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## NEUROLOGICAL AND PSYCHONEUROLOGICAL MANIFESTATIONS IN COVID 19 PATIENTS

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### ABSTRACT

The article presents a review of scientific literature, clinical observations, containing data on the features of neurological manifestations and mental disorders, complications from the nervous system in a new coronavirus infection, illustrated with clinical examples. Neurological manifestations are not leading in the clinic for diseases caused by coronaviruses. However, the development of the nervous system is also possible with respiratory, sensory, motor, autonomic and other disorders of the central and peripheral nervous system. In addition, COVID-19 can worsen the course of already existing neurological diseases, therefore, this article provides basic recommendations for the management of certain groups of patients with nervous diseases. Given the earlier epidemics of other coronavirus infections, neurologists most often face cognitive and psycho-emotional disorders and other pathologies in the subsequent period. Therefore, it is important to choose the appropriate treatment and monitor the development of early and long-term consequences of neurological manifestations and complications of COVID-19 and then evaluate the effectiveness of effective individual rehabilitation programs for patients.

### KEYWORDS

Covid 19, nervous system, neurological symptoms, disease, coronavirus, rehabilitation, complicated by neuropsychiatric disorders, program, traditional oriental (Korean) medicine.

## INTRODUCTION

The realities of the last months of the coronavirus pandemic forced us to re-evaluate the features of neurological pathology, the degree of detection of new and decompensation of existing diseases, when this comorbidity becomes sharply threatening to health, including leading to tragic outcomes. COVID-19 (Coronavirus Disease 2019) is a new viral infection that has a number of features, such as a fast spread rate, a high mortality rate, significant social and economic consequences that destroy the usual way of life [1, 2]. The virus is capable of mutating, and all forms of it can be potentially dangerous to humans. Bats serve as a natural reservoir of SARS-CoV, camels and Himalayan civets are intermediate hosts. Confirmation of COVID-19 infection is a positive laboratory test for the presence of SARS-CoV-2 RNA by the polymerase chain reaction (PCR) method, regardless of clinical manifestations. In 97.5% of people, the incubation period is 11.5 days, ranging from 2 to 14 days, on average 5–7 days. COVID-19 is characterized by the presence of clinical symptoms of acute respiratory viral infection: increased body temperature (> 90%); cough (dry or with a small amount of phlegm) in 80% of cases; shortness of breath (55%); fatigue (44%); a feeling of congestion in the chest (> 20%), sore throat, rhinitis. There may also be a decrease in smell and taste, signs

of conjunctivitis [3]. A triad of symptoms characterizes the clinical picture: fever, cough, shortness of breath. In addition to systemic and respiratory symptoms, the virus causes neurological disorders, as it is neurotropic. Neurological disorders occur in approximately 36.4% of patients with COVID-19 [4]. Recently, severe viral hemorrhagic encephalitis, toxic encephalopathy, acute demyelinating lesions, acute cerebrovascular accidents (ACVA) and other complications have been described. The direct effect of coronavirus on the nervous system, the likelihood of its penetration through the olfactory and trigeminal nerves and through the hematogenous pathway through the endothelial cells of the blood-brain barrier (BBB) is discussed [5]. The SARS-CoV-2 virus, like SARS-CoV-1, enters human cells through the receptor for angiotensin converting enzyme 2 (ACE2) [6]. The outbreak of coronavirus infection around the world will remind of itself with various kinds of consequences for a long time. In addition, mainly complications in patients who have undergone COVID-19, up to neurological and psychiatric ones. This phenomenon has received the name "pandemic" (from the Greek. Πανδημία - "the whole people") - an unusually strong epidemic that spread over the territory of countries and continents. Most people who are personally affected by the coronavirus will

