alkaline proteins and catecholamines in erythrocytes require the inclusion of hypolipidemic drugs in the therapeutic complex, which reduce the content of atherogenic lipoproteins in the blood plasma, prevent the development or promote the regression of the atheromatous process.

REFERENCES

1. Korshniak V.O. Vplyv vybukhovoï khvyli na formuvannia nevrolohichnoi symptomatyky u khvorykh z boiovoiu cherepno-mozkovoïu travmoïu [Impact of blast wave on the formation of neurological symptoms in patients with combat traumatic brain injury]. *International Journal of Neurology*. 2016; 5 (83): 83-87. (In Ukrainian).
2. Korshnyak VO. Gostra boyova kontuziyna cherepno-mozkova travma: patogenez, diagnostika, likuvannya [Acute combat traumatic brain injury: pathogenesis, diagnosis, treatment]. After edition of Korshnyak V.O. Kharkiv. IE Liburkina L.M. Publ. 2018; 156. (In Ukrainian).
3. Korshniak VA, Nasybullyn BA, Korshniak T.V. Sravnytelnaiia otsenka sostoiania hemodynamyky u bolnykh s cherepno-mozghovoi travmoi y aterosklerozom s nachalnymi proiavlenniamy nedostatochnosti mozghovoho krovoobrashcheniia [Comparative assessment of hemodynamics in patients with craniocerebral trauma and atherosclerosis with initial manifestations of cerebral circulatory insufficiency]. *Medical rehabilitation, balneology, physiotherapy*. 2012; 2: 20-22. (In Ukrainian).
4. Korshniak VO, Nasibullin BA. Suchasni pohliady na mekhanizm vplyvu vybukhovoï khvyli na tsentralnu nervovu systemu ta formuvannia nevrolohichnoi symptomatyky [Modern views on the mechanism of blast wave impact on the central nervous system and formation of neurological symptoms]. *International Journal of Neurology*. 2016; 6 (84): 136-142. (In Ukrainian).
5. Shkolnyk V.M., Baranenko O.M., Pogoryelov O.V. Paraklinichni metody doslidzhennia v nevrologiyi [Paraclinical research methods in neurology]. Dnipropetrovsk. «ART-Press» Publ. 2003; 42-48. (In Ukrainian).

ORCID and contributionship:

Volodymyr O. Korshnyak: 0000-0002-3041-3944^{A,B,D,E}

Julia V. Bovt: 0000-0002-0693-2242^{B,C,E}

Oleksandr R. Pulyk: 0000-0002-8717-047X^{F,E}

Oleksandr M. Stoyanov: 0000-0002-3375-0452^{B,D}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Volodymyr O. Korshnyak

State Institution «Institute of Neurology, Psychiatry

And Narcology of The National Academy of

Medical Sciences of Ukraine», Kharkiv, Ukraine

e-mail: korshnyak.doc@gmail.com

Received: 10.11.2022

Accepted: 30.05.2023

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article



Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

EFFECT OF SCORPION VENOM TOXINS ON STRUCTURAL AND FUNCTIONAL PARAMETERS OF INTERNAL ORGANS, INCLUDING KIDNEYS (REVIEW)

DOI: 10.36740/WLek202306124

Ruzhena Matkivska¹, Inga Samborska², Oleksandr Maievskiy³¹BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE²NATIONAL PIROGOV MEMORIAL MEDICAL UNIVERSITY, VINNYTSIA, UKRAINE³EDUCATIONAL AND SCIENTIFIC CENTER "INSTITUTE OF BIOLOGY AND MEDICINE" OF TARAS SHEVCHENKO NATIONAL UNIVERSITY OF KYIV, KYIV, UKRAINE

ABSTRACT

The aim: To establish patterns of structural and functional changes in internal organs, including kidneys, under the conditions of exposure to scorpion venom toxins.**Materials and methods:** A thorough literature analysis was conducted on the basis of PubMed, Google Scholar, Web of Science, and Scopus databases. When processing the search results, we chose the newest publications up to 5 years old or the most thorough publications that vividly described the essence of our topic.**Conclusions:** The venom of various species of scorpions exhibits a wide range of biological activity. Acting on the structures of the central and peripheral nervous system, the toxins of scorpion venom cause the development of paralysis, convulsions, brain inflammation, hemorrhagic and ischemic strokes. Under conditions of influence on the cardiovascular system, damage to the endothelial lining of the vascular wall, disturbances in heart rhythm, conduction, and the development of destructive changes in the myocardium are characteristic. Data on kidney damage due to scorpion bites require a more detailed study, as information on microscopic and submicroscopic changes in the structure of the organ is too limited. However, cases of the development of tubular necrosis, interstitial nephritis, and kidney infarction are currently known.**KEY WORDS:** scorpions, venom, toxicity, voltage-gated ion channels, kidneys

Wiad Lek. 2023;76(6):1491-1498

INTRODUCTION

According to the WHO, about 1.5 million cases of poisoning due to scorpion bites are registered annually in the world, resulting in 2,000-3,000 deaths. Cases of scorpionism are common in the United States of America, Canada, Europe, and Australia, but this problem is most widespread in Africa, India, Mexico, Brazil, Iran, Saudi Arabia, and Venezuela, where more than 2 billion people are under constant threat. Climate changes, together with the rapid development of cities near the areas where scorpions usually live, significantly increase the probability of meeting them. In particular, in Brazil alone, since 2012, the number of scorpion stings has increased from 64,000 to 124,000 per year [1].

To date, there is information about the existence of about 2,000 species of scorpions. The vast majority of them are dangerous to humans, especially representatives of the families Buthidae, Scorpionidae and Hemiscorpionidae. Clinical manifestations of poisoning by scorpion toxins vary significantly, depending on their

species, the amount of poison that entered the victim's body. Researchers note that the content of their venom is extremely complex and heterogeneous [2].

THE AIM

The aim was to establish patterns of structural and functional changes in internal organs, including kidneys, under the conditions of exposure to scorpion venom toxins.

MATERIALS AND METHODS

A thorough literature analysis was conducted on the basis of PubMed, Google Scholar, Web of Science, and Scopus databases. When searching for information on the prevalence of the problem of scorpionism in the world, the composition of scorpion venom, its biological effects on the body of mammals, we used the following combinations of keywords: «scorpions»,

«venom», «toxicity», «voltage-gated ion» channels», «kidneys». When processing the search results, we chose the newest publications up to 5 years old or the most thorough publications that vividly described the essence of our topic. After conducting a detailed review of the abstracts of the articles and getting acquainted with their full content, 40 sources were selected that fully corresponded to the results of the request.

