ORIGINAL ARTICLE

POSSIBILITIES OF METABOLIC AND FUNCTIONAL DISORDERS CORRECTION IN OSTEOARTHRITIS WITH COMPLEX COMORBIDITY

DOI: 10.36740/WLek202203114

Iryna M. Halabitska[1], Liliya S. Babinets[1], Volodymyr I. Vysotskyi[2]
[1]I. HORBACHEVSKY TERNOPIL NATIONAL MEDICAL UNIVERSITY, TERNOPIL, UKRAINE
[2]BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE

ABSTRACT

The aim: To assess the impact of complex metabolic therapy of primary osteoarthritis and type 2 diabetes mellitus under conditions of comorbidity on the course and progression of these pathologies. Patients with comorbidities of primary osteoarthritis and diabetes mellitus are a special group of patients because the importance of these comorbidities is the additional difficulty in diagnosing and conducting adequate therapy, given the close etiopathogenetic links of these conditions, which leads to poor quality of life, increased costs of diagnosis and treatment, increasing the frequency and duration of hospital stay.

Materials and methods: We examined 67 patients with primary osteoarthritis in comorbidity with diabetes mellitus. Patients were comparable by clinical, gender criteria, the severity of primary osteoarthritis, and treatment received and were divided into two groups: 1st group (n=32) - patients received treatment for OA and diabetes mellitus in accordance with international recommendations; 2nd group (n=35) - patients received treatment as in group 1 + drug alpha-lipoic acid. Determination of the level of the studied parameters was performed before and after treatment.

Results: The analysis of the obtained results revealed statistically significant positive dynamics after treatment for symptoms of primary osteoarthritis in both study groups of patients ($p<0.05$), but the therapeutic effect in the 2nd group was more significant ($p<0.05$). There was a statistically significant positive dynamics on the scale of VAS at rest and movement ($p<0,05$), WOMAC index for pain, stiffness, and functional insufficiency ($p<0,05$), and Leken index in the 2nd group after treatment compared with the 1st ($p<0.05$).

Conclusions: The obtained results indicate a statistically significant positive effect of alpha-lipoic acid on the course and progression of primary osteoarthritis under conditions of comorbidity with diabetes mellitus.

KEY WORDS: primary osteoarthritis, diabetes mellitus, exocrine pancreatic insufficiency, family medicine

Wiad Lek. 2022;75(3):645-648

INTRODUCTION

Osteoarthritis (OA) is one of the most common diseases of the joints, which is accompanied by high comorbidity, which greatly complicates the drug therapy of this disease. Diseases of the pancreas with a high frequency are detected as a comorbid pathology in primary OA [1-3]. Most diseases of the pancreas are considered diseases affecting both the secretory and incretory parts of the pancreas, leading to the development of chronic pancreatitis (CP) and diabetes mellitus (DM) [3-5]. The problem of diabetes is becoming increasingly important, as this disease is one of the world's most common chronic diseases. Type 2 diabetes (DM2) is now seen as a social problem. This is due to the fact that there is an increase in the number of people suffering from diabetes and an increased risk of developing various complications [5-7]. Exocrine pancreatic insufficiency (EPI) often develops on the background of DM2, which worsens the course of comorbid pathologies, as well as complicates the choice of treatment tactics [3, 5, 7]. Patients with comorbidities of primary OA and diabetes mellitus are a special group of patients because the importance of these comorbidities is the additional difficulty in diagnosing and conducting adequate therapy, given the close etiopathogenetic links of these conditions, which leads to poor quality of life, increased costs of diagnosis and treatment, increasing the frequency and duration of hospital stay [5-7].

THE AIM

The aim of the study was to assess the impact of complex metabolic therapy of primary OA and DM2 under conditions of comorbidity on the course and progression of these pathologies.

MATERIALS AND METHODS

We examined 67 patients with primary OA in comorbidity with diabetes mellitus, who were on outpatient treatment at the Ternopil Center for Primary Health Care during 2019-2020. The average age of patients was (58.56±7.97) years (from 28 to 79 years); there were 34 women (50.75%) and 33 men (49.25%). The control group consisted of 30 healthy people. Exclusion criteria were cancer, acute and exacerbation of chronic pathologies of vital organs, type 1 diabetes, active gastric and duodenal ulcers, viral hepatitis

Table I. Dynamics of symptoms of primary OA in the study groups before and after treatment

