

міжнародний конгрес **З ІНФУЗІЙНОЇ ТЕРАПІЇ** 27.04.2021 СОVID-19: КЛІНІЧНЕ ОБГОВОРЕННЯ ОСНОВНИХ СИНДРОМІВ ЗАХВОРЮВАННЯ





RESOLUTION

Online Teleconference «COVID-19: Clinical Discussion of Disease Syndromes»

April 27, 2021

Almost 15 000 health care specialists have registered to participate in Online Teleconference «COVID-19: Clinical Discussion of Disease Syndromes».

The practical format of the Teleconference was assured by involvement of key specialists who have been treating the patients with COVID-19 from the very first days.

Teleconference agenda consisted of several topical units of reports: «Leading experts' view of the COVID-19 problem», «The strategy for treatment of patients with neurological and pulmonary complications of COVID-19», «Practical experience of a comorbide patient management», «Microcirculation disorders».

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.

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

- Comprehensive treatment of patients with severe forms of COVID-19.
- Methods for correction of neurological disorders of patients with COVID-19.
- COVID-19 and diabetes mellitus an ideal storm in a context of ICU.
- Practical experience of treatment of patients with pneumonia.
- Inhaled steroids for treatment of COVID-19. Why the response is like that and what should we know?
- Clinical cases and practical recommendations.
- Interdisciplinary discussion of recent problems.

Conclusions and decisions based on discussion of reports:

1. Rhythm disturbance in case of COVID-19 became one of challenges for specialists in all fields. The etiology of such disturbances is comprehensive and requires individual approach to their treatment. The European Society of Cardiology (ESC) mentions that despite of politological origin application of beta-blockers of ultra-short action for rhythm stabilization is a first line therapy. The preference should be given to Esmolol among other beta-blockers. It has the following features: fast onset of action – 2 minutes, short half-life – withdrawal within 9 minutes. Esmolol is a first line therapy for patients with supraventricular and ventricula rhythm disturbances.

- 2. Redundant and uncontrolled release of proinflammatory cytokines and chemokines is the main reason for multiorgan lesion and death of patients with severe forms of COVID-19. So direct impact on an aggressive inflammatory response can potentially decrease mortality, and lesion of organs and systems. In such a case antioxidants are important medicines as far as reactive oxygen intermediates play an important role in an inflammatory reaction and cytokine storm. In case of acute diseases related to high concentration of reactive oxygen intermediates, mitochondrial antioxidants should be applied at an early stage of disease. Edaravone is an ischemic cascade blocker, a low-molecular antioxidant penetrating through cell membranes thanks to passive diffusion and actively removing peroxy radicals through the mechanism of electron donation. It absorbs and neutralizes free radicals and in such a way it suppresses development of cytokine storm and ischemic processes of cerebrovascular disorders.
- 3. An increased frequency of myocardial infarction, ischemic stroke, pulmonary artery thromboembolism and other thrombotic complications are observed in case of COVID-19. The most promising directions of acute ischemic stroke therapy are perfusion pressure improvement in brain vessels by means of reasonable infusion therapy and impact on the glutamate cascade stages, achieved by the use of cytoprotective drugs. Edaravone, citicolinum and electrolytes were used to optimize the treatment of cerebrovascular complications in patients with COVID-19. The study analyzed the clinical and paraclinical data of 34 patients. It is proved that the abovementioned combination of drugs helps to reduce neurological deficits, increase the frequency of favorable functional recovery on the MRS scale and is recommended for widespread use in medical practice.
- 4. Cytokine storm does not pass without consequences for target organs. SARS-CoV-2 binds to type 2 angiotensin converting enzyme receptors (ACE-2) which is in the vessels and heart. Lesions are due to additional disregulation of the RAAS/ACE-2 system due to coronavirus infection, resulting in cardiovascular damage.
- 5. Neurological manifestations are typical for a new coronavirus disease. The frequency of definite neurological features (alteration of consciousness, headache, anxiety, uneasiness, depression) used to depend on severity of COVID-19 and was usually observed in patients with severe disease. Use of edaravone, combination of L-arginine and L-carnitine, and hyperosmolar balanced solution as a complex therapy for patients with COVID-19 contributes to the regression of clinical manifestations and normalization of laboratory performance in comparison with standard pathogenetic therapy.
- 6. The third wave of COVID-19 has brought new challenges. Mutations of the virus accelerate the lung phase. While previously the cytokine storm symptoms appeared on the 5-7th day, now the cytokine storm develops faster and appears on the 2nd-3rd day. So the pathogenic and syndromic treatment should be used right after hospital admission: addition of three drugs of the «Breakwater» scheme to the basic treatment (edaravone, fixed combination of L-arginine and L-carnitine, and hyperosmolar balanced solution subject to low volume infusion therapy regime).
- 7. According to the international studies, one in three carriers of the virus suffers from the impact of COVID on the nervous system condition. Therefore, strokes are not rare. Such patients need additional therapy. The results of combined usage of drugs with powerful antioxidative and cytoprotective action (edaravone and balanced solution of Ringer's lactate with citicoline) have demonstrated quite high efficiency in the schemes for treatment of ischemic stroke in patients with COVID-19, in comparison to a standard scheme that reduces neurological deficit, increases the frequency of favorable functional recovery.
- 8. Respiratory failure development, changing of blood rheological and fibrinolytic properties, excessive thrombus formation, cardiovascular and nervous system damage, and increased fibrosis formation in lungs are the processes taking place in the body of patients with coronaviral infection. An additional pathogenic treatment with edaravone, L-arginine and L-carnitine, and Reosorbilact resulted in better blood oxygen saturation, drop in body temperature and reduced patient stay in the in-patient facility.

