Efficiency of comprehensive rehabilitation of chronic fatigue syndrome due to coronavirus infections COVID-19

Z.I. Adambaev[1*], *I.A.* Kilichev[1], *A.B.* Nurzhonov[2], *N.Yu.* Khudoyberganov[1], and *M.R.* Niyazmetov[1]

[1]Urgench branch of the Tashkent Medical Academy, Urgench, 220100, Uzbekistan
[2]Khorezm Regional Multidisciplinary Medical Center, Urgench, 220100, Uzbekistan

Abstract: The aim of the study was to study the effectiveness of complex rehabilitation in patients with chronic fatigue syndrome caused by coronovirus infections. In 120 patients with a confirmed diagnosis of SARS-CoV-2 (COVID-19) aged 20-58 years, post-COVID syndrome or chronic fatigue syndrome was detected, 52 men and 68 women. Patients had asthenic, cognitive, vegetative manifestations, sleep disorders, smell and taste disorders, anxiety and depression. Patients received drug therapy: succinic acid preparations, brain metabolic drugs, stimulating antidepressants, sleeping pills - melatonin and B vitamins, among other things, received micropolarization of the head and translingualneurostimulation. The results of treatment confirmed the effectiveness of the proposed conservative therapy. The neurological symptoms of post-COVID syndrome - chronic fatigue syndrome (CFS) were studied in 120 patients with a confirmed diagnosis of SARS-CoV-2 (COVID-19), aged 20-58 years. Patients were examined according to the “Questionnaire for the detection of asthenia”, "Mini Mental State Assessment (MMSE)", et.al. Sleep disorders were studied using the Epworth Sleepiness Scale, anxiety and depression were studied using the “Questionnaire for Determining Anxiety and Depression”. The patients were divided into 2 groups: the main group (MG) - 69 patients and the control group (CG) - 51 patients. Patients with MG and CG received drug therapy: succinic acid preparations, brain metabolic drugs, stimulating antidepressants, sleeping pills - melatonin and B vitamins. And patients with MG, among other things, received micropolarization of the head and translingualneurostimulation.

1 Introduction

In December 2020, the code U09 was added to the International Classification of Diseases of the 10th revision (ICD-10) - Condition after COVID-19, which includes post-COVID syndrome [1].

* Corresponding author: goodluck_0714@mail.ru

In October 2021, the World Health Organization (WHO) published a consensus on post-COVID syndrome. Post-Covid Syndrome is defined by this Consensus as a post-COVID-19 condition in people with a probable or confirmed history of infection, usually occurring 3 months after the onset of COVID-19 symptoms and lasting at least 2 months, and which cannot be explained by an alternative diagnosis [2].

During COVID-19, an acute stage is distinguished, lasting from 1 to 4 weeks, subacute - from 4 to 12 weeks, and chronic - from 12 weeks or more [3].

According to the WHO, the proportion of patients with long-term consequences after acute COVID-19 is 10-20% [2, 4, 5], and in patients undergoing inpatient treatment due to severe coronavirus infection, it can reach 76-85% [6, 7, 8].

Some reports talk about the undulating course of post-COVID syndrome or “Long Covid”. So, Salmon-Ceron D., et al. (2020) describe that 43% of people seen after being discharged from a Parisian hospital had an asymptomatic period before relapse. They also report that 76% developed new symptoms that were not present during the acute phase of their COVID-19 infection [9]. And in a study by Davis et al (2020), who conducted an online survey among patients with “Long Covid”, it is reported that 86% of respondents experienced relapses irregularly or in response to certain triggers (such as physical or mental activity, stress, menstruation, heat or alcohol) [6].

Long-term symptoms have been reported in COVID-19 patients from the first wave of the pandemic. Women were significantly more likely to report residual symptoms, including anxiety ($p = 0.001$), fatigue ($p = 0.004$), and myalgia ($p = 0.022$) [10]. According to some data, in the examined patients with confirmed COVID-19 infection, one persistent symptom was reported after six to eight months [11, 12]. A systematic review of neurological symptoms in COVID-19 by Wildwing and Holt (2021) reports two types of neurological symptoms; life-threatening symptoms such as Guillain-Barré syndrome and encephalitis; and chronic symptoms consistent with post-COVID syndrome in the form of fatigue and myalgia, which are very similar to other neurological conditions such as chronic fatigue syndrome and functional neurological disorder [13]. Currently, post-COVID asthenia is considered as a decrease in physical and/or mental performance as a result of changes in central, psychological and/or peripheral mechanisms due to COVID-19 [14].

Asthenia/fatigue, inability to concentrate or so-called "brain fog", depression, anxiety, sleep disturbances, as well as numerous and varied autonomic disorders (pulse and blood pressure lability, orthostatic tachycardia and hypotension, gastrointestinal disorders, dermatological disturbances in the form of local hyperemia, pruritus, sweating disorders, etc. Symptoms occur some time after infection or develop later and persist for several months [15].

