ORIGINAL ARTICLE

PREVENTION OF ASTHENIC SYNDROME AS CONCOMITANT CIRCUMSTAINS IN POST-COVID-19 PATIENTS

DOI: 10.36740/WLek202105110

Igor V. Kireyev, Natalia V. Zhabotynska, Inna M. Vladimirova, Lilia V. Ocheredko
NATIONAL UNIVERSITY OF PHARMACY, KHARKIV, UKRAINE

ABSTRACT

The aim: Is research into development of asthenic syndrome and its effect on the productivity in post-COVID-19 patients.

Materials and methods: All patients underwent neuropsychological testing immediately after the COVID-19 treatment and one month after a comprehensive rehabilitation program.

Results: The research proved that of all post-COVID-19 patients, who showed signs of asthenic syndrome from predominantly moderate to extreme severity, the patients who followed the complete comprehensive rehabilitation intervention significantly reduced verifiable severity of asthenic syndrome as well as the disability duration.

Conclusions: Early administration of combined rehabilitation methods enables preventing the development of long-term side effects, reduces recovery time and enchases the productivity in post-COVID-19 patients.

KEY WORDS: COVID-19, asthenic syndrome, rehabilitation, productivity

Wiad Lek. 2021;74(5):1104-1108

INTRODUCTION

The incidence of coronavirus disease in the world exceeds 105 million people, with 58 million recovery cases and over than 2 million death [1]. The concomitants problem in post-COVID-19 rehabilitation period include reduced productivity, respiratory and voice disorders, impaired swallowing reflexes, abnormalities of psychoemotional state i.e. impaired attention span, pour memory retention, abrupt swings from anxiety or depression and overload deterioration in quality of life [2]. Separate studies also point out in post-acute-COVID-19 state some convalescent patients may experience long-term side effect such sustained fatigue, diffused myalgia, emotional impairment, and sleeping disorders [3, 4]. On the other hand, the development of all this symptoms exacerbated by rapid fatigue, sustained weakness and exhaustion are commonly recognised as symptoms of asthenic syndrome. Asthenia lasting for over 6 months is considered chronic.

The appearance of signs of asthenic syndrome sings may be primarily related to the accumulation of cytokines in the central nervous system due to a cytokine storm caused by coronavirus [5,6]. Pro-inflammatory cytokines, passing through the blood-brain barrier, lead to autonomic dysfunction, which is acutely manifested as high fever, and in the long term leads to sleeping disorders, cognitive dysfunction and deep anergia. Such signs are also characteristic of chronic fatigue syndrome, which is a long-term manifestation of asthenic syndrome. Post-COVID-19 patients may continue to develop severe post-viral syndrome in the form of a long-term state of chronic fatigue characterized by neuroimmune exhaustion after physical load [7].

Physical exercise contributes to the synthesis of neurotransmitters responsible for good mood, activity, and stress resilience. Intensive physical exercise builds up a new dominant in the central nervous system, which relieves tension in the other parts of the brain [8]. This redistribution of agitation and inhibition processes leads to an improved brain performance after physical exercise, the effect felt immediately after physical load with a possible retention span.

Severe asthenia symptoms lead to detrimental social and economic consequences and marked deterioration in the patient's quality of life [9]. Significantly researchers have carried out a study in general disability related to chronic fatigue syndrome in a post-COVID-19 patient which required additional treatment, with a suggestion of an in-depth investigation into the possible link to the fatigue symptoms with COVID-19 infection. As well as development of relatively low-cost treatment for post-viral fatigue to relief the symptoms and to restore the pre-COVID-19 quality of life [4].

