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MINI REVIEW

Post-COVID Syndrome During the COVID-19 Pandemic and the Impact of COVID-19 on the Brain

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ABSTRACT

The review provides information on the classification, mechanisms of development of infection and multiple organ damage, as well as clinical manifestations of post-COVID syndrome (Post-COVID Conditions, Long COVID, Post-acute COVID). The issues of the impact of the new coronavirus infection COVID-19 on the human brain are also considered, its psychiatric and neurological aspects are discussed. The experience of international observations indicates a high prevalence of post-COVID symptoms.

INTRODUCTION

Much has changed in the familiar world since the coronavirus infection known as COVID-19 (Corona virus Disease 2019), which is caused by Sars-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), has entered our lives. At the moment, there are many known strains of coronavirus, four of which have received the status of variants of concern to WHO (Variants of Concern - VOC).

Through the spike protein, namely its Receptor-Binding Domain (RBD fragment), SARS-CoV-2 interacts with ACE2 on the surface of the host cell, resulting in the association of the cell membrane with the virus envelope, followed by the release of the genome into the cytoplasm. Further, vesicles containing the newly formed virion are formed, and the subsequent release of the virus outside the affected cell [1].

DISCUSSION

At this stage, it is impossible to speak with confidence about the real prevalence of post-COVID syndrome due to the lack of large, multicenter studies involving a large number of patients. Also, the lack of clear criteria, the standard of laboratory, instrumental and clinical markers of long-term COVID does not currently allow us to talk about a clear number of patients in need of assistance. However, already at this stage there are many works around the world, and their data are not comforting. For example, according to Sandra Lopez-Leon, et al. [2] about 80% of people diagnosed with COVID-19 had at least one persistent symptom of the disease two weeks after recovery. Most often they were fatigue, headache, decreased attention, hair loss and shortness of breath.

Scientists from Italy provided data that after 60 days from the onset of the first symptom of a coronavirus infection, in a group of patients of 143 people, none of them had a fever or other signs of an acute illness. However, only 13% of them had

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no symptoms and returned to their pre-illness condition. While 32% of the subjects had 1 or 2 persisting symptoms, and 55% had 3 or more. The most common symptoms were fatigue, shortness of breath, joint pain, and chest pain [3].

According to the U.S. Centers for Disease Control and Prevention (CDC), the five most common symptoms of long-term COVID are:

- Increased Fatigue
- Shortness of Breath
- Cough
- Joint Pain
- Pain in the Chest [4].

Olalekan Lee Aiyegbusi, et al. [5] in their review for SAGE journals provided the following data regarding the most common symptoms:

- Fatigue 47%
- Shortness of Breath 32%
- Myalgia 25%
- Joint Pain 20%
- Headache 18%
- Cough 18%
- Chest Pain 15%
- Altered Odor 14%
- Altered Taste 7%
- Diarrhea 6%.

As another confirmation of the above, we can cite the studies of Swiss scientists. According to their systematic review, in adults under 50 years of age, the effects of COVID-19 persisted from two weeks to three months. They were manifested by such symptoms as constant fatigue (39-73% of the assessed persons), shortness of breath (39-74%). 44-69% of the surveyed noted a decrease in the quality of life. There is also a high incidence of abnormal CT findings, including pulmonary fibrosis (39-83%), signs of peri-/perimio-/myocarditis (3-26%), changes in the microstructure and functional integrity of the brain with persistent neurological symptoms (55%), increased frequency of psychiatric diagnoses (5.8% versus 2.5-3.4% in the control group), incomplete recovery of olfactory and gustatory dysfunction [6]. Let's note the mental and neurological aspects of the impact of COVID-19 on the brain.

Various studies have shown that there is a bidirectional relationship between mental disorders and COVID-19: not only the new coronavirus infection increases the risk of developing mental disorders, but mental disorders themselves significantly increase the risk of contracting coronavirus, as well as an adverse outcome of COVID-19 [5]. According to Wang Q, et al. [6], the risk of contracting coronavirus is 5-7 times higher in people with mental disorders than in the general population. At the same time,

the results of a meta-analysis by Toubasi, et al. [7] suggest that mental disorders by 60.3% (OR = 1.52; 95% CI 1.20-1.93; $p < 0.001$) increase the risk of being admitted to the intensive care unit for mechanical ventilation, as well as death. In addition, it was found that such a mental disorder as delirium is an indicator of a complicated course of COVID-19 and an unequivocal indication for transferring a patient to an intensive care unit [7].

