

RESOLUTION

Euroasian Online Teleconference «Focus on POST-COVID patients. «Long-haulers» – who are they?»

April 15, 2021

Almost 15 000 health care specialists have registered to participate in the Euroasian Online Teleconference «Focus on POST-COVID patients. «Long-haulers» – who are they?».

International format of the Teleconference was assured by involvement of foreign speakers, organizers and participants. There were doctors from Ukraine, Uzbekistan, Tadzhikistan, Kirgizstan, Kazakhstan, Moldova, Georgia and Azerbaijan as registered participants.

Teleconference agenda consisted of several topical units of reports: «General clinical aspects of treatment and rehabilitation of post-COVID patients», «Long-haulers in pulmonology, neurology, cardiology, and endocrinology».

Interdisciplinary format of the Teleconference was assured by speakers from different special fields: anesthesiologists, neurologists, cardiologists, endocrinologists, infectious disease specialists, family doctors, pulmonary specialists, and allergologists.

Thirteen main reports were offered to the participants for review and discussion and they were dealing with the following issues:

- Post-COVID syndrome as seen by the eyes of different specialists.
- Post-COVID cardiac syndrome. Will our hearts withstand this pandemic too?
- How to make life of post-COVID patients with pulmonological and neurological complications easier?
- What should we do for a post-COVID patient with diabetes mellitus in 2021?
- Clinical cases and own experience.
- Interdisciplinary discussion of topical issues.

Conclusions and decisions based on discussion of reports:

1. The severity of acute COVID-19 and development of post-COVID complications are not interrelated. Any person, even those who had COVID-19 without any symptoms and with negative PCR test are in «Long-COVID Risk» zone. Long-hauler is a term offered by Harvard School, USA, and means a person who had diagnosed COVID-19 and whose level of health and functioning was not restored to the initial level in 3-6 months after the disease.
2. The frequency of neurological or psychiatric diagnoses within the next 6 months after COVID-19 is equal to 33.62%, among them 12.84% of neuropsychiatric disorders are diagnosed for the first time. Sleep disorder syndromes related to the increased level of anxiety are the most widespread. As far as structures responsible for sleep and emotional state regulation are located close to each other, it causes high co-morbidity of anxious disorders and sleep disorders. It was proved that high anxiety is one of

factors of chronic insomnia. Ethylmethylhydroxypyridine succinate (Lodyksem®) reduces anxiety during post-COVID period, restores sleep and improves cognitive functions.

3. Endotheliitis and system background inflammation as resonance of cytokine storm and oxidative stress during the outbreak of the disease have a great importance for pathogenesis of post-COVID changes. That is why monitoring of respiratory function, cardiac symptoms, state of nervous system and psychological functions is obligatory after acute symptoms of COVID-19, as well as pathogenic and syndromic approach to rehabilitation of patients focused on suppression of system background inflammation, improvement of endothelial function and decrease of asthenia signs.
4. Pathogenic and syndromic approach is important for relief of general state and improvement of quality of life of a patient with post-COVID syndrome. It is possible thanks to infusion therapy with edaravone, L-arginine and L-carnitine, and electrolyte solution in combination with xylitol having marked energy action.
5. 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. The first study of use of dry powder budesonide 1600 mcg in case of mild COVID-19 demonstrates good clinical effect – reduction of hospital admissions by 90%, 2 days shorter period of symptoms, reduction of residual effects of COVID-19 on the 14th and 28th day. Use of inhaled glucocorticosteroids during COVID-19 for reduced risk of hospital admission and alleviation of symptoms has demonstrated first positive results and is a promising method for reduction of hospital admission and less COVID-19 morbidity.
6. The accumulated experience of treatment of patients with COVID-19 proves that pulmonitis is a pulmonary fibrosis triggering mechanism: more than 50% of patients suffer with respiratory function disorders during post-COVID period and 25% of patients in the hospital demonstrate decrease of VC due to pulmonary fibrosis. Pathogenetic processes are based on further affection of respiratory endothelium and alveolar complex as a result of release of proinflammatory mediators and synthesis of free radicals. Adding of Edaravone to the treatment scheme let us slow down release of proinflammatory cytokines, neutralize aggressive free radicals and protect vessels endothelium from damaging. Edaravone is able to prevent development of increased endothelial permeability of micro-circulatory lung bed caused by proinflammatory cytokines. Injectable acetylcysteine is a powerful pneumoprotector and anti-oxidant decreasing release of IL-6, IL-8, and alveolar cells apoptosis.
7. All patients with severe and critical progression of COVID-19-associated community-acquired pneumonia had a greatly increased level of ST-2 – new marker of acute myocardial injury. Moreover, many patients have an increased level of ST-2 even at the moment of hospital discharge. Use of a fixed combination of L-arginine and L-carnitine for cardioprotection and restoration of the cardio-vascular system functioning during post-COVID period is pathogenetically substantiated.