THE AIM

Our study was aimed at determining presence of the asthenic syndrome as a possible manifestation of a post-COVID-19 syndrome with an assessment of its effect on productivity in post-COVID-19 patients. To reach this objectives the following tasks were set: processing the complaints that show signs of the development of asthenic syndrome; studying the types and degree of severity of this syndrome; investigating changes in manifestations

Table I. Distribution of the frequency of complaints among the groups of post-COVID-19 patients

Complaints	Test group 1 (n=22)	Test group 2 (n=6)	Control Group (n=12)
General weakness	100%	100%	100%
Reduced productivity	100%	100%	100%
Increased fatigue	100%	100%	100%
Lack of sleep after awakening	86%	83,3%	83,3%
Sleeping disorder	54,5%	50%	66,6%
Mood swings	72,7%	50%	58,3%
Anxiety	77,3%	66,6%	58,3%
Impaired attention span	86,4%	50%	50%
Pour memory retention	86,4%	50%	50%

Table II. WAM test performance rates: well-being, activity and mood of post- COVID-19 patients

Indicator WAM scales	Test group 1 (n=22)		Test group 2 (n=6)		Control Group (n=12)	
	1	2	1	2	1	2
Well-being	43,55 ±1,33	51,63 ±1,47*	42,01 ±2,28	48,32 ±2,04*	42,78 ±1,80	46,38 ±1,61*
Activity	49,21 ±0,97	55,23 ±1,25*	47,46 ±1,3	49,15 ±1,37	48,33 ±1,13	49,2 ±1,28
Mood	42,08 ±0,90	57,32 ±1,21*	41,64 ±1,10	55,28 ±1,16*	41,85 ±1,10	48,33 ±1,01*

1 – Prior to the post-COVID-19 rehabilitation program

2 – After the post-COVID-19 rehabilitation program

* $p<0,01$ – verified increasing in WAM indicators after the post-COVID-19 rehabilitation program

of asthenic syndrome upon the comprehensive rehabilitation program and assessing the effect of comprehensive rehabilitation program on the terms of convalescence and productivity of post-COVID-19 patients.

MATERIALS AND METHODS

We examined 28 post-COVID-19 patients (18 female and 10 male), aged 25 to 83, 5 (17.8%) of whom suffering mild form of COVID-19 (treated on an outpatient basis); 14 (50%) patients suffering moderate COVID-19 and 9 (32.2%) after severe form of coronavirus disease (all treated in a hospital environment). During the treatment none of the patients needed artificial ventilation of lungs; 23 (82.1%) patients of whom however received oxygen inhalation using either in the form oxygen concentrators or an oxygen supply system in hospital. Following either outpatient, or inpatient treatment, an assessment of the state of the nervous system was carried out in order to determine the presence and nature of the disorders. The complaints obtained, a neuropsychological testing based on the use of assessment scales was applied. To determine the psychoemotional state of patients, the questionnaire was used: self assessment of well-being, activity and mood (WAM) [10]. The WAM table contains 30 pairs of opposing characteristics of a person's psychoemotional state. The patients were offered to mark the degree of severity of a particular characteristic of their condition. In order to determine the prevailing type of asthenic syndrome, a subjective asthenia assessment scale was applied, Multidimensional Fatigue Inventory (MFI-20) [11]. The questionnaire consists of 20 questions and provides 5 sub-scales to determine general, physical or mental asthenia, reduced activity and motivation. To determine the degree of asthenic syndrome, the L. D. Malkov questionnaire, Asthenic State Scale (ASS) was used [12]. The questionnaire contains 30 questions, with possible answers estimated from 1 to 4 points. After the results of the test, the absence of asthenia or its presence in a weak, moderate or extreme degree was assessed. Upon the initial assessment of the nervous system, the patients were offered a comprehensive rehabilitation program that included physical exercise and brain activity stimulators. All types of exercises were selected in complain with recommendations for rehabilitation of patients after COVID-19 issued by the WHO Regional Office for Europe [13]. The set of physical exercises consisted of 5 warm-up exercises, 4 aerobic, 7 power exercises, and exercises to stretch all muscle groups. The set was elaborated for 30 minute-duration 5 days a week. To increase brain activity, patients were offered a daily doing of puzzles of various complexity of 48, 96 and 108 pieces with a gradual increase in complexity; a daily memorisation of short verse and daily séances of favourite music. The

Table III. Determination of asthenic syndrome type by MFI-20 in post-COVID-19 patients