- 9. At a time when etiotropic drugs that directly affect virus SARS-CoV-2 have not been developed yet, a pathogenic and syndromic approach to treatment of patients with severe COVID-19 is extremely important, as far as it considers individual characteristics and provides maximum support to the body. In this context use of combined therapy consisting of edaravone, combination of L-arginine and L-carnitine, and Reosorbilact is very promising, as far as it helps to improve the state of patients with COVID-19-associated pneumonia and to prevent disability and loss of patients' quality of life after the disease.
- 10. Damaging of pancreatic cells by coronavirus leads to the development of diabetes mellitus in patients who have not previously contracted it, leading to further disabling of such patients. First, the virus enters the endothelium of pancreatic vessels, and then directly into pancreas cells. L-arginine, which provides a protective and restorative effect on endothelium, is used for protection of the endothelium the first barrier the virus faces. Restoration of the endothelium is the way to protect the pancreas gland.
- 11. Use of pentoxifylline to intensify treatment of patients with COVID-19 is quite promising as far as:
 - it suppresses synthesis of proinflammatory cytokines (tumour necrosis factor α, IL-1, IL-6);
 - it prevents activation, proliferation, adhesion, polarization and chemotaxis of T-cells and neutrophils;
 - it counteracts inhibitory effect of TNF-α, depressing surfactant synthesis with type II pneumocytes, that is a key mechanism for ARDS pathogenesis;
 - it inhibits platelet aggregation and promotes fibrinolithic activity, which can reduce the risk of thrombosis;
 - it has hemoreologic, antiplatelet and anti-inflammatory effect.
- 12. Lung damage with further development of respiratory failure and the spread of pathological processes to other body systems is one of the main reasons of complicated progression of COVID-19 and further death. Acetylcysteine is used for treatment of patients with respiratory distress syndrome to reduce and prevent lung damage. Acetylcysteine counteracts oxidative stress and reduces inflammatory reaction in respiratory epithelium, which forms a pneumoprotective effect. The ability to prevent the death of the respiratory system epithelium is a basis of acetylcysteine's pneumoprotective properties. Parenteral administration of acetylcysteine ensures maximum bioavailability of the drug and the development of a pneumoprotective effect.
- 13. Many countries of the world have noticed lack of high incidence of COVID-19 among patients with asthma. Such phenomenon is explained by permanent use of inhaled corticosteroids by such patients. It was proved that inhaled steroids have 3 effects:
 - Reduced enrichment of membrane proteins of ACE-2 receptors, ACE-2 and TMPPSS2, directly participating in entry of SARS-CoV-2 virus into the cells.
 - Inhibiting of SARS-CoV-2 replication in infected epithelium cells.
 - Reduced production of cytokines, including IL-6 and IL-8.
 - The protective action of inhaled glucocorticosteroids in case of COVID-19 decreasing the viral load and hyperinflammatory immune reaction is considered.
 - The study conducted in Great Britain with participation of 146 patients demonstrated high efficiency of use of dry powder budesonide 1600 mcg in case of mild COVID-19. Good clinical effect was proved: reduction of hospital admissions by 90%, higher level of saturation in patients using budesonide, reduction of symptoms and fever, 3 days faster recovering of patients, 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 COVID-19 severity. Dry powder budesonide is represented by Easyhaler inhaler in Ukraine.

- 14. Insulin resistance leads to hyperglycemia, decreases the uptake of glucose, cells suffer from energy deficiency. It's a pathogenic cause of asthenic syndrome. The pathogenic approach to the treatment of patients with hyperglycemia and asthenic syndrome is the energy support of cells. Under insulin resistance conditions, a substance with an insulin-independent mechanism of action, such as xylitol, may operate. Therefore it is necessary to use xylytol-containing solutions for pathogenic treatment of asthenic syndrome.
- 15. Hypercoagulation, thrombosis and microcirculation disorders are among the most dangerous conditions in patients with COVID-19. They are direct consequences of damage to the endothelial system by SARS-CoV-2 virus and result in damage to target organs. In conjunction with drugs that prevent thrombus formation (heparins), it is necessary to provide endothelial protection and protection of organs with L-arginine and L-carnitine.

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