Of great interest is a meta-analysis of 7 studies (47.910 patients aged 17 to 87 years with a follow-up period of 14-110 days) devoted to the study of the prevalence of symptoms specifically of long-term COVID-19. These studies show that 80% of patients with COVID-19 persist with post-COVID symptoms. The most common are fatigue (58%), headache (44%), attention disorders (27%), hair loss (25%), shortness of breath (24%) [16].

Thus, neurological manifestations of post-COVID syndrome are mainly represented by asthenic symptoms (resembling chronic fatigue syndrome), loss of smell and taste, autonomic, cognitive and sleep disorders. The frequency of detection of these disorders in patients after COVID-19, according to the literature, varies from 2.3% to 89%, lasting up to 8 months and having an undulating course in some patients. Such a huge scatter of data is apparently due to the lack of uniform criteria for identifying post-COVID manifestations.

American researchers believe that COVID-19 can cause chronic fatigue. Based on the similar symptoms of post-COVID syndrome (long-term covid) and chronic fatigue syndrome, American researchers studied the biological basis of these two conditions and found much in common [8]. Myalgic encephalomyelitis, or chronic fatigue syndrome, is a

complex disease of the central nervous system. It is characterized by symptoms such as severe, debilitating fatigue that does not go away even after prolonged rest, sleep disturbances, difficulty thinking, commonly called "brain fog", anomalies of the autonomic nervous system. As a rule, all these symptoms are exacerbated after physical or cognitive stress. In almost the same way, patients with post-COVID syndrome describe their condition, who after suffering COVID-19 for several weeks and even months, fatigue, shortness of breath, problems with sleep, memory and concentration of attention persist. Both in the syndrome of increased fatigue and in long-term covid, the authors note the central role of oxidative stress, leading to the occurrence of redox imbalance at the cellular level associated with inflammation, and metabolic disorders, which are observed in both diseases [7, 17, 18, 19].

In the pathogenesis of asthenic syndrome after suffering COVID-19, Russian authors [20] consider the multifactorial nature of its development, namely, the following links are distinguished:

1) activation of lipid peroxidation leads to the accumulation of free radicals and hydroperoxides in the brain tissue and blood, malondialdehyde in the blood;

2) activation as a result of tissue hypoxia of anaerobic metabolic pathways in the brain tissue and muscles;

3) neurotransmitter disorders that develop as a result of a weakening of the functions of biogenic amines of the noradrenergic, dopaminergic and serotonergic systems in the structures of the reticular activating system of the brain and the limbic system lead to the disconnection of neurofunctional connections with the hippocampus, the center of regulation of cognitive processes and emotional reactions.

The neurometabolic mechanism of asthenic syndrome development is based on hypoxia and hypoxemia, which entail energy deficiency of neuronal structures, weakening of the biosynthesis of macroergic compounds, disruption of tissue respiration, and activation of free radical oxidation processes with subsequent damage to neuronal and mitochondrial cell membranes [20].

At the initiative of Russian therapists, a separate code appeared in the ICD-10 to describe the post-COVID syndrome: U09.9 - Condition after COVID-19. Postcovid asthenia is classified in the ICD-10 as G93.3 - Fatigue syndrome after a viral infection [21].

2 Results of own research

The aim of the study was to study the effectiveness of complex rehabilitation in patients with chronic fatigue syndrome caused by coronovirus infections.

3 Materials and methods

The neurological symptoms of post-COVID syndrome - chronic fatigue syndrome (CFS) were studied in 120 patients with a confirmed diagnosis of SARS-CoV-2 (COVID-19), aged 20-58 years. Of these, 52 men and 68 women. Patients had asthenic, cognitive, vegetative manifestations, sleep disorders, smell and taste disorders, anxiety and depression.

Asthenic manifestations were examined according to the “Questionnaire for the detection of asthenia”, in which there are 11 questions: the maximum score is 11, the higher the score, the higher the asthenia [22].

For the study of CI, the "Mini Mental State Assessment (MMSE)" was used. On this scale, 0-10 points - severe dementia, 11-19 points - moderate dementia, 20-23 points - mild

dementia, 24-27 points - cognitive impairment, 28-30 points - no cognitive impairment [22].

Vegetative disorders were examined according to the "Questionnaire for identifying signs of autonomic changes", according to which autonomic disorders are detected when the score exceeds 15 [22].

Sleep disorders were studied using the Epworth Sleepiness Scale, according to which: 1-6 points - normal sleep, 7-8 points - moderate drowsiness, 9-24 points - abnormal (pathological) drowsiness [22].