REVIEW AND DISCUSSION

GENERAL INFORMATION REGARDING THE TOXIC COMPONENTS OF THE VENOM OF DIFFERENT SPECIES OF SCORPIONS

Currently, the most studied components of scorpion venom are small peptides, mainly due to their diversity and broad pharmacological properties. According to the structure, small peptides are classified into three large superfamilies: peptides containing cysteine-stabilized (CS) α/β motifs with disulfide bridges, calcins, and peptides that do not contain disulfide bridges. However, it has been established that enzymes, mixtures of inorganic salts, free amino acids, nucleotides, and lipids are among the toxic components of scorpion venom. [3, 4].

Peptides with CS motifs are built from an α -helix connected with two- or three-stranded β -sheet by disulfide bridge. They affect mammalian ion channels by blocking or modulating their action and can be divided into short- and long-chain peptides. Long-chain toxins consist of 55-76 amino acid residues and about four disulfide bridges. According to their mechanism of action, they are often called Na^+ channel toxins (NaTx), namely α and β , depending on their specific interaction with voltage-gated Na^+ channels. α -NaTx block site-3 in ion channels and, therefore, inhibit their inactivation and prolong the action potential. β -NaTx interact with site-4 Na^+ channels, shift the activation voltage to a more negative potential, which leads to their inactivation [5].

Short-chain peptides consist of 23-64 amino acid residues and 3-4 disulfide bridges. They are also known as K^+ channel toxins (KTxs), acting as K^+ channel blockers. KTxs are divided into α , β , γ , κ , δ , λ . It was established that the δ -KTxs group, in addition to influencing K^+ channels, has inhibitory activity against serine proteases [6].

Calcins belong to a small but ever-growing family of scorpion venom toxins consisting of Ca^{2+} ion channel modulator peptides. Among them, imperacalcin (imperatoxin), maurocalcine, hemicalcin, hadrucalcin, opicalcin, urocalcine, and veioalcine are distinguished. These types of peptides have a high similarity of amino acid sequences in their structure (more than 78% iden-

tity) and are stabilized by two disulfide bridges. Data from the scientific literature indicate that calcines act mainly as agonists of ryanodine receptors, which are intracellular ligand-activated Ca^{2+} channels, located in the membranes of the endoplasmic and/or sarcoplasmic reticulum. Ryanodine receptors play a key role in the processes of excitation and contraction of cardiac and skeletal muscles, ensuring the release of Ca^{2+} from intracellular depots. Therefore, in general, calcines induce an excessive contraction of muscle fibers, an increase in the intracellular level of Ca^{2+} , which leads to the development of spastic paralysis. Calcins also have the ability to penetrate cell membranes without causing their lysis. It was hypothesized that this property is caused by the presence of positively charged amino acid residues at one end of the molecule, which probably interacts with negatively charged gangliosides of the host's plasmolemma. This facilitates the association between the hydrophobic region of the toxin and the inner surface of the cell membrane, allowing calcin to move. Further electrostatic interactions with negatively charged molecules in the cytoplasm cause the entry of the toxin into the cell, without causing the lysis of its membrane [7].

Peptide toxins without disulfide bridges are compounds represented by 13-56 amino acid residues with an extremely heterogeneous composition. Unlike disulfide-bridged toxins, they do not exhibit properties that suggest structure-function relationships. Most of them are cationic molecules that show remarkable structural flexibility. This characteristic allows them to interact with a wide range of biological targets, however, no specific targets for them have been identified so far [8].

To date, there is limited data on enzymes as components of scorpion venom, because the focus of research has always been on small peptides. Among the studied enzymes, hyaluronidase, PLA_2 , MMP, serine proteases, LLAOs are components of the venom of most scorpions, which exhibit a wide range of biological effects [9]. Hyaluronidase found in the families Buthidae, Bothriuridae, Urodacidae is capable of disrupting the integrity of the extracellular matrix and connective tissue components in the perivascular areas of venom inoculation sites, facilitating systemic diffusion of other toxic compounds to target organs [10]. PLA_2 scorpion venoms belong to the III group of PLA_2 , have a heterodimeric structure, consist of long and short chains connected by a disulfide bridge. They show neurotoxicity, myotoxicity, anticoagulant and angiogenic properties. PLA_2 act as hemolytic agents because they destroy cell membranes of erythrocytes by hydrolysis of phospholipids [11]. They also cause tissue necrosis and hemorrhage. The activity of this family of enzymes has been established

in several species of scorpions, including *Opisthacanthus cayaporum* and *Heterometrus laoticus*. PLD (phospholipase D or sphingomyelinase D), which has a cytotoxic effect and was isolated from the venom of *Heterometrus lepturus*, was also detected [12].

Scientific research shows that the venom of *Tityus* scorpions has a pronounced proteolytic activity, and the first MMP was studied in *Tityus serrulatus*. MMPs and serine proteases are toxic compounds of the scorpions *Tityus discrepans* and *Hemiscorpius lepturus*. It is believed that proteases play a key role in the activation of toxin precursors through post-translational modifications. In addition, they inhibit platelet aggregation, modulate the production of NO by cytokines, and activate the complement system. These enzymes contribute to the diffusion of toxic compounds of the venom through the degradation of matrix proteins such as collagen and glycoproteins [13].

In scientometric databases, information regarding scorpion venom enzymes such as LAAOs was found. They have a cytotoxic effect, since the product of their catalytic activity, primarily H_2O_2 , induces apoptosis of endothelial cells of the vascular wall, causing hemorrhages, edema [14].

In addition to the above-mentioned components of scorpion venom, certain types of metals, such as copper, zinc, iron, plumbum, manganese and nickel, have been studied in their composition. The latter are isolated from the toxins of *Androctonus bicolor*, *Androctonus crassicauda* and *Leiurus quinquestriatus*. Their connection with the activity of enzymes has been proven, since they probably act as enzyme cofactors [15].

At the moment, it is known that in addition to protein toxins, the scorpion venom includes a significant amount of non-peptide low molecular weight substances (< 1 kDa). Thus, it has been experimentally proven that *Diplocentrus melici* has 1,4-benzoquinone derivatives, *Heterometrus laoticus* – adenosine, and *Centruroides sculpturatus* – citric acid. In other published materials, information about such components as spermidine in the scorpions *Palamneus phipsoni* (*Heterometrus phipsoni*), 5-hydroxytryptamine in *Leiurus quinquestriatus* and *Buthotus minax* (*Hottentotta minax*) was found. [16]. These components are still poorly understood, especially their biological role and mechanisms of action. Therefore, currently modern analytical methods of research are increasingly directed at this problem. It is known that low molecular weight compounds can act directly as toxins or enhance the effects of other poison substances. Evans E. R. Et al. [17] established the presence of such substances in the venom of *Hormurus waigiensis* scorpions as adenosine and AMP. Adenosine is a common component of the venom

of many predatory animals. It has been proven to have a wide range of physiological effects in mammals, including induction of vasodilation, increased permeability of vessel walls, inhibition of platelet aggregation, and prolongation of blood clotting time. Based on this, it can be argued that adenosine contributes to increasing the toxicity of venom components and facilitates their delivery to target organs. AMP in *Hormurus waigiensis* scorpions has hypotensive properties and, together with adenosine, increases the pathological effect of venom peptide substances.