Indicator	Test group 1 (n=22)		Test group 2 (n=6)		Control Group (n=12)	
	1	2	1	2	1	2
General asthenia	16,81 ±3,71	8,47 ±2,47*	13,76 ±2,28	8,13 ±2,83*	12,86 ±1,80	9,81 ±4,4
Physical asthenia	17,61 ±2,26	8,85 ±2,35*	13,83 ±2,75	8,15 ±3,37*	15,43 ±4,16	9,24 ±3,42
Mental asthenia	11,07 ±4,33	5,01 ±1,71*	10,71 ±3,91	6,84 ±2,61*	10,27 ±4,22	8,73 ±3,06
Low activity	16,9 ±3,61	10,8 ±2,91*	15,76 ±4,27	8,37 ±3,5*	14,64 ±4,43	9,31 ±3,56
Low motivation	11,1 ±4,73	5,98 ±1,78*	9,76 ±4,26	5,64 ±1,34*	9,33 ±4,21	7,01 ±2,93

1 – Prior to the post-COVID-19 rehabilitation program
2 – After the post-COVID-19 rehabilitation program
* p<0,01 – verified increasing in MFI-20 indicators after the post-COVID-19 rehabilitation program

Table IV. Asthenic syndrome severity levels on the ASS

Asthenia level	Test group 1 (n=22)				Test group 2 (n=6)				Control Group (n=12)			
	1		2		1		2		1		2	
Extreme	115 ±3,31	46,8%	0*		109,01 ±5,28	50%	0*		112,87 ±7,80	50%	102± 0,01*	16,6%*
Moderate	85,5 ±6,91	33,2%	78,4 ±4,52*	22,7%*	83,64 ±5,43	33,4%	79,25 ±1,37	33,3%	81,23 ±7,3	33,3%	79,27 ±2,26	41,7%*
Weak	64,08 ±6,25	20%	57,32 ±1,21*	54,6%*	69,64 ±3,25	16,6%	60,77 ±1,26	50,1%*	66,85 ±5,10	16,6%	61,12 ±6,01	33,4%*
No signs of asthenic syndrome	0		32,12 ±1,5*	22,7%*	0		37 ±0,01*	16,6%*	0		35 ±0,01*	8,3%*

1 – Prior to the post-COVID-19 rehabilitation program
2 – After the post-COVID-19 rehabilitation program
* p<0,01 – verified changes asthenia level after the post-COVID-19 rehabilitation program

integrated program was performed on 22 patients of test group 1 for 1 month. The test group 2 consisted of 6 patients who declined physical exercises and thus were engaged only brain activity stimulators. The control group embraced 12 post-COVID-19 patients aged 32 to 74, who underwent evaluation the nervous system state wire the same questionnaire immediately after the treatment and 1 month in the wake and who refused perform rehabilitation program. In addition, the duration of disability in all groups was assessed. All methods applied during the study complied with requirements of the Helsinki Declaration of the World Medical Association.

RESULTS

During the anamnesis, all patients voiced complaints typical of asthenic syndrome. 100% patients complained about general weakness, reduced productivity and sustained fatigue. Over 50% patients complained about lack of sleep after awakening, sleeping disorders, mood swings, anxiety, impaired attention span and pour memory retention (Table I).

According the WAM questionnaire the study showed a decrease in all health indicators patients of test groups (Table II) with a slight up with trend and none significantly different among the groups. Upon the complication of the four-week rehabilitation program verified increase (p<0,01) well-being, activity and mood in the test group 1 was observed. Test group 2 showed only verified increase in the well-being and mood assessment, with an activity index verifiable. The control group showed verified increasing in the well-being and mood assessment, with an activity index verifiable and even so the observed changes in the group remained within the medium level. At the same time, after the rehabilitation program test group 1 displayed high levels of convalescence per all indicators, while test group 2 the high level indicators were reached only in well-being and mood position (Table II).

In compliance MFI-20 as to the determination of the type of asthenic syndrome, all types of asthenic syndrome, i.e. general, physical and mental asthenia, including decrease in activity and motivation were observed in post-COVID-19 suffers (Table III). No verifiable difference

among the groups as to the type of asthenic syndrome revealed immediately upon the termination of treatment of coronaviral disease. After the comprehensive rehabilitation program, both the test groups and the control group proved a decrease in the sings of asthenic syndrome, with test groups 1 and 2 displayed verified effect ($p<0,01$). The control group showed a tendency to decrease in general, physical and mental asthenia along with increased activity and motivation, these changes however being unverified. Note-worthy, all groups of patients displayed the prevalence of general and physical asthenia over mental with a marked decrease in activity. Upon the completion the rehabilitation program a significant verified decrease in the manifestations of general, mental and physical asthenia observed, with an increase motivation against the background of an insignificant activity increase in test groups 1 and 2 (Table III).