experience acute stress disorder, many will experience post-traumatic stress disorder (PTSD), but some people will have a deeper trauma in the form of lingering anxiety disorders, depressive episodes, neurotic disorders and personality deformities. Thus, touching upon the topic of mental disorders triggered by the COVID-19 pandemic, we can talk about the "coronavirus syndrome." [8]. In humans, ACE2 is expressed by most organs and tissues, and, according to H. Zou et al. (2020), the most vulnerable to the SARS-CoV-2 virus are the lungs and lower parts of the respiratory tract, heart, kidneys, intestines, as well as smooth muscle cells of the vascular wall (mainly the microvasculature). It is necessary to evaluate the damaging effect of the virus on the brain and other parts of the central and peripheral nervous system, taking into account the fact that neurons, glial cells, and endothelial cells [9] express ACE2. Considering previous publications on neurological disorders in SARS-CoV-1 and MERS-CoV infections, the neurological disorders due to SARS-CoV-2 virus can be divided into two groups. The first group of disorders is direct damage to the central and peripheral nervous system by the SARS-CoV-2 virus. The second is a change in the course of neurological diseases against the background of an infection caused by the SARS-CoV-2 virus, especially with the development of pneumonia and SARS. Neurological disorders caused by human coronaviruses, including SARS-CoV-2, are attracting the attention of researchers [10].

Experimental models have shown that the SARS-CoV-2 virus related to the SARS-CoV-1 virus is able to enter the brain and cause serious neurological disorders [11]. The pathophysiology of neurological disorders in infection with the SARS-CoV-2 virus is probably similar to that in SARS-CoV-1, and penetration into the brain can occur by the hematogenous and / or perineural route.

To date, works have been published that consider the issues of damage to the nervous system by the SARS-CoV-2 virus. The first review of neurological manifestations was carried out by L. Mao et al. (2020) in patients with a confirmed diagnosis of COVID-19 who were in a hospital in Wuhan. According to the materials presented by L. Mao et al., (2020) of 214 patients, 88 (41.1%) patients had a severe course of the disease, 126 (58.9%) had mild or moderate severity. The group with a severe course was characterized by an older age ( $58.7 \pm 15.0$  and  $48.9 \pm 14.7$  years) and more frequent concomitant pathology (47.7 and 32.5%). Neurological symptoms were detected in 78 (36.4%) of 214 patients and were more often observed in severe cases (45.5 and 30.2%). In the same group, cerebral strokes (5.7 and 0.8%), impaired consciousness (14.8 and 2.4%) and muscle damage (19.3 and 4.8%) developed more often. In general, if we summarize the publications available now, we can distinguish three variants of damage to the nervous system in COVID-19: damage to the central nervous system; damage to the peripheral nervous system and damage to the muscular system. One of

the variants of damage to the peripheral nervous system with the subsequent possible penetration of infection into the brain is damage to the olfactory nerves. Previously, it was experimentally established that the SARS-CoV-1 virus, related to the SARS-CoV-2 virus, from the nasal cavity through the olfactory nerves penetrated into the cranial cavity and further into the brain, causing its severe damage [12]. L. Mao et al. (2020) diagnosed olfactory disorders in patients with COVID-19 in 5.1% of cases, and somewhat more often in patients with a mild form of the disease. The latter may be due to difficulties in identifying olfactory disorders in patients with a severe form. According to S. Gane et al. (2020), loss of smell may not only precede infectious symptoms, but also be the only clinical manifestation of COVID-19. This is confirmed by the publication of M. Eliezer et al. (2020) that a significant decrease or loss of smell in the absence of other clinical and CT / MRI changes in the nasal cavity and nasal passages may be the only early sign of COVID-19. According to the British Association of Otorhinolaryngologists [ETN UK], in the current situation, the acute decrease / loss of smell should be considered as a marker of COVID-19. It is important to note that the impairment of smell in COVID-19 differs to some extent from changes in the sense of smell in other viral diseases in which nasal congestion is present. In cases of the development of hypo / anosmia in COVID-19, the question of the possibility of further penetration of the virus through the olfactory