PATTERNS OF THE PATHOLOGICAL EFFECT OF SCORPION VENOM ON THE NERVOUS SYSTEM OF MAMMALS

It was previously mentioned that scorpion toxins mainly have a neurotoxic effect. The last is vividly described on the example of *Tityus serrulatus*. From the venom of these scorpions, certain types of compounds capable of affecting the structures of the central nervous system were experimentally isolated [18]. TS_1 is the most common and dangerous toxin, which makes up about 16% of the soluble fraction of the venom. It acts as a classic β -toxin, modulating the processes of activation of Na^+ channels – Nav1.6 and Nav1.3 during the resting potential. Intracerebral injection of TS_1 in rats has been shown to induce epileptiform seizures, hind limb paralysis, and severe respiratory distress followed by death. This toxin is able to stimulate the body's immunological response, increasing the levels of TNF- α and IFN- γ in the brain of experimental animals [19]. TS_3 from *Tityus serrulatus* scorpions is considered an α -toxin associated with severe and fatal consequences. Even small doses of it after intracerebral administration to experimental rats are able to affect the structures of the brain stem involved in the neurovegetative control of the functions of the cardiovascular and respiratory systems. When injected subcutaneously, the toxin overcomes the blood-brain barrier and reaches the indicated centers. Its main action is aimed at delaying inactivation of voltage-gated Na^+ channels, which increases the permeability of cell membranes for Na^+ ions, increasing the release of neurotransmitters in synapses. After intrahippocampal injection, TS_3 promotes the release of glutamate, the development of seizures and the death of a significant number of neurons in certain areas of the hippocampus [20]. This toxin causes Ca^{2+} -dependent release of glutamate from cortical synaptosomes. Its role in the development of pulmonary edema and cerebral inflammatory process with increasing levels of TNF- α and increased leukocyte migration has been established. TS_4 from the venom of these scorpions is considered a weaker toxin. However,

it induces the secretion of neurotransmitters such as glutamate and GABA from rat brain synaptosomes. Ts₅ is an α -neurotoxin capable of delaying inactivation of voltage-dependent Na⁺ channels. It specifically acts on Nav1.2, Nav1.3, Nav1.4, Nav1.5, Nav1.6, Nav1.7., shows the property of influencing the level of catecholamines in the blood and reducing the concentration of GABA, dopamine in vitro. It acts as a pro-inflammatory toxin, stimulating the production of TNF- α , IL-6. It should be noted that a large number of toxins that block K⁺ channels in the CNS, such as Ts₆, Ts₇, Ts₈, Ts₁₅, Ts₁₆, Ts₁₉, are also isolated from the venom of *Tityus serrulatus* scorpions [21].

Among the adult and children's population, such a complication from the central nervous system during scorpion bites as a violation of cerebral blood circulation is reported. The development of both ischemic and hemorrhagic stroke is characteristic [22, 23]. The latter arise as a result of significant intracranial hemorrhages. Available data on cerebral infarction, which occurs more often in the parietal-occipital and cerebellar regions. Scorpion venom often affects the vessels of the brain, including the anterior and middle cerebral arteries. Scientists note that ischemic changes in the thalamus, brain stem, and the development of lateral medullary syndrome are possible. It is known that the mortality due to cerebral circulation disorders under these conditions is about 28%, however, in addition to CNS lesions, most of the victims after inoculation with scorpion venom toxins had symptoms of shock, coagulopathy, rhabdomyolysis, and acute renal failure, which increased the risk of a fatal outcome [24].

In separate published scientific sources of information, it is stated that in the initial stages of the scorpion venom toxins action, the symptoms of the parasympathetic nervous system disruption, which are manifested by nausea, vomiting, diarrhea, sweating, salivation, lacrimation, bradycardia, arterial hypotension are prevailing. In the future, disorders of the functioning of the sympathetic nervous system, accompanied by hypertension, arrhythmias, and heart failure, become dominant [25, 26]. Damage of the peripheral nervous system structures in cases of scorpionism is also proven. In particular, it is known the development of such phenomena as abnormal eye movements, facial paralysis, Guillain-Barre syndrome, myelitis, fasciculations, convulsions. However, one of the most serious complications is paralysis of the respiratory muscles, which causes respiratory failure [27, 28].

MECHANISMS OF THE CARDIOVASCULAR SYSTEM INJURY IN SCORPION BITES

According to scientific sources, poisoning due to scorpion bites, can lead to the development of heart failure

and hemodynamic disorders. The etiology of disturbances in the normal functioning of the cardiovascular system in these conditions is associated with the effect of the poison on the sympathetic nervous system and / or on the structure of the myocardium itself, as well as with the release of catecholamines, neuropeptide Y (NPY), angiotensin II and endothelin-1 (ET-1). Proteases such as angiotensin-converting enzyme (ACE), endothelin-converting enzyme (ECF), isolated from *Tityus* scorpion venom, lead to hemodynamic disturbances. At the same time, activation of inflammatory pathways and excessive production of reactive oxygen species (ROS) contribute to heart tissue damage. As a rule, venom toxins bind to pattern recognition receptors (PRRs), in particular toll-like receptor-2 (TLR₂) and TLR₄, and activate NF- κ B, the production of proinflammatory mediators, oxidative stress (OS) in the myocardium. According to the latest studies, an increase in the concentration of the vasoconstrictor ET-1 in the blood serum of victims and experimental animals was associated with a violation of the activity of the cardiovascular system precisely due to an increase in blood pressure, a violation of the rhythm and an increase in the frequency of heart contractions. It has also been proven that ET-1, through the activation of the ET-A receptor, triggers and/or modulates the body's inflammatory reactions, the development of vascular wall fibrosis. It increases the production of superoxide anion and the growth of cytokines such as IL-1, TNF- α , IL-6. It was also established that MMP-2 and MMP-9, which grew in the homogenates of rat heart samples, were involved in the processes of heart tissue damage during scorpion bites, compared to the control [29]. According to scientists' findings, ET-A receptors are involved in the processes of activation and sequestration of neutrophils, which causes the release of myeloperoxidase from their azurophilic granules. They investigated the development of OS in the myocardium, which was confirmed by the increase in the content of reactive forms of NO, H₂O₂, and malondialdehyde in the supernatants of experimental animals. At the same time, a sharp decrease in the levels of compounds of antioxidant protection – catalase and glutathione peroxidase was recorded. Under these conditions, microscopic studies revealed a severe degree of the heart muscle damage, degeneration of muscle fibers, the presence of areas of hemorrhages and edema. Foci of myonecrosis and pronounced histio-lymphocytic infiltration were observed. The increase in specific markers of heart damage was characteristic, namely the CPK-MB isoform, LDH_{1,2}. In the aorta, areas of aneurysm, media hypertrophy, and its infiltration by leukocytes were noted [30, 31]. An interesting fact is that scorpion bites cause a so-called

vegetative storm (adrenergic or cholinergic), which leads to the appearance of tachycardia and arterial hypertension, thereby increasing the heart contraction and leading to myocardial dysfunction. In addition, the development of an imbalance between oxygen needs and its consumption due to vasoconstriction of the coronary vessels, which causes ischemia, is characteristic. Various mediators that grow in these conditions contribute to the development of myocarditis or stress cardiomyopathy [32, 33].