According to the ASS, 46.8-50% of post-COVID-19 patients, revealed extreme degree of asthenia; 33% of the patients were diagnosed as a suffering the moderate degree of asthenia and the remaining 16.6-20% suffering the weak degree of asthenia with no significant differences verified among the groups (Table IV). After the four-week rehabilitation program the following verified positive changes in the level of severity of asthenic syndrome were observed. Thus, in test groups 1 and 2, no extreme asthenic syndrome case was observed, as opposed to the control group, in which the extreme asthenic syndrome case was steel observed in one patient. Test group 1 showed a verified ($p<0,01$) decrease in moderate asthenic syndrome cases (from 33.2% to 22.7%) and an increase in weak asthenic syndrome cases (from 20% to 54.6%) with a simultaneous decrease in the intensity of manifestation of asthenic syndrome. Test group 2 displayed no reduction in moderate asthenic syndrome cases after the rehabilitation program (33.4% before and 33.3% after the rehabilitation program, respectively) and a verified ($p<0,01$) increase in weak asthenic syndrome cases (from 16.6% to 50.1%) with a decrease in the intensity of asthenic syndrome manifestations. The control group showed a verified ($p<0,01$) decrease in moderate asthenic syndrome cases (from 33.3% to 41.7%) and an increase in weak asthenic syndrome cases (from 16.6% to 33.4%), these changes being unverified as compared to test groups 1 and 2. No verified decrease in the intensity of asthenic syndrome was discovered with the test group. After four-weeks, no signs of asthenic syndrome were identified in 22.7% cases in the test group 1; 16.6% cases in the test group 2 and 8.3% cases in the control group – all cases were verified ($p<0,01$) (Table IV).

All patients were evaluated as to the duration of thick leave. 16 patients (72%) in test group and 2 patients (33.3%) in test group 2 resumed work immediately after the termination of the rehabilitation program in comparison with 5 patients (41.6%) in the control group. On average, the duration of thick leave with patients of the test group 1 was 12.3±5.2 days shorter than those in test group 2 and 16.4±3.2 shorter than those of the control group – all date were verified ($p<0,01$).

DISCUSSION

Asthenic syndrome is virtually always present in the scope of psychoemotional disorders and can significantly impair patients' productivity of and their quality of life. It is note-worthy, in our research 100% patient post-COVID-19 state give complaints characteristic of asthenic syndrome with a prevalence of moderate to extreme severity of types of asthenic syndrome. All patients who performed a complete comprehensive rehabilitation program showed an improvement in well-being, activity and mood up to a high level while the patients whom declined a physical load in favour mental exercises displayed a verified average medium level of activity, which can be attributed to age limitations (69±5.74) and lack of physical exercises. After the rehabilitation program, the following redistribution of asthenic syndrome cases was observed: in both the test groups no extreme asthenic syndrome cases were identified, with some asthenic syndrome cases eliminated all together. Reduced with also of the number of moderate asthenic syndrome cases with a simultaneous increased in weak asthenic syndrome. The control group claimed to have experience similar changes; however the claims remained unverifiable and extreme asthenic syndrome cases still observed at the end of period under review. The original representative results obtained in the present study indicate the efficacy of the low cost comprehensive rehabilitation program for the speedy convalescence of post-COVID-19 patients with the use of techniques of neuro-psychological examination in view to the further rehabilitation intervention with corresponds to the aims of the research.

CONCLUSIONS

The present research proved that of all post- COVID-19 patients, who showed signs of asthenic syndrome from predominantly moderate to extreme severity, the patients who followed the complete comprehensive rehabilitation intervention significally reduced verifiable severity of asthenic syndrome as well as the disability duration. It was also shown that administration of only brain activity stimulators without corresponding physical loads tend to have an overall lesser effect than comprehensive rehabilitation program. An early rehabilitation intervention after the termination of the acute phase in COVID-19 effectively prevents the development of long-term side effects in the form of asthenic syndrome and reduces the convalescence time and enhances productivity in post-COVID-19 patients.

