

04.11.2021 ЕВРОАЗИАТСКИЙ ТЕЛЕМОСТ «ЖИЗНЬ ПОСЛЕ COVID-19: ВЕРНУТЬ АКТИВНОСТЬ»



RESOLUTION OF

Eurasian Teleconference «Life after COVID-19: how to restore activity»

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Almost 10 000 health care specialists from Uzbekistan, Tadzhikistan, Kirghizia, Ukraine, Kazakhstan, Azerbaijan, Georgia, Moldova and other countries have registered to participate in the Teleconference "Life after COVID-19: how to restore activity" (Kyiv, Ukraine).

Interdisciplinary format of the Teleconference, which took place on November 4, 2021, was assured by speakers from different special fields: cardiologists, neurologists, anesthesiologists, pulmonary specialists, general practitioners, allergologists and obstetrician-gynecologists.

12 main speeches were offered to the participants and they were dealing with the following issues:

- Main pathophysiological mechanisms and clinical manifestations of the Long COVID syndrome.
- Rehabilitation directions in the Post COVID period.
- Long-term consequences of the COVID-19 infection and the ways for correction of neurological and cognitive disorders.
- Ways to reduce the risk of premature birth during Post COVID period.
- What is Kounis syndrome and how is it interrelated with Long COVID syndrome.

Brief outlines of reports

- 1. As reported by experts at least 10-20% of patients who had coronavirus disease suffered from Long COVID syndrome or Post COVID syndrome. Millions of people cannot return to normal life. Pathophysiological syndromes are distinctive feature of Long COVID: systemic "simmering" inflammation, which is "aftersound" of cytokine storm of acute COVID-19 phase, endotheliitis, pneumonitis and asthenic syndrome. Drug-free rehabilitation methods should be combined with drug-induced ones to achieve significant clinical results and complete functional recovery especially in patients of working age.
- 2. Coronaviral infection causes serious damage to the body. The nervous system is particularly vulnerable. The virus is neurotropic and neuroinvasive, it damages nerve fibers and brain neurons. Neurological symptoms may appear even 79 days after coronaviral infection. Some months later the patients are diagnosed with depressive disorders, thrombosis, strokes and autoimmune disorders, caused by accumulation of pro-inflammatory cytokines, reactive oxygen intermediates and arising systemic background inflammation. Edaravone inhibits high levels of cytokines influencing upon systemic "simmering" inflammation, and improves brain metabolism reducing neuroinflammation by means of neutralization of free radicals and iNOS (inducible nitric oxide synthase), reduction of microglia activation, glutamate-mediated excitotoxicity and activation of antioxidant defense enzymes SOD.