It has been experimentally established that the venom of some species of scorpions can affect the coagulation system. Thus, the toxins of *Buthotus judaicus*, *Heterometrus spinnifer*, *Parabuthus transvaalicus*, *Androctonus australis*, *Scorpio maurus palmatus*, *Leiurus quinquestriatus habraeus* and *Pandinus imperator* caused a prolongation of blood clotting time. In particular, the toxins of the species *Pandinus imperator* and *Parabuthus transvaalicus* increased this indicator by 2.5 and 2.3 times, respectively, while the others by 0.8-2 times. Literary sources indicate that *Buthus tamulus* scorpions can even cause the development of disseminated intravascular coagulation syndrome. In vitro studies of the action of *Palamneus gravimanus* and *Leiurus quinquestriatus* venoms showed that the toxic compounds of the first type have both pro- and anticoagulant properties, while the toxic compounds of the second scorpion type exhibit a weak anticoagulant effect, reducing the coagulation time of recalcified plasma by only 5-20%. Fibrinolytic activity in both of these representatives was not established. Further experiments with *Palamneus gravimanus* venom fractions partially purified by chromatography showed that they promote the activation of factor X and interfere with the interaction of thrombin and fibrinogen. It was found that a high concentration of *Tityus discrepans* venom in human blood plasma is associated with changes in the activity of partial thromboplastin and prothrombin time. It should also be noted that some fibrinolytic enzymes were isolated from the venom of the scorpion mentioned above. Two of their fractions showed a fibrinolytic effect by degrading α -chains of fibrin and affected tissue plasminogen activator, inducing it. Only one fraction of enzymes carried out its activity exclusively in relation to fibrinogen. It is also known that two types of toxins - imperatoxin from the venom of scorpions *Pandinus imperator* and phaiodactylipin from *Androctonus pahiodactylus* have a hemolytic effect and prolong blood clotting time [34].

Scientific databases indicate that low molecular weight venom compounds isolated from *Buthus martenssi* induce platelet aggregation in the blood of rabbits in vivo and in vitro, thrombus formation, and

changes in thromboxane B_2 levels. Recent experimental studies have established that adenosine and two dipeptides – LeuTrp and IleTrp – found in *Heterometrus laoticus* scorpions had anticoagulant properties. They prolonged the bleeding time in laboratory mice. Dipeptides also inhibited the secondary phase of platelet aggregation induced by ADP and collagen [35].

STRUCTURAL AND FUNCTIONAL CHANGES IN THE KIDNEYS OF MAMMALS IN POISONING WITH SCORPION TOXINS

Among the currently known pathological processes associated with scorpionism, according to experimental studies, kidney damage is considered one of the most critical complications, which is often fatal [36]. In particular, it is noted that *Hemiscorpius lepturus* and *Androctonus australis* exhibit pronounced nephrotoxic effects. The toxic compounds of their venom can directly or indirectly affect kidney tissue, causing mesangiolytic, the development of glomerulonephritis, vasculitis, interstitial nephritis, cortical and tubular necrosis, as well as hypoxia and kidney infarction [37]. Among these pathologies, tubular necrosis is most often observed in victims, which is characterized by a decrease in reabsorption and an increase in the secretion processes of Na^+ , K^+ , Cl^- . Venom inoculation has been shown to affect Na^+ channels in the kidney. At the same time, there is an increase in the levels of catecholamines in the blood of affected individuals. The concentration of Ca^{2+} ions increases in the cytosol of nephron tubule cells under the conditions of poisoning with scorpion toxins. The body's protective mechanisms promote the growth of pro-inflammatory cytokines in the kidney parenchyma, namely IL, TNF- α , NO, as well as platelet aggregation factor, PGs, leukotrienes, kinins, angiotensin, and ET. To date, clinical cases of bites accompanied by rhabdomyolysis, hemolysis and disseminated intravascular blood coagulation are known. These processes contributed to the development of acute renal failure due to damage of the glomerular apparatus and were associated with hemoglobinuria and proteinuria. Acute kidney injury can also be caused by PLA₂ of the venom. Under these conditions, the enzyme exhibits hemolytic and cytotoxic effects in the body. In addition, it promotes the growth of arachidonic acid and, accordingly, the synthesis of eicosanoids. There is also evidence of increased activity of the hypothalamic-pituitary-adrenal system, which stimulates the production of corticosteroids. At the same time, an increase in the levels of acute phase proteins and significant hemodynamic disorders are recorded. It is known that the phenomena of hemolysis are accompanied by the accumulation of a significant

amount of hemoproteins. Under these conditions, the presence of heme groups increases the production of free radicals that accumulate in the cortex of kidneys, exerting a toxic effect. The production of ROS is facilitated by increasing activity of NADPH oxidase. In this case, apoptosis or necrosis of kidney cells is a frequent consequence [38].

Movahed A. et al. [39], studying the effect of *Hemiscorpius lepturus* scorpion venom on the morphology of the kidneys, during histological examination revealed the expansion of the lumens and thinning of the walls of the proximal tubules of the nephron, and the accumulation of fibrin in the glomerular apparatus. The capillaries of the glomerulus contained clusters of erythrocytes, the endothelium of their walls was swollen 4 hours after the injection of the venom to laboratory animals. In the proximal tubules, the flattening of the epithelial cells of the inner layer, their loss of the brush border, and the atypical reaction of the nuclei of these cells, which indicated the development of acute tubular necrosis, were noted.

A thorough analysis of the scientific literature demonstrated the involvement of macrophages in the development of acute kidney injury due to scorpion bites. Thus, the MCP level rises in the victim's body, which indicates the start of an inflammatory process in the body and signals about the risk of complications, since it directly affects the migration of macrophages, proliferation and differentiation of leukocytes in the epithelium of human kidney tubules. *Monocyte chemoattractant protein-1* (MCP-1) stimulates the secretion of IL-6 and intercellular expression molecule-1 (ICAM-1). In addition, by binding to receptors of the chemokine-2 (CC₂) on the surface of podocytes, it can reduce the expression of both miRNA and nephrin protein. The last participates in the formation of filtration slits, therefore defects of

this protein lead to the development of kidney failure, disruption of the cytoskeleton of podocytes, disorders of the filtration process [40].