pathways into the brain remains open and important. The data on taste changes are also interesting. L. Mao et al. (2020) revealed changes in taste in 5.6% of cases, while they were somewhat more common in mild than in severe cases of the disease (7.1 and 3.4%). Differences in frequency, as well as changes in the sense of smell, probably need to be interpreted taking into account the complexity of their determination in patients with severe form. In 1.5% of cases, taste changes preceded infectious symptoms; their frequency did not differ between patients with mild and severe forms of the disease. The question of the localization of the process and the pathogenetic mechanisms of taste disturbance in COVID-19 remains open. Given that, ACE2 receptors are abundantly present on the taste surface of the tongue, the direct effect of the virus on taste buds and / or on nerve fibers cannot be ruled out.

## METHODS

Our survey included 125 percent who had a coronavirus infection and showed signs of damage to the nervous system. They were on outpatient treatment at the COYCA Oriental Medicine Center at the RCH # 2, polyclinic # 2. Of these - 57 men (45.6%), 68 women (54.4%), aged 20 to 60 years. The examination program included patients who underwent COVID 19 from 3 to 8 months (average 5.5) which, Covid 19 was confirmed by laboratory and instrumental data. Depending on the ongoing rehabilitation program, the



patients were divided into 4 groups. In the first group, the methods of traditional oriental medicine were used to restore patients. In the second group, patients received physiotherapy procedures. In the third group - the complex application of physical factors and methods of traditional oriental (Korean) medicine. The fourth group is the control group, in which patients received only drug therapy.

To take into account the results of treatment, we used:

- neurological status;
- assessment of exercise tolerance according to the Borg Scale,
- assessment of muscle strength on the MRC scale (muscles),
- assessment of the intensity of anxiety and depression according to the Hospital Anxiety and Depression Scale (HADS).

## RESULTS OF INVESTIGATION

In this study, 78 (62.4%) of 125 patients with COVID 19 had neurological manifestations with damage to the central and peripheral nervous system and skeletal muscles. In most cases, these neurological symptoms were observed early in the disease before the typical symptoms of COVID 19 developed. The presence of neurological general cerebral symptoms during the manifestation of COVID-19 infection was described in 36.4% of patients in the form of confusion, headache (13.1%), nausea, vomiting, seizures, dizziness (16.8%),

impaired sense of smell (5.1%), taste (5.6%), epileptic seizures (20%), "musculoskeletal syndromes" (10.7%), changes in mental status (15%), as well as in the form of ataxia and acute cerebrovascular syndrome. A study involving 125 patients showed that more than half (50.7%) had depressive symptoms, 44.7% had anxiety symptoms and 36.1% had sleep disorders. The clinical manifestations of PTSD were: fear, anticipation of a threat, nightmares, irritability, anger, impulsive decisions to flee quarantined communities, feelings of loneliness, decreased memory and attention, frustration and hopelessness. Associations with the deterioration of the mental health of the population have been formed. Neurological disorders associated with COVID 19 had clinical manifestations of damage to various structures of the nervous system - the central nervous system, peripheral nervous system and cranial nerves, as well as mental disorders. Undoubtedly, further in-depth studies of the lesions of the nervous system in COVID-19 are needed, which will greatly complement the information available today. For the first time, the experience of using physical factors and methods of traditional oriental (Korean) medicine in the rehabilitation of patients who have undergone coronavirus infection complicated by neuropsychiatric disorders will be analyzed, and an approach to the differentiated prescription of the most optimal method of rehabilitation therapy will be developed.

## CONCLUSION

Because of the study, the data available to date suggest the possibility of damage in COVID-19 and the central and peripheral nervous systems. The defeat of the nervous system is realized through the direct action of the virus.

All data presented and summarized in this article are preliminary. We will study the features of rehabilitation programs for patients who have undergone COVID19, complicated by neuropsychiatric disorders. A neurorehabilitation program will be developed using the methods of traditional oriental (Korean) medicine

Evaluated the effectiveness of various rehabilitation programs in a comparative aspect.

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