REFERENCES

1. Koronavirus COVID-19: zahalna statystyka [Coronavirus COVID-19: general statistics]. Kyiv: MinfinMedia; 2021. https://index.minfin.com.ua/ua/reference/coronavirus/. (in Ukrainian).
2. Pan American Health Organization. Rehabilitation considerations during the COVID-19 outbreak. 2020; 1–22. https://iris.paho.org/bitstream/handle/10665.2/52035/NMHMHCOVID19200010_eng.pdf?sequence=6&isAllowed=y.

3. Mizrahi B., Shilo S., Rossman H. et al. Longitudinal symptom dynamics of COVID-19 infection in primary care. 2020;1–32. https://www.medrxiv.org/content/10.1101/2020.07.13.20151795v2.full.pdf.
4. Perrin R., Riste L., Hann M. Into the looking glass: Post-viral syndrome post COVID-19. Med Hypotheses. 2020;144:110055. doi: 10.1016/j.mehy.2020.110055.
5. Yujun Tang, Jiajia Liu, Dingyi Zhang et al. Cytokine Storm in COVID-19: The Current Evidence and Treatment Strategies. Front Immunol. 2020;11:1708. doi: 10.3389/fimmu.2020.01708.
6. Hojyo Sh., Uchida M., Tanaka K. et al. How COVID-19 induces cytokine storm with high mortality. Inflamm Regen. 2020;40:37. doi: 10.1186/s41232-020-00146-3.
7. Carruthers B.M., van de Sande M.I., De Meirleir K.L. Myalgic encephalomyelitis: international consensus criteria. J Intern Med. 2011;270:327–338.
8. Karpukhina Yu.V., Tarasova O.O. Vplyv fizychnoho navantazhennia ta relaksatsii na pratsezdatnist holovnoho mozku [The influence of physical activity and relaxation on the brain performance]. Pedahohika, psykholohiia ta medyko-biolohichni problemy fizychnoho vykhovannia. 2012;66–70. (in Ukrainian).
9. Young P., Finn B.C., Bruetman J. et al.The chronic asthenia syndrome: a clinical approach. Medicina (B Aires). 2010;70(3):284–92.
10. Doskyn V.A., Lavrenteva N.A., Sharai V.B. et al. Oprosnyk SAN: samochuvstvye, aktyvnost, nastroenye [SAN questionnaire: health, activity, mood]. 2015. https://psmetodiki.ru/index.php/vzroslye/lichnost/141-oprosnik-san-samochuvstvie-aktivnost-nastroenie-v-a-doskin-n-a-lavrenteva-v-b-sharaj-i-m-p-miroshnikov. (in Russian).
11. Smets E.M., Garssen B., Cull A. et al. Application of the multidimensional fatigue inventory (MFI-20) in cancer patients receiving radiotherapy. Br J Cancer. 1996;73(2):241–245.
12. Netrusova S. Test-opytuvalnyk dlia diahnostyky astenii. Shkala astenichnoho stanu L. D. Malkova [Test questionnaire for the diagnosis of asthenia. L. D. Malkova's scale of asthenic state]. 2019. https://psyhosoma.com/uk/test-opituvalnik-dlya-diagnostiki-asteniiyi-shkala-astenichnogo-stanu-l-d-malkova/. (in Ukrainian).
13. World Health Organization. Support for Rehabilitation Self-Management after COVID-19-Related Illness. Copenhagen. 2020; 4–18. https://apps.who.int/iris/bitstream/handle/10665/333287/WHO-EURO-2020-855-40590-54571-eng.pdf.

ORCID and contributionship:
Igor V. Kireyev: 0000-0002-5413-9273 [A, E, F]
Natalia V. Zhabotynska: 0000-0003-3744-492 [B, D]
Inna M. Vladimirova: 0000-0002-6584-4840 [E, F]
Lilia V. Ocheredko: 0000-0002-9142-0208 [C]

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

CORRESPONDING AUTHOR
Natalia V. Zhabotynska
National university of pharmacy
53 Pushkinskaya Street, 61000 Kharkiv, Ukraine
tel: +380671230106
e-mail: bronkevih@gmail.com

Received: 24.12.2020
Accepted: 29.03.2021

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