

RESOLUTION

Of Teleconference «Therapeutic strategies in case of COVID-19»

December 9, 2021

Kyiv, Ukraine

Almost 10 000 health care specialists have registered to participate in the Teleconference "Therapeutic strategies in case of COVID-19".

Interdisciplinary format of the Teleconference was assured by involvement of speakers from different special fields, such as: infectious disease specialists, anesthesiologists, pulmonologists.

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

- Delta variant of SARS-CoV-2: distinctive features of diagnostics and treatment.
- Doctor's behavior at different stages of new coronaviral infection.
- How to avoid serious mistakes at early stages of disease and to prevent development of severe or critical form of COVID-19?
- Reasonable antibiotic treatment of SARS-CoV-2-associated pulmonary involvement.
- Cytokine storm and premature ageing.
- Managing the risks of complications in case of COVID-19.

Conclusions and decisions based on discussion of reports:

1. The delta variant of SARS-CoV-2 does not operate under the laws of epidemiology. Usually, mutations of the virus weaken its aggressive properties, but in the case of the Delta strain, the situation is different: virus became more aggressive, complications develop on the 6-7th day of disease, case fatality rate has increased, children and pregnant women get sick, mortality among young people increases. Specific features of clinical progression of Delta include "dramatic" progressive course of disease; strongly-pronounced diarrheic syndrome; higher frequency of thrombosis. Early detection of patients with severe illness enables a rapid start of optimized supportive therapy and timely referral to a facility designated according to the clinical route of patient with COVID-19 (where there is access to oxygen and respiratory support).
2. Endotheliitis and endothelial dysfunction are among key syndromes in case of COVID-19 and they are accompanied with coagulation activation and higher risks of thrombotic complications. Besides, production of nitrogen oxide (NO) decreases greatly because of excessive production of free radicals resulting in vasoconstrictors domination and increased platelet and white blood cell adhesion. That is why exogenous admission of L-arginine as substrate for NO synthesis is a pathogenetically justified way to reduce signs of endothelial dysfunction. Combination of L-arginine and L-carnitine may be used for this purpose. According to the data of randomized, double, blind, placebo-controlled research "Results of adding of peroral L-arginine to the standard treatment of patients with COVID-19", conducted by G. Fiorentino and his co-authors, adding of peroral L-arginine to the standard treatment of patients with severe COVID-19 greatly reduces length of hospital stay and decreases respiratory support. It makes sense to use hyperosmolar crystalloid solution to reduce intoxication syndrome as far as it provides fluid transfer from the intercellular sector to the vascular bed thanks to its hyperosmolarity and in such a way it improves microcirculation and perfusion of tissues.

3. Excessive production of pro-inflammatory cytokines, so called cytokine storm, is one of the reasons of ARDS and multiple organ failure syndrome on the background of COVID-19. It was established by clinical studies. That is why effective depression of excessive production of pro-inflammatory cytokines is considered to be an efficient way to prevent fatal affection of patients with COVID-19 and to rescue their lives. Edaravone therapy, initiated at an early stage and/or in the second transition period, may prevent disease progression to cytokine storm in high-risk patients. Edaravone prevents lung damaging and weakens the formation of inflammatory cells and pro-inflammatory cytokines, such as IL-6, TNF α , keratinocyte-derived chemokine and macrophage inflammatory protein-2 (MIP-2) in fluid bronchoalveolar lavage. Edaravone suppresses activation of phospholipase A2 and synthesis of platelet-activating factor, and removes pulmonary edema and extravasation of white blood cells.
4. Pathomorphological image in lungs during COVID-19 coincides with viral interstitial pneumonia in the form of diffuse alveolar damage. Bilateral, basal peripheral changes in the sort of “ground glass”, usually small in size, prevail at an early stage of disease progression and they are premonitory signs of development of viral pneumonia during COVID-19. As the disease progresses, areas of lung tissue change in the sort of “patchwork quilt” are formed, consolidation sectors resembling pneumonia signs to be formed – “reversed halo”. In case of severe disease with development of severe pneumonia or acute respiratory distress syndrome, usually, fibrosis is formed to varying degree. Such changes may later lead to respiratory failure, secondary pulmonary hypertension and pulmonary heart. Complex protocol therapy and adding of syndromic and pathogenetic approach, including control of hypercytokinaemia, in the form of edaravone, fixed combination of L-carnitine and L-arginine, hyperosmolar balanced solution, improves the condition of patients with COVID-19-associated pneumonia and contributes to the alleviation of the disease. “Ground glass” pattern is important but not pathognomonic for COVID-19 and it may be observed in different diseases, so it should be taken into account in diagnosis.
5. 83 patients with coronaviral disease were examined and divided into groups depending on the prescribed therapy in Kharkiv Oblast Clinical Infectious Hospital. In the main group the basic therapy was accompanied with syndromic and pathogenetic approach aimed at prevention of the risk of development of fatal complications. On the background of treatment according to the scheme including edaravone, fixed combination of L-carnitine and L-arginine, hyperosmolar balanced solution, possibly faster regression of fever, headache, sleep disturbances, anxiety, and general weakness were observed; lab test values normalized: downregulation of D-dimer, C-reactive protein, IL-6, ALT activity, AST, GGT in blood serum ($p < 0,001$).
6. Bacterial infection is a widespread complication of coronaviral disease. The reason for that is weakening of patient’s immunity both as a result of SARS-CoV-2 infection and concomitant treatment. The indicator for empirical antibacterial therapy in patients with COVID-19 is the addition of bacterial co-infection and/or superinfection (bacterial community-acquired pneumonia, ventilator-associated pneumonia, urinary tract infection, sepsis, infectious-toxic shock, etc.). For start-up treatment of bacterial complications, 3-generation cephalosporins are recommended (for example, protected cephalosporin cefoperazone + sulbactam) in combination with macrolide. If not effective 4-generation respiratory fluoroquinolone are prescribed, for example, moxifloxacin in the form of concentrate, which should be previously dissolved in the proper volume of normal saline, allowing optimization of infusion therapy.
7. 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. Positive results stimulated the scientific community to conduct “PRINCIPLE” research among 4700 patients with COVID-19, where the efficiency of dry powder budesonide is studied. The preliminary results of the

research are quite positive, as far as patients from the budesonide group recovered 2.94 days earlier and had sustainable recovery of their health, the number of requests for emergency medical care has decreased and reduction of hospital admission was observed. 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 severe progression of COVID-19. In Ukraine dry powder budesonide is represented in Easyhaler inhaler.

8. Current data demonstrate that patients infected with SARS-CoV-2 and having concomitant wheezing belong are a vulnerable group of persons with a high probability of impaired flow and adverse results. Short-acting bronchial spasmolytics and inhaled steroids should be considered to eliminate bronchial obstruction in such patients. If there is a need, nebulizer therapy should be used to deliver medication directly to the respiratory tract. Current recommendations of the British Thoracic Society do not consider nebulizer as a potential risk for carry-over of COVID-19, as far as aerosol, being formed in the nebulizer chamber, does not contain a virus.

Лоскутов Олег Анатолійович

Керівник Асоціації анестезіологів, перфузіологів та лікарів інтенсивної терапії, д.мед.н., професор, зав.кафедри анестезіології та інтенсивної терапії НМАПО імені П. Л. Шупика (Київ)



Шумаков Валентин Олександрович

Голова ГО «Асоціація кардіореабілітації України», Заслужений лікар України, д.м.н., професор