It should be noted that for mental disorders, compared with neurological disorders, the relationship with markers of the severity of COVID-19 is less typical, which confirms the importance of psychological factors. These factors include: the potential threat of infection with a new coronavirus infection, the restrictions associated with the pandemic, the abundance of unreliable and conflicting information in the media [8].

Thus, according to a meta-analysis the overall prevalence of psychological distress during the COVID-19 pandemic is 34% (95% CI 27-42%). At the same time, at the beginning of the pandemic, more than 95% of stable patients with COVID-19 experienced clinically significant symptoms of post-traumatic stress. It is worth remembering that a number of studies have shown that high levels of psychological stress are associated with increased levels of inflammatory markers and greater vulnerability to upper respiratory tract infections.

The increased risk of SARS-CoV-2 infection and its adverse course in individuals with mental disorders is also explained by maladaptive behavioral patterns that are characteristic of many mental disorders. For example, patients under the influence of delusions and hallucinations cannot correctly assess their condition, as a result of which they may not seek medical help and not be tested for coronavirus. People suffering from attention deficit hyperactivity disorder have difficulty adhering to the mask-and-glove regimen and maintaining social distance. Low medical attendance by patients with depression was found, which is presumably associated with impairments in the motivational sphere inherent in this disorder [9].

In addition, people with mental disorders are characterized by an unfavorable addict logical profile: they smoke more often and also smoke more cigarettes than the average person from the general population [10,11]. Smoking has previously been shown to increase the risk of both COVID-19 infection [12] and its adverse course [13].

Another factor negatively affecting the outcome of COVID-19 in people with mental disorders is the high prevalence in this population of diseases such as obesity, diabetes mellitus, and chronic obstructive pulmonary disease [14]. These disorders are usually the result of a sedentary lifestyle of patients, an unhealthy diet, and may also occur due to the undesirable effects of treatment with psychotropic drugs. Many of these disorders have previously

been identified as independent predictors of negative COVID-19 outcomes [15].

Infection with coronavirus leads to the defeat of a number of systems and organs. Along with the lungs, the process often involves the heart, kidneys, intestines, endocrine organs, skin, blood vessels, structures of the eyeballs, as well as various parts of the nervous system with the formation of the so-called neuro-COVID syndrome [16].

As it is known, advanced age, the presence of arterial hypertension and diabetes mellitus in a patient, obesity, and cerebrovascular diseases worsen the prognosis in patients infected with COVID-19.

Viral infection, including COVID-19, can be a factor causing the worsening of a number of pre-existing, both acquired and hereditary neuromuscular diseases. In particular, cases of worsening of the course of autoimmune myasthenia gravis against the background of a coronavirus infection have been described. In patients with metabolic myopathies, an infectious disease may be accompanied by an increased risk of rhabdomyolysis.

The risks of a more severe course of COVID-19 in patients receiving immunosuppressive therapy for autoimmune neuromuscular diseases have been widely discussed. It was noted that, contrary to expectations, long-term systemic administration of glucocorticoids does not lead to a significant increase in the severity of coronavirus infection in these patients. Also, there was no more severe course of COVID-19 in patients receiving immunoglobulin preparations or plasmapheresis.

CONCLUSION

Thus, the presence of long-term symptoms in such a wide population is a topical public health problem throughout the world, which should not be neglected in a pandemic. Since the post-COVID syndrome is still unknown in its essence, scientists have yet to understand the causes, mechanisms of development and ways to prevent the post-COVID state.

Also over the course of almost two years, COVID-19 has become more virulent, undergoing frequent mutations, making it difficult to link a specific strain to disease severity. Therefore, it is necessary to conduct large-scale studies in order to establish a relationship between the strain of the virus and the duration of post-COVID manifestations of the disease.

The pandemic has exposed the fragility of the health care system around the world, and has shown the need for a more reliable and highly effective science, technology and innovation system. The lack of test kits and other personal protective equipment, insufficient training of healthcare workers, the lack of adequate funds for the treatment of patients infected with COVID-19 – all these factors have

led to a rethinking of priorities, in particular to increase investment in science, technology and innovation. Various vaccines have been created to provide a choice, but the economy needs about five years to get up to speed. The results of the analysis show that the global recession will be prolonged, and no country will escape its consequences, regardless of its mitigation strategy.

The impact of COVID-19 on the brain is vast and largely under-researched. After a thorough examination, a personalized pharmacotherapy is selected, combining a combination of psycho- and somatotrophic drugs, as well as a complex of non-drug methods, which, depending on the indications, includes physiotherapy exercises and physiotherapy, biofeedback, transcranial micro polarization of the brain and axial loading suits. The program has shown high efficiency, including improving the quality of life in most areas related to health.

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