CONCLUSIONS

Thus, the venom of various species of scorpions exhibits a wide range of biological activity. Acting on the structures of the central and peripheral nervous system, the toxins of scorpion venom cause the development of paralysis, convulsions, brain inflammation, hemorrhagic and ischemic strokes. Under conditions of influence on the cardiovascular system, damage to the endothelial lining of the vascular wall, disturbances in heart rhythm, conduction, and the development of destructive changes in the myocardium are characteristic. These changes in the organs of the cardiovascular system are often accompanied by disorders in the hemostasis system. Data on kidney damage due to scorpion bites require a more detailed study, as information on microscopic and submicroscopic changes in the structure of the organ is too limited. However, cases of the development of tubular necrosis, interstitial nephritis, and kidney infarction are currently known. Significant achievements in the field of research into the proteome, peptidome and biological activity of the constituent components of scorpion venom make it possible to understand in more detail the specifics of the morpho-functional changes that occur in the body of victims under the conditions of their bites. However, the huge variety of these species of animals somewhat complicates and slows down the process of studying all the key components of their venom, and therefore the pathophysiological mechanisms of the development of certain complications remain unknown.

REFERENCES

1. Lacerda AB, Lorenz C, De Azevedo TS et al. Scorpion envenomation in the state of São Paulo, Brazil: Spatiotemporal analysis of a growing public health concern. *PLoS One*. 2022; 17 (4): e0266138. doi: 10.1371/journal.pone.0266138.
2. Godoy DA, Badenes R, Seifi S et al. Neurological and systemic manifestations of severe scorpion envenomation. *Cureus*. 2021; 13 (4): e14715. doi: 10.7759/cureus.14715.
3. Abd El-Aziz FEA, El Shehaby DM, Elghazally SA et al. Toxicological and epidemiological studies of scorpion sting cases and morphological characterization of scorpions (*Leiurus quinquestriatus* and *Androctonus crassicauda*) in Luxor, Egypt. *Toxicol Rep*. 2019; 6: 329-335. doi: 10.1016/j.toxrep.2019.03.004.
4. Ozkan O, Alcigir ME. A comparative pathomorphological findings between *Leiurus abduhbayrami* and *Androctonus crassicauda* (Scorpion: Buthidae) envenomation in rabbit animal model. *J Arthropod Borne Dis*. 2019; 13 (1): 104-115.
5. Dueñas-Cuellar RA, Santana CJC, Magalhães ACM et al. Scorpion toxins and ion channels: potential applications in cancer therapy. *Toxins (Basel)*. 2020; 12(5):326. doi: 10.3390/toxins12050326.
6. Freire MCLC, Silva de Menezes YA, Ferreira Ferraz MV et al. Molecular basis of *Tityus stigmurus* alpha toxin and potassium channel *kV1.2* interactions. *J Mol Graph Model*. 2019; 87: 197-203. doi: 10.1016/j.jmgm.2018.11.012.
7. Uzair B, Bint-E-Irshad S, Khan BA et al. Scorpion venom peptides as a potential source for human drug candidates. *Protein Pept Lett*. 2018; 25(7):702-708. doi: 10.2174/0929866525666180614114307.