- 3. In the State Institution "Institute of Neurology, Psychiatry and Narcology of the National Academy of Medical Sciences of Ukraine" the open comparative research of efficiency of combined application of edaravone, fixed combination of L-arginine and L-carnitine and solution based on xylitol and electrolytes was conducted with participation of 30 patients with neurological disorders in the Post COVID period. The duration of treatment was 14 days. The comparison group consisted of 30 patients with neurological disorders in the Post COVID period who received standard basic treatment (vitaminotherapy, antihypertensive therapy, antidiabetic therapy, statins if medically required, vasoactive agents). Syndromic and pathogenic approach in the active treatment group had an impact on cognitive functions that was manifested in faster mental activity, better short-term and operative memory, more stable mental processes, decreased level of state and trait anxiety. The treatment conducted in the active treatment group reduced asthenia intensity signs and improved quality of life indicators. Post-COVID patients with neurological complications had higher than normal serum levels of pro-inflammatory marker cytokines IL-6 and VEGF. Adding of edaravone, fixed combination of L-arginine and L-carnitine and solution based on xylitol and electrolytes to the basic therapy resulted in decrease of IL-6 and VEGF levels, so we may assume that this treatment scheme has an anti-inflammatory impact. The efficiency and safety of syndromic and pathogenic approach determines its prospects for further prescription for treatment of patients with neurological Post COVID disorders.
- 4. COVID-19 is directly connected with damaging of cardio-vascular system. So myocarditis develops in patients with COVID-19 a few days after the outbreak of the fever. This indicates myocardial damage caused by viral infection. 25% of patients with Long COVID syndrome mention new chest cavity pain and it may be related to coronary function disorders caused by SARS-CoV-2. Vasomotor disorders associated with endothelial dysfunction are found in 79% of patients and are often associated with microvascular vasodilation disorders or high microvascular resistance. Fixed combination of L-carnitine and L-arginine may reduce signs of endothelial dysfunction, reduce the risk of development of blood clots and improve energy supply of myocardium. Ethylmethylhydroxypyridine succinate, identical to the original, is able to reduce the level of anxiety of Post COVID Longhaulers if it is administered parenterally at a dose of 700 mg (14 ml) per day.
- 5. SARS-CoV-2 may induce coronary spasm, directly damage endothelium, cause cytokine storm and higher frequency of stent thrombosis that is related to hypercoagulation condition and clinically similar with three main variants of Kounis syndrome: coronary spasm, acute myocardial infarction, stent thrombosis. COVID-19-induced cytokine storm and hyper coagulopathy may manifest themselves as Kounis syndrome and result in higher risk of fatality in Post COVID patients. Application of fixed combination of L-arginine and L-carnitine in case of Long COVID syndrome helps to improve the condition of vessels and heart of such patients and to prevent complications in the future.
- 6. Accumulated experience of treatment of patients with COVID-19 proves that pulmonitis is a pulmonary fibrosis triggering mechanism: more than 50% of patients suffer from respiratory function disorders in the Post COVID period, 25% of inpatients demonstrate reduced vital capacity as a result of pulmonary fibrosis. Pathogenetic processes are based on further damaging of respiratory endothelium and alveolar complex as a result of discharge of pro-inflammatory mediators and synthesis of free radicals. Adding of edaravone to the treatment scheme helps to suppress release of pro-inflammatory cytokines, to neutralize aggressive free radicals and to protect vascular endothelium against damaging. Edaravone may prevent development of increased permeability of lungs microvasculature endotheliocytes caused by pro-inflammatory cytokines. Injectable acetylcysteine is a powerful pneumoprotector and antioxidant, which contributes to reduced release of IL-6, IL-8, and reduced apoptosis of alveolar cells.

- 7. Many countries of the world have noticed lack of high incidence of COVID-19 among patients with asthma. The patients with allergic diseases have a reduced level of expression of ACE-2 receptors in the cells of airways, so it prevents replication of SARS-CoV-2 virus in the respiratory epithelium. Such effect is explained by permanent use of inhaled glucocorticosteroids. The dose-related reduction of expression of ACE-2 receptors caused by use of inhaled glucocorticosteroids was clearly demonstrated. The protective action of inhaled glucocorticosteroids in case of COVID-19 decreasing the viral load is considered. Use of inhaled glucocorticosteroids during COVID-19 has demonstrated first positive results and is a promising method for reduction of hospital admission and less COVID-19 morbidity and Post COVID complications.
- 8. The consequences of a new coronaviral infection, especially in severe form, during pregnancy is an increase in the frequency of premature births due to the need for early delivery caused by the development of complications of pregnancy due to endothelium dysfunction (placental insufficiency and severe preeclampsia), that defines such pregnant women as a high-risk group for unfavourable perinatal and obstetric events. This fact suggests a common pathogenesis for endothelial dysfunction in coronaviral infection, preeclampsia and placental insufficiency. Use of levorotatory nitrogen oxide donator (L-arginine) for pregnant women in the acute period of coronavirus disease and after it may be a potential solution for such problem.

Akilov Khabibulla Ataullaevich Professor, Director of the Center for the Development of Professional Qualifications of Medical Workers under the Ministry of Health of the Republic of Uzbekistan





Shumakov Valentin Oleksandrovich

Chairman of the Association of Cardiac Rehabilitation of Ukraine, Honored Doctor of Ukraine, MD, Professor