Symptom of OA	Comparison group				
	Control (n=30)	1st group (n=32)		2nd group (n=35)	
		Before treatment	After treatment	Before treatment	After treatment
VAS index, calm, mm	1,11±0,12	35,54±3,76 p_{1-2}<0,05	29,16±1,54 p_{2-3}<0,05	34,41±2,88 p_{1-4}<0,05	21,54±1,28 p_{4-5}<0,05
VAS index, movement, mm	2,12±0,43	48,65±3,48 p_{1-2}<0,05	39,71±1,88 p_{2-3}<0,05	49,17±3,69 p_{1-4}<0,05	31,65±1,75 p_{4-5}<0,05
WOMAC index, pain, points	0,79±0,09	16,85±1,97 p_{1-2}<0,05	13,26±1,47 p_{2-3}<0,05	17,01±1,71 p_{1-4}<0,05	10,59±1,22 p_{4-5}<0,05
WOMAC index, stiffness, points	0,12±0,02	5,58±0,89 p_{1-2}<0,05	4,18±0,12 p_{2-3}<0,05	5,69±0,83 p_{1-4}<0,05	3,89±0,15 p_{4-5}<0,05
WOMAC index, func. insufficiency, points	1,15±0,03	43,77±3,43 p_{1-2}<0,05	37,95±2,03 p_{2-3}<0,05	43,81±3,77 p_{1-4}<0,05	32,14±2,08 p_{4-5}<0,05
WOMAC index, total, points	2,38±0,05	72,89±5,23 p_{1-2}<0,05	65,77±2,19 p_{2-3}<0,05	73,53±5,02 p_{1-4}<0,05	61,22±3,07 p_{4-5}<0,05
Leken index, points	0,21±0,04	6,76±0,97 p_{1-2}<0,05	5,54±0,54 p_{2-3}<0,05	6,51±0,88 p_{1-4}<0,05	4,63±0,52 p_{4-5}<0,05

Notes:
1. p_{1-2} , p_{1-4} – statistically significant difference between groups in relation to the control group;
2. p_{2-3}, p_{4-5} – statistically significant difference in relation to their group before treatment.

and liver cirrhosis, Crohn's disease, nonspecific ulcerative colitis, cystic fibrosis.

The materials of the clinical study were considered at the meeting of the commission of bioethics of I. Horbachevsky Ternopil National Medical University Minute № 60 from 01.09.2020 The work was carried out in accordance with the Code of Ethics of the Declaration of Helsinki. All patients signed an information agreement to participate in the study.

The diagnosis of OA was established on the basis of diagnostic criteria of the International Association for the Study of OA (OARSI (2019)), the American Association of Rheumatologists (ACR (2020), and the European Association of Rheumatologists (European League Against Rheumatism, EULAR, 2017). Examination of the joints included examination, palpation, and objective assessment of pain at rest and during VAS movements. OA symptoms were also assessed by the WOMAC index (Western Ontario and McMaster University) and the Leken index. Radiological stages of OA were evaluated according to the classification of J.H. Kellgren and J.S. Lawrence.

The diagnosis of diabetes mellitus 2 was verified by the Order of the Ministry of Health of Ukraine from № 1118 from 21.12.2012 "On approval and implementation of medical and technological documents for standardization of medical care for type 2 diabetes". Fecal α-elastase was determined by an enzyme-linked immunosorbent assay. Also, to determine the presence and depth of reduction of exocrine function of the pancreas and concomitant enterocolitis was evaluated coprogram on a 5-point scale. To diagnose incretory insufficiency of the pancreas used to determine the level of fasting blood glucose, glycosylated hemoglobin (HbA1c) (using a kit for rapid determination of HbA1c by ion-exchange chromatography), and the HOMA-IR index, calculated by the formula:

HOMA = (fasting glucose (mmol/l) × fasting insulin (μIU/l))/22.5.

The assessment of the state of the pancreas was performed according to the parameters of ultrasound examination of the pancreas, which was summarized to determine the severity of the process according to the criteria of the Marseille-Cambridge classification of CP in points.

Patients were comparable by clinical, gender criteria, the severity of primary OA, and treatment received and were divided into two groups:

1st group (n=32) - patients received treatment for OA and diabetes mellitus in accordance with international recommendations;

2nd group (n=35) - patients received treatment as in group 1 + drug alpha-lipoic acid by intravenous administration of the drug at a dose of 20 ml per day, corresponding to 600 mg of alpha-lipoic acid 1 time per day for 2 weeks. After this course, patients orally took the drug alpha-lipoic acid 2 capsules (600 mg) 1 time per day for 4 weeks. Determination of the level of the studied parameters was performed before and after treatment.