8. Valdez-Velázquez LL, Cid-Urbe J, Romero-Gutierrez MT et al. Transcriptomic and proteomic analyses of the venom and venom glands of *Centruroides hirsutipalpus*, a dangerous scorpion from Mexico. *Toxicon*. 2020; 179: 21-32. doi: 10.1016/j.toxicon.2020.02.021.
9. Amorim FG, Longhim HT, Cologna CT et al. Proteome of fraction from *Tityus serrulatus* venom reveals new enzymes and toxins. *J Venom Anim Toxins Incl Trop Dis*. 2019; 25: 1-11. doi: 10.1590/1678-9199-jvatitd-1482-18.
10. Guerra-Duarte C, Rebello Horta CC, Ribeiro Oliveira-Mendes BB et al. Determination of hyaluronidase activity in *Tityus* spp. Scorpion venoms and its inhibition by Brazilian antivenoms. *Toxicon*. 2019; 167: 134-143. doi: 10.1016/j.toxicon.2019.06.019.
11. Soltan-Alinejad P, Alipour H, Meharabani D et al. Therapeutic potential of bee and scorpion venom phospholipase A2 (PLA2): A narrative review. *Iran J Med Sci*. 2022; 47 (4): 300-313. doi: 10.30476/IJMS.2021.88511.1927.
12. Krayem N, Gargouri Y. Scorpion venom phospholipases A2: A minireview. *Toxicon*. 2020; 184: 48-54. doi: 10.1016/j.toxicon.2020.05.020.
13. Furtado AA, Daniele-Silva A, Silva-Júnior AAD et al. Biology, venom composition, and scorpionism induced by brazilian scorpion *Tityus stigmurus* (Thorell, 1876) (Scorpiones: Buthidae): A mini-review. *Toxicon*. 2020; 185: 36-45. doi: 10.1016/j.toxicon.2020.06.015.
14. Desales-Salazar E, Khusro A, Cipriano-Salazar M et al. Scorpion venoms and associated toxins as anticancer agents: update on their application and mechanism of action. *J Appl Toxicol*. 2020; 40 (10): 1310-1324. doi: 10.1002/jat.3976.
15. Boghazian A, Nazem H, Fazilati M et al. Toxicity and protein composition of venoms of *Hottentotta saulcyi*, *Hottentotta schach* and *Androctonus crassicauda*, three scorpion species collected in Iran. *Vet Med Sci*. 2021; 7 (6): 2418-2426. doi: 10.1002/vms3.593.
16. Das B, Patra A, Mukherjee AK. Correlation of venom toxinome composition of Indian red scorpion (*Mesobuthus tamulus*) with clinical manifestations of scorpion stings: Failure of commercial antivenom to immune-recognize the abundance of low molecular mass toxins of this venom. *J Proteome Res*. 2020; 19 (4): 1847-1856. doi: 10.1021/acs.jproteome.0c00120.
17. Evans ERJ, McIntyre L, Northfield TD et al. Small molecules in the venom of the scorpion *Hormurus waigiensis*. *Biomedicines*. 2020;8(8):259. doi: 10.3390/biomedicines8080259.
18. Bahloul M, Souissi B, Turki O et al. Evidence of direct toxicological effects of scorpion venom on central nervous system in Tunisian children. *Case Rep Crit Care*. 2018; 2018: 8304375. doi: 10.1155/2018/8304375.
19. Rodriguez RV, Dorce VA, de Freitas LA et al. Intrahippocampal injection of TstX-I increases the levels of INF- γ in the cerebral tissue but not the levels of glutamate. *Toxicon*. 2015; 103: 155-159. doi: 10.1016/j.toxicon.2015.07.006.
20. Beraldo Neto E, Freitas LA, Pimenta DC et al. Tb1, a Neurotoxin from *Tityus bahiensis* scorpion venom, induces epileptic seizures by increasing glutamate release. *Toxins (Basel)*. 2020; 12 (2): 65. doi: 10.3390/toxins12020065.
21. Li X, Wu X, Li N et al. Scorpion venom heat-resistant synthesized peptide ameliorates 6-OHDA-induced neurotoxicity and neuroinflammation: likely role of Nav 1.6 inhibition in microglia. *Br J Pharmacol*. 2021; 178 (17): 3553-3569. doi: 10.1111/bph.15502.
22. Bordón L, Paredes W, Pacheco R et al. Intracerebral hemorrhage secondary to scorpion toxin in the Northwest of Argentina; a case report. *Bull Emerg Trauma*. 2018; 6 (3): 253-256. doi: 10.29252/beat-060312.
23. Tao J, Yin S, Song Y et al. Novel scorpion venom peptide Hstx2 ameliorates cerebral ischemic brain injury in rats via the MAPK signaling pathway. *Biochem Biophys Res Commun*. 2021; 534: 442-449. doi: 10.1016/j.bbrc.2020.11.062.
24. Bucaretychi F, De Capitani EM, Fernandes CB et al. Fatal ischemic stroke following *Tityus serrulatus* scorpion sting in a patient with essential thrombocythemia. *Clin Toxicol (Phila)*. 2016; 54 (9): 867-870. doi: 10.1080/15563650.2016.1204454.
25. Cajado-Carvalho D, Kuniyoshi AK, Duzzi B et al. Insights into the hypertensive effects of *Tityus serrulatus* scorpion venom: Purification of an angiotensin-converting enzyme-like peptidase. *Toxins (Basel)*. 2016; 8 (12): 348. doi: 10.3390/toxins8120348.
26. Romero-Imbachi MR, Cupitra N, Ángel K et al. *Centruroides margaritatus* scorpion complete venom exerts cardiovascular effects through α -1 adrenergic receptors. *Comp Biochem Physiol C Toxicol Pharmacol*. 2021; 240: 108939. doi: 10.1016/j.cbpc.2020.108939.
27. Saad K, El-Hamed MAA, Abo-Elala MGM et al. Neurologic complications in children with scorpionism: A retrospective study in upper Egypt. *J Child Neurol*. 2017; 32 (6): 537-542. doi: 10.1177/0883073817690091.
28. Thomas VV, George T, Mishra AK et al. Lateral medullary syndrome after a scorpion sting. *J Family Med Prim Care*. 2017; 6 (1): 155-157. doi: 10.4103/2249-4863.214988.
29. Reis MB, Rodrigues FL, Lautherbach N et al. Interleukine-1 receptor-induced PGE2 production controls acetylcholine-mediated cardiac dysfunction and mortality during scorpion envenomation. *Nat Commun*. 2020; 11 (1): 5433. doi: 10.1038/s41467-020-19232-8.
30. Ahmed AE, Hassan MH, Rashwan NI et al. Myocardial injury induced by scorpion sting envenoming and evidence of oxidative stress in Egyptian children. *Toxicon*. 2018; 153: 72-77. doi: 10.1016/j.toxicon.2018.08.008.
31. Gökay SS, Kendir ÖT, Güllü UU et al. Myocarditis and early markers of cardiac response associated with scorpion stings in children. *Wilderness Environ Med*. 2018; 29 (4): 471-478. doi: 10.1016/j.wem.2018.06.013.
32. Hasan HF, Radwan RR, Galal SM. Bradykinin-potentiating factor isolated from *Leiurus quinquestriatus* scorpion venom alleviates cardiomyopathy in irradiated rats via remodelling of the RAAS pathway. *Clin Exp Pharmacol Physiol*. 2020; 47 (2): 263-273. doi: 10.1111/1440-1681.13202.
33. Khalaf MA, El-Deen MAB, Hishmat AM. Scorpion sting: N-terminal fragment of proB-type natriuretic peptide as an early predictor of pediatric cardiotoxicity. *Hum Exp Toxicol*. 2021; 40 (5): 754-760. doi: 10.1177/0960327120968863.

34. Thien TV, Anh HN, Trang NTT et al. Low-molecular-weight compounds with anticoagulant activity from the scorpion *Heterometrus laoticus* venom. *Dokl Biochem Biophys.* 2017; 476 (1): 316-319. doi: 10.1134/S1607672917050052.
35. Brazón J, Guerrero B, D'Suze G et al. Fibrin(ogen)olytic enzymes in scorpion (*Tityus discrepans*) venom. *Comp Biochem Physiol B Biochem Mol Biol.* 2014; 168: 62-69. doi: 10.1016/j.cbpb.2013.11.007.
36. Galíndez-Cerón JD, Jorge RJB, Chavez-Acosta MH et al. Renal alterations induced by the venom of Colombian scorpion *Centruroides Margaritatus*. *Curr Top Med Chem.* 2019; 19 (22): 2049-2057. doi: 10.2174/1568026619666190731143523.
37. Dizaji R, Sharafi A, Pourahmad J et al. The effects of *Hemiscorpius lepturus* induced-acute kidney injury on PGC-1 α gene expression: From induction to suppression in mice. *Toxicon.* 2020; 174: 57-63. doi: 10.1016/j.toxicon.2019.12.154.
38. Saidani C, Béchohra L, Laraba-Djebari F et al. Kidney inflammation and tissue injury induced by scorpion venom: comparison with a nephrotoxic model. *Toxin Reviews.* 2019; 38 (3): 240-247. doi: 10.1080/15569543.2018.1446028.
39. Movahed A, Fatemikia H, Tanha K et al. Serological, pathological, and scintigraphic assessment of *Hemiscorpius lepturus* effects on renal dysfunction in rats. *Iran J Basic Med Sci.* 2018; 21 (12): 1221-1225. doi: 10.22038/ijbms.2018.31426.7585.
40. Haller H, Bertram A, Nadrowitz F et al. Monocyte chemoattractant protein-1 and the kidney. *Curr Opin Nephrol Hypertens.* 2016;25 (1): 42-9. doi: 10.1097/MNH.000000000000186.