Anxiety and depression were studied using the “Questionnaire for Determining Anxiety and Depression”, in which 7 questions (for each section) are marked with 4 answers (from 0 to 3 points) - from 0 to 21 points: the higher the score, the less anxiety and depression [22].

The patients were divided into 2 groups: the main group (MG) - 69 patients and the control group (CG) - 51 patients. Patients with MG and CG received drug therapy: succinic acid preparations, brain metabolic drugs, stimulating antidepressants, sleeping pills - melatonin and B vitamins. And patients with MG, among other things, received micropolarization of the head and translingualneurostimulation.

Micropolarization is the impact on the brain of an ultra-small electric current (up to 1 mA), thereby causing a change in the level of polarization of neuronal and synaptic membranes, which is comparable to natural physiological processes. The mechanism of action of micropolarization is associated with an activating effect on the neurohumoral, axonodentritic components of the brain and spinal cord, on the autonomic nervous system, there is a change in the level of membrane excitability of neurons, the synaptic apparatus, and sensitivity to the perception of ascending afferent flows increases. In other words, a new structure of interneuronal connections is formed in the damaged brain. Excessive, unnecessary connections break up, and instead of them, new, more physiologically effective ones are established [23].

Translingualneurostimulation (TLNS) is a modern rehabilitation method of influencing the central nervous system through the stimulation of tongue receptors. TDNS is carried out using a device whose electrodes are placed directly on the tongue. The device generates electrical impulses, stimulates receptors on the tongue. Impulses are transmitted to the brainstem and then distributed along the ascending, descending and horizontal paths to all parts of the central nervous system. A 20-minute TLNS procedure improves the functioning of various parts of the brain [23].

4 Results and discussion

In the study of asthenic manifestations in patients according to the "Questionnaire for the Detection of Asthenia", it was found that, on average, moderately pronounced asthenic manifestations were detected in our patients. When analyzing the results of the MMSE scale, our patients revealed moderate and mild cognitive impairment. Studies of autonomic disorders according to the "Questionnaire for identifying signs of autonomic changes" revealed in our patients, on average, moderate autonomic manifestations. Sleep disturbances in our patients according to the Epworth Sleepiness Scale revealed moderate disturbances. Detection of anxiety and depressive manifestations in our patients revealed moderate anxiety and mild depressive manifestations (Table).

Thus, in our patients with post-COVID syndrome, asthenic, cognitive, vegetative manifestations, sleep disorders, anxiety and depression were detected.

The next stage of our work was to identify the effectiveness of our proposed treatment. As can be seen from the table, when comparing the treatment indicators before and after treatment in the MG and the CG, it can be seen that in both compared groups there was a

positive trend. However, in the MG, compared to the CG, there are significantly better indicators for all indicators of the questionnaires and scales. As can be seen from the data obtained, in the MG, who received complex therapy with the inclusion of head micropolarization and translingualneurostimulation, the effectiveness of treatment was better. This confirms that micropolarization and neurostimulation improves the broken neuronal connections in the brain broken by coronovirus infection. Our studies confirm that "the stable effect of brain micropolarization is based on the physiologically adequate action of a small direct current on various areas of the brain and spinal cord with the activation of interstructural and intersystem relationships, supported by self-regulation mechanisms. As a result of micropolarization, a new functional state of the CNS is formed, closer to the norm, with the achievement of the physiological level of dynamic homeostasis disturbed during the pathological process, which provides a new level of implementation of various types of activity" [23].

5 Conclusion

The complex rehabilitation of neurological manifestations of post-covid syndrome proposed by us in the form of succinic acid preparations, brain metabolic agents, stimulating antidepressants, hypnotics, B vitamins, as well as micropolarization of the brain and translingualneurostimulation, have proven to be a complex effective rehabilitation of this category of patients.

Table 1. Indicators of post-covid syndrome according to questionnaires and scales in the dynamics of treatment in the compared groups

	MG n=69		CG n=51	
	beforetreatment	aftertreatment	beforetreatment	aftertreatment
Asthenia Questionnaire	7.7±0.3	1.8±0.4*	7.6±0.4	3.7±0.5
MMSE	25.5±1.02	28.1±1.0*	25.3±1.01	27.3±1.01
Questionnaire for Autonomic Disorders	25.3±1.0	18.3±1.1*	24.8±1.1	22.3±1.2
Epworth Sleepiness Scale	8.5±0.6	4.8±0.5*	8.6±0.7	6.6±0.5
Anxiety Questionnaire	12.6±0.8	19.5±0.6*	12.5±1.0	17.7±0.8
Depression Questionnaire	14.5±0.7	19.2±0.5*	14.6±0.8	17.6±0.5

*-$p<0.05$ – between MG and CG after treatment

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