The correspondence of the data distribution of the clinical study to the law of normal distribution was checked by the Kolmogorov-Smirnov test. The arithmetic mean and standard error (M±m) were used to describe the data in the normal distribution. Because the data obtained from the clinical study had deviations from the normal distribution of the variation series, we used nonparametric statistical methods to compare the groups - Mann-Whitney U-test (for independent groups)

Table II. Dynamics of indicators of the functional state of the software in the study groups before and after treatment

Indicator functional state of the pancreas	Comparison group				
	Control (n=30)	1st group (n=32)		2nd group (n=35)	
		Before treatment	After treatment	Before treatment	After treatment
α-elastase, μg/g	251,63±5,28	132,77±4,65 p_{1-2}<0,05	135,36±4,54 p_{2-3}>0,05	129,21±4,97 p_{1-4}<0,05	144,81±3,58 p_{4-5}<0,05
Blood glucose, mmol/l	4,14±0,12	7,61±0,51 p_{1-2}<0,05	7,53±0,44 p_{2-3}>0,05	7,87±0,49 p_{1-4}<0,05	6,49±0,35 p_{4-5}<0,05
HbA1c, %	4,57±0,12	7,25±0,87 p_{1-2}<0,05	7,06±0,47 p_{2-3}>0,05	7,11±0,31 p_{1-4}<0,05	6,59±0,21 p_{4-5}<0,05
HOMA index	1,47±0,11	3,54±0,19 p_{1-2}<0,05	3,48±0,12 p_{2-3}>0,05	3,37±0,11 p_{1-4}<0,05	3,11±0,12 p_{4-5}<0,05
Coprogram, points	0,12±0,03	5,89±0,69 p_{1-2}<0,05	5,15±0,33 p_{2-3}>0,05	5,68±0,38 p_{1-4}<0,05	4,73±0,29 p_{4-5}<0,05
Ultrasound indicator of pancreas structure, points	1,06±0,02	5,67±0,42 p_{1-2}<0,05	5,23±0,36 p_{2-3}>0,05	5,47±0,59 p_{1-4}<0,05	4,72±0,39 p_{4-5}<0,05

Notes:
1. p_{1-2}, p_{1-4} – statistically significant difference between groups in relation to the control group;
2. p_{2-3}, p_{4-5} – statistically significant difference in relation to their group before treatment.

and Wilcoxon test (for dependent groups). We used the software and mathematical complex for the personal computer "Microsoft Exel 2016" (Microsoft) and computer programs for statistical analysis and data processing "STATISTICA® 8.0".

RESULTS

The analysis of the obtained results revealed statistically significant positive dynamics after treatment for symptoms of primary OA in both study groups of patients (p<0.05), but the therapeutic effect in the 2nd group was more significant (p<0.05). There was a statistically significant positive dynamics on the scale of VAS at rest and movement (p<0,05), WOMAC index for pain, stiffness, and functional insufficiency (p<0,05), and Leken index in the 2nd group after treatment compared with the 1st (p<0.05) (Table I).

According to the indicators of the functional state of the pancreas in the 1st group, no statistically significant improvement was found for any indicator, but there was a positive trend (p> 0.05) (Table II). In the 2nd group after treatment, there was a statistically significant increase in the level of fecal α-elastase (p<0,05), there was also a statistically significant decrease in blood glucose (p<0,05) and a statistically significant decrease in the level of glycated hemoglobin and HOMA index (p<0.05), a similar statistically significant trend was observed for the scores of the coprogram and ultrasound criteria of the pancreas structure (p<0.05) (Table II).

DISCUSSION

An important result of our study is that the use of alpha-lipoic acid in patients with comorbidity of primary OA and DM2 contributes to the positive dynamics of symptoms of both diseases. The most studied is the effect of exogenous alpha-lipoic acid in DM [7]. According to the results of many studies, alpha-lipoic acid when taken orally or intravenously has a positive effect on various conditions in which oxidative and inflammatory processes are involved [8, 9]. Against the background of diabetes, oxidation leads to the development of hyperglycemia, which, in turn, causes even more pronounced oxidative processes, which in turn causes the development of a vicious pathophysiological cycle. Alpha-lipoic acid, by inhibiting oxidation, is able to break this cycle, and this makes it a promising tool in the treatment of prediabetes and diabetes [10, 11]. Understanding the structure of alpha-lipoic acid and its use as an exogenous drug makes it possible to consider alpha-lipoic acid in the treatment of diabetes and diabetic peripheral neuropathy [12]. However, we have not found studies aimed at studying the pathogenetic mechanisms of the influence of alpha-lipoic acid on the course of primary OA under conditions of comorbidity with DM2, which makes our work relevant.