ORCID and contributionship:

Ruzhena Matkivska: 0000-0002-4082-2899^D

Inga Samborska: 0000-0002-6812-489X^{A,B}

Oleksandr Maievskyi: 0000-0002-9128-1033^{E,F}

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Inga Samborska

National Pirogov Memorial Medical University

56 Pirogov str., 21018 Vinnytsia, Ukraine

e-mail: samborska1990@gmail.com

Received: 13.12.2022

Accepted: 24.05.2023

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

CASE STUDY

CHRONIC MIGRAINE. CASE REPORT

DOI: 10.36740/WLek202306125

Oleksandr Pulyk¹, Myroslava Hyryavets¹, Vladyslava Ahij²¹UZHHOROD NATIONAL UNIVERSITY, UZHHOROD, UKRAINE²LTD DIA-LAB, UZHHOROD, UKRAINE**ABSTRACT**

We report a case of a 40-year-old male who had the clinical signs of chronic migraine. The diagnosis of chronic migraine is based on International Headache Society diagnostic criteria. The patient was bothered by unilateral and localized pain in the frontotemporal and ocular area, which lasts 4–72 hours, sensitivity to light and sound. Headache has pulsating quality, moderate or severe pain intensity. Attacks of headache bothered about 15–20 days a month. According to the standard MR scanning protocol, single areas of increased MR signal were detected in the mode T2, Flair, which do not limit diffusion and do not cause a change in the MR signal in the SWI mode. The foci are located subcortically in the white matter of the frontal lobes of the brain, corresponding to foci of gliosis of the white matter of the frontal lobes. The patient received antiepileptic drugs, β -Blockers, triptans, antidepressants. The patient is recommended to inject botulinum toxin.

KEY WORDS: chronic migrane, primary headache, MRI

Wiad Lek. 2023;76(6):1499-1501

INTRODUCTION

Chronic migraine is one of the most common and debilitating neurological disorders, it is often underdiagnosed and undertreated. In one study, only 25% of patients with chronic migrane received a correct diagnosis [1]. According to the Global Burden of Disease study in 2019, migraine remains the second most common cause of disability [1]. The adjusted prevalence of migraine is highest in North America, followed by South and Central America, Europe, Asia, and Africa [2]. Chronic migraine, a condition characterized by the experience of migrainous headache on at least 15 days per month, is highly disabling [3]. Many patients with chronic migraine also have medication overuse, defined as using a compound analgesic, opioid, triptan or ergot derivative on at least 10 days per month [3]. Chronic migraine imposes a substantial economic burden on society [3]. Chronic migraine is an important treatable cause of neurological disability. It is vital to make a diagnosis and ensure that any concomitant medical or psychological conditions are treated in parallel with interventions aimed at reducing the biological tendency to headaches [4]. Specific trials in patients with chronic migraine are sparse, and in many cases the evidence for the use of standard preventive medications has to be extrapolated from studies in patients with high-frequency episodic migraine [3]. New acute and preventive options should become available

over the next 3–6 years, including calcitonin gene-related peptide (CGRP) antagonists and antibodies, and drugs targeted at other serotonin receptor subtypes [3]. The diagnosis of migraine is based on patient history, based on International Headache Society diagnostic criteria [2], these features must not have been attributable to another disorder too. The choice of laboratory and/or imaging studies is determined by the individual presentation [2]. Magnetic resonance imaging together with clinical data migraines identify areas of white matter in both hemispheres of the brain hypertensive in T2 mode, Flair, which is not related to stroke, chronic small vessel deep white matter ischemic change, multiple sclerosis/demyelination, cerebral vasculitis [5]. Migraineurs, male and female, have a 2.5-fold increased risk of subclinical cerebellar stroke and those with migraines with aura and increased headache frequency are at the highest risk [2]. Chronic migraine is associated with higher headache-related disability/impact, medical and psychiatric comorbidities, health care resource use, direct and indirect costs, lower socioeconomic status, and health-related quality of life [4].

THE AIM

To describe the course and results of neuroimaging of chronic migraine in the patient.

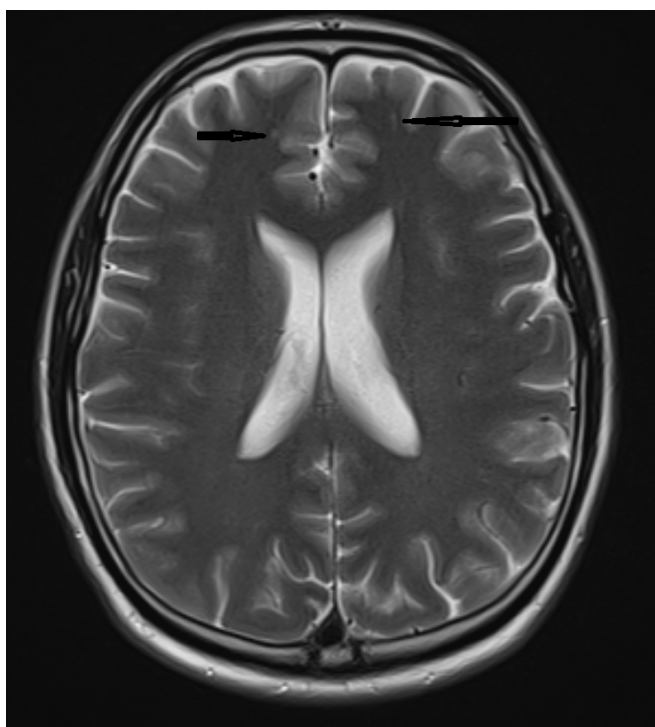


Fig. 1. Axial T2-weighted MRI. In the subcortical white matter of the frontal lobes, the presence of lesion of increased MR signal is determined (indicated by an arrow).

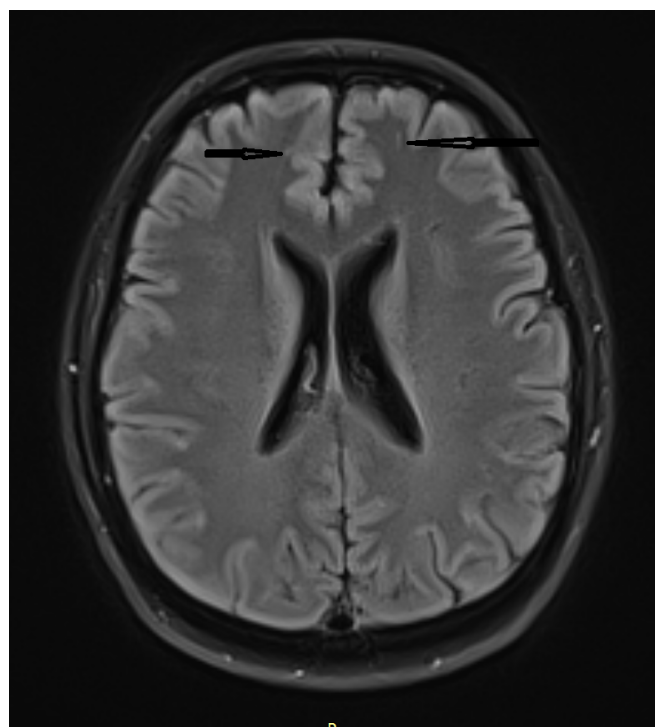


Fig. 3. Axial T2-weighted MRI. In the subcortical white matter of the frontal lobes is determined by the presence of areas of increased MR signal (indicated arrow).