8. Cardiac complications of COVID-19 go along with most of long-haulers. It is important to conduct dynamic evaluation of the state of patients with post-COVID cardiac syndrome within more than 6 months after hospital discharge. Endotheliitis and myocarditis form pathogenesis of complications of the cardiac patient. Besides, adrenergic activity caused by continuing inflammation, release of proinflammatory cytokines, disruption of RAAS and metabolic processes in myocardium play an important role too. These are the mechanisms that need to be carefully addressed in the treatment of such patients.
9. Lightning-quick development of myocarditis proves myocardial damage caused by SARS-CoV-2 viral infection, related to release of proinflammatory cytokines, and there is no time for delay! Accompanying pathologies of patients with COVID-19, such as CHD, hypertensive disease, diabetes mellitus and Chronic Lung Disease just make it worse. And lack of evidence of myocardial damage on ECG in most patients may bring the doctors to their wit's end. It is difficult to choose the correct strategy under such conditions. As far as it is not safe enough to use statins, the medicines with proved efficiency have to be chosen: the combination of L-arginine and L-carnitine helps to protect myocardium in the presence of ischemia, increases EF, decreases necrotic zone, number of arrhythmia and frequency of cardiac deaths.
10. The aggressive attack on pancreas gland by SARS-CoV 2 virus leaves to thyroid specialists no choice: most patients have a risk to acquire diabetes mellitus during post-COVID period! It is evident that endothelium of vessels as a main barrier preventing affection of pancreas gland by corona virus has to be protected. Endothelium damage is clinically manifested in asthenic syndrome. Adding of xylitol-containing solution and levorotatory arginine to the standard treatment scheme has demonstrated good results. A sufficient decrease of asthenization intensity in comparison to the results of the reference group was observed on the 5th-6th day of the infusion therapy. So, L-arginine protects endothelium against damaging and restores its integrity. Xylitol based solutions provide energetic support in the presence of insulin resistance of patients with COVID-19.
11. Systemic inflammation promotes development of neurological complications and long-term asthenic syndrome. High level of cytokines correlates with severity of asthenia. Edaravone decreases systemic inflammation by neutralization of free radicals and cytokines, and in such a way it may indirectly decrease severity of asthenia. Xylitol based solutions are source of energy with insulin independent metabolism and they provide efficient energetic support to COVID Long-haulers.
12. Dysregulated immune-inflammatory response with an increased level of cytokines may explain long-term symptoms of post-COVID syndrome. Hyperreactive brain microglia may modulate a large number of CNS symptoms and correlates positively with the level of inflammatory markers in the patient's blood. Edaravone inhibits high level of cytokines influencing systemic inflammation and improves brain metabolism decreasing neuroinflammation. Mechanisms: neutralization of free radicals and iNOS (inducible NO synthase), reduction of microglia activation, glutamate-mediated cytotoxicity and activation of SOD antioxidant enzymes.
13. Post-COVID patient or Long-hauler demands multidisciplinary decisions, comprehensive rehabilitation and pharmacotherapeutic approach to treatment of three major pathogenic syndromes: systemic inflammation, endotheliitis and asthenic syndrome. Long-hauler scheme assures pathogenic and syndromic approach: Edaravone reduces systemic inflammation, a fixed combination of

L-arginine and L-carnitine restores functioning of the cardio-vascular system, an infusion solution containing xylitol is a source of energy with insulin independent mode of action.

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