CONCLUSIONS

The use of alpha-lipoic acid in the complex treatment of patients with comorbidity of primary OA and DM2 has a positive effect on the course of both comorbid pathologies (p<0.05). In the group of additional appointment of alpha-lipoic acid was found a statistically significant decrease in the index of VAS at rest and in movement (p<0,05), statistically significantly decreased WOMAC index in the group with additional appointment of alpha-lipoic acid after treatment compared with the group protocol treat-

ment was found (p<0.05). There was also a statistically significant decrease in the Leken index in the group with the additional prescription of alpha-lipoic acid compared with the group in which only protocol treatment was used (p<0,05). The obtained results indicate a statistically significant positive effect of alpha-lipoic acid on the course and progression of primary OA under conditions of comorbidity with diabetes mellitus (p<0.05). There was also a statistically significant positive effect of alpha-lipoic acid on the indicators of exocrine and endocrine functions of the pancreas (p<0.05), which indicates the feasibility of using alpha-lipoic acid in the treatment of patients with primary OA and diabetes mellitus under comorbidity conditions.

REFERENCES

1. Osteoarthritis Guideline Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee. American College of Rheumatology [serial online]. 2020. https://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice-Guidelines. [date access 20.05.2021]
2. Bannuru R.R., Osani M.C., Vaysbrot E.E. OARSI Guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthritis and Cartilage. 2019;27(11):1578-1589. doi: 10.1016/j.joca.2019.06.011.
3. Babinets L.S., Halabitska I.M. Chronic inflammatory process and bone tissue changes in patients with osteoarthritis and exocrine pancreatic insufficiency. Lekarsky Obzor. 2020; 69 (1): 7-10.
4. Sakellariou G., Conaghan P.G., Zhang W. et al. EULAR recommendations for the use of imaging in the clinical management of peripheral joint osteoarthritis. Ann Rheum Dis. 2017;76:1484–1494. doi:10.1136/annrheumdis-2016-210815.
5. Babinets L.S., Halabitska I.M. Characteristics of joint pain in patients with primary osteoarthritis and comorbid conditions with exocrine pancreatic insufficiency. Lekarsky Obzor. 2021;70(2):62-64.
6. Cho N.H., Shaw J.E., Karuranga S. Et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res. Clin. Pract. 2018. doi: 10.1016/j.diabres.2018.02.023.
7. Kahn S.E. The relative contributions of insulin resistance and beta-cell dysfunction to the pathophysiology of Type 2 diabetes. Diabetologia. 2003;46:3–19.
8. Erdem Guzel E., K. Tektemur N., Tektemur A. Alpha-lipoic acid may ameliorate testicular damage by targeting dox-induced altered antioxidant parameters, mitofusin-2 and apoptotic gene expression. Andrologia. 2021; 53 (3). doi: 10.1111/and.13990.
9. El-Sayed E-M., Mansour A.M., El-Sawy W.S. Alpha lipoic acid prevents doxorubicin-induced nephrotoxicity by mitigation of oxidative stress, inflammation, and apoptosis in rats. J Biochem Mol Toxicol. 2017;31(9). doi: 10.1002/jbt.21940.
10. Eser Faki H., Tras B., Uney K. Alpha lipoic acid and vitamin E improve atorvastatin-induced mitochondrial dysfunctions in rats. Mitochondrion. 2020;52:83-88. doi: 10.1016/j.mito.2020.02.011.
11. Mohamed H.K., Meligy F.Y. The possible protective effects of alfa lipoic acid on diethanolamine-induced renal toxicity in adult male albino rats: A histological and immunohistochemical study. Egyptian Journal of Histology. 2018; 41 (4). doi: 10.21608/ejh.2018.3929.1010.
12. Corrêa L.B.N.S., Ramos C.S.C.B., Abboud R.S. et al. Influence of alpha lipoic acid supplementation on urinary bladder morphology of diabetic rats. International Journal of Morphology 2020; 38 (3):627-633. doi: 10.4067/s0717-95022020000300627.

The work was performed within the framework of the research project "Comprehensive approach to the control of symptoms, direct and distant prognosis in conditions of comorbid pathology in the clinic of internal diseases and the practice of a family medicine" carried out at the Department of Primary Health Care and General Practice of Family Medicine, I. Horbachevsky Ternopil National Medical University, State registration number: 0118U000361.

ORCID and contributionship:
Liliya S. Babinets: 0000-0002-0560-1943 [A, C-F]
Iryna M. Halabitska: 0000-0002-9028-7230 [A-F]
Volodymyr I.Vysotskyi: 0000-0001-6010-6614 [A, C-E]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Liliya S. Babinets
I. Horbachevsky Ternopil National Medical University
14 Kupchyns'ky St., 46400 Ternopil, Ukraine
tel: +380673520743
e-mail: lilyababinets@gmail.com

Received: 14.06.2021
Accepted: 15.08.2021

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