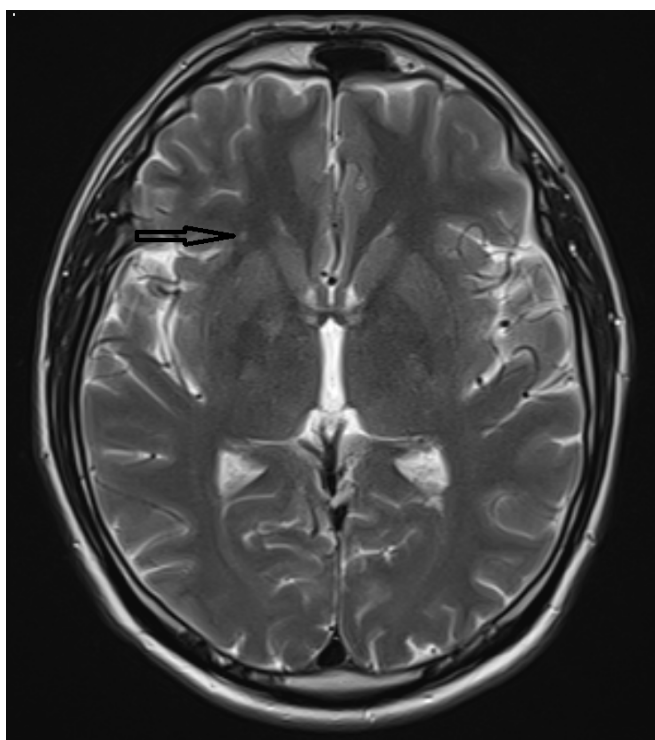


Fig. 2. Axial T2-weighted MRI. In the subcortical white matter of the right frontal lobe, the presence of a focus of increased MR signal is determined (indicated by an arrow).

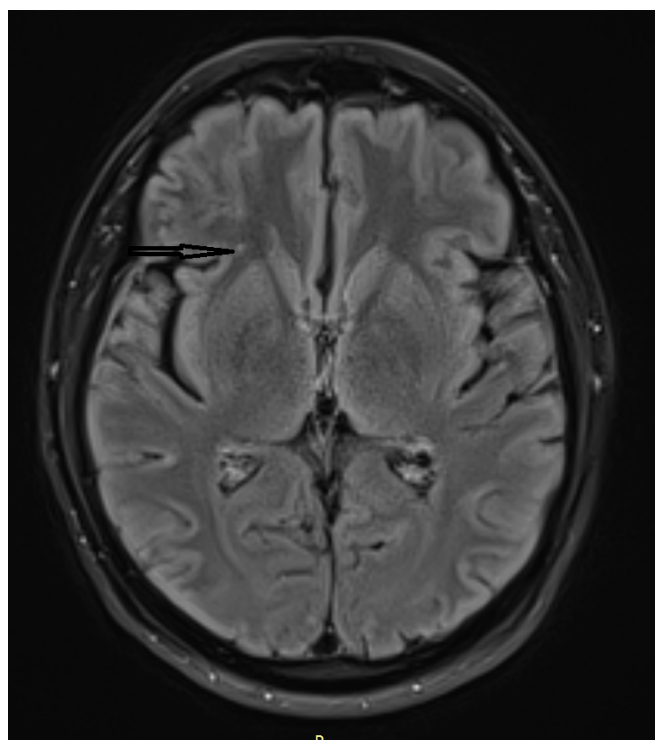


Fig. 4. Axial T2-weighted MRI. In the subcortical white matter of the right frontal lobe, the presence of areas of increased MR signal is determined (indicated by an arrow).

CLINICAL CASE

A 40-year-old male consulted a neurologist with complaints on unilateral and localized pain in the frontotem-

poral and ocular area, which lasts 4–72 hours, sensitivity to light and sound. Headache has pulsating quality, moderate or severe pain intensity. The patient has been ill for 8 years.

Repeatedly examined in Ukraine and abroad. The patient received antiepileptic drugs (topiramate, gabapentin, valproic acid, clonazepam), β -Blockers (propranolol), triptans (sumatriptane, zolmitriptane, rizatriptane, eletriptan), antidepressants (duloxetine, venlafaxine, amitriptyline).

On neurological examination, we found normal mental status and higher functions and no meningismus. No cerebellar ataxia, sensitivity, surface and deep tendon reflexes were normal, pathological reflexes were not found. A general physical examination was normal. Blood tests as well as liver and kidney function were normal. MRI of the brain (1,5 Tl without enhancement) showed the following changes (Fig 1-4). During the MRI examination of the patient according to the standard scanning protocol, single areas of increased MR signal were detected in the

mode T2 (Fig.1, Fig.2), Flair (Fig.3, Fig.4), which do not limit diffusion and do not cause a change in the MR signal in the SWI mode. The foci are located subcortically in the white matter of the frontal lobes of the brain, corresponding to foci of gliosis of the white matter of the frontal lobes. The diagnosis of chronic migraine based on clinical symptoms, International Headache Society diagnostic criteria and MRI brain findings was done.

CONCLUSIONS

Since the patient with chronic migraine was taking antidepressants, antiepileptic drugs, β -Blockers and triptans - botulinum toxin administration was recommended.

REFERENCES

1. Kung D, Rodriguez G, Evans R. Chronic Migraine: Diagnosis and Management. *J. Neurologic Clinics*. 2023 Feb;41(1):141-159. doi: 10.1016/j.ncl.2022.05.005.
2. Headache Classification Committee of the International Headache Society. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. *Cephalalgia*. 2018 Jan;38(1):1-211.
3. Weatherall M. The diagnosis and treatment of chronic migraine. *Ther Adv Chronic Dis*. 2015 May;6(3):115-123. doi: 10.1177/2040622315579627.
4. Burch RC, Buse DC, Lipton RB. Migraine: Epidemiology, Burden, and Comorbidity. *J. Neurologic Clinics*. 2019;37(4):631-649. doi: 10.1016/j.ncl.2019.06.001.
5. Palm-Meinders IH, Koppen H, Terwindt GM et-al. Structural brain changes in migraine. *JAMA*. 2012;308 (18):1889-97. doi:10.1001/jama.2012.14276.

ORCID and contributionship:

Oleksandr Pulyk: 0000-0002-8717-047X

Myroslava Hryavets: 0000-0001-8419-0590

Vladyslava Ahij: 0000-0003-0677-7278

Conflict of interest:

The Authors declare no conflict of interest

CORRESPONDING AUTHOR

Oleksandr Pulyk

Uzhhorod National University

14 Universytetska St., Uzhhorod 88000, Ukraine

e-mail: apulyk@gmail.com

Received: 10.10.2022

Accepted: 30.05.2023

A - Work concept and design, **B** - Data collection and analysis, **C** - Responsibility for statistical analysis, **D** - Writing the article, **E** - Critical review, **F** - Final approval of the article

 Article published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0)

