

RESOLUTION

Of Online Teleconference «Infusion Therapy School»

May 13, 2021

Almost 11 000 health care specialists have registered to participate in Online Teleconference «Infusion Therapy School».

Our school has several specific features: use of the most recent data of global researches and clinical case studies in simple words. So the practitioner can get practical knowledge and has a chance to apply it right after the event.

Teleconference agenda consisted of several topical units of reports:

- Intoxication season. Specific features of infusion detoxification.
- Multidisciplinary aspects of management of POST-COVID patients.
- Infusion support of endocrinological patient.
- Microcirculation disorders in the context of different disease areas.

Involvement of speakers from different fields of medicine let us have a look at the problem of infusion therapy from different angles and to get the whole picture in order to choose the right treatment strategy for the patient with corresponding nosology.

The participants had a chance to listen to and to ask the questions regarding 14 reports dealing with the following issues:

- Actualization of detoxification therapy during intoxication season.
- Infusion therapy for «Long-haulers» (patients with POST-COVID). Specific features of application in various fields of medicine.
- Patients with hyperglycaemia and insulin resistance – the step to diabetes mellitus. Treatment.
- Complication of the main disease as a result of tissue perfusion disorder.

Conclusions and decisions based on discussion of reports:

1. Treatment of pyelonephritis demands application of infusion solutions preserving excretory function of kidneys and efficiently reducing toxic syndrome signs. In case of acute kidney injury use of diuretics is limited so the balanced hyperosmolar solution should be used, as far as it improves kidney blood circulation and decreases the level of urea and creatinine in plasma. The solution can be used without restriction in patients with a little bit low kidney function. The treatment plan makes up 200 ml per day for patients under 60 kg, and 400 ml for patients above 60 kg. The treatment duration is 7-10 days. Oral dehydration of 1,200-1,800 ml of liquid with balanced electrolyte composition (for example, ReO Water) should also be applied.

2. The number of patients in the world with different hepatobiliary system problems exceeds 2 billion people. In Ukraine, as in other countries, there is a growing trend of hepatobiliary system diseases. Toxic syndrome in the patients with digestive disorders is the main one and the overall severity of the disease and the length of hospitalization depend on its intensity. Such patients need infusion therapy with application of special solutions for detoxification. A balanced hyperosmolar solution can quickly eliminate the cause of intoxication by accelerating the exchange of substances between tissues and capillaries. Detoxification quickly improves the overall health of the patient and reduces the time spent in hospital.
3. Systemic inflammation and endotheliitis cause neurological complications and damaging of target organs. High levels of cytokines correlate with the severity of neurological symptoms. Edaravone reduces systemic inflammation by means of neutralization of free radicals and cytokines, and combination of L-arginine and L-carnitine protects endothelium being the first to be attacked by proinflammatory substances and protects target organs against virus. As a result, the bodies of the central and peripheral nervous system are protected to prevent severe neurological complications in patients after COVID-19 (long-haulers).
4. Rheo-STAT Pneumonia Research is the first international, multicenter research on application of hyperosmolar solution Reosorbilact in case of pneumonia that has an international evidence base and is included into the register of the international resource ClinicalTrials.gov. It is in the treatment of pneumonia that there has been no significant or fundamental change in the last 30 years. And mortality has remained the same. According to the study we can see that the use of hyperosmolar solution has significantly improved almost all initial clinical and laboratory indicators on the third day already. But the most important is that there was no pulmonary edema and pleural fluid when Reosorbilact was used. The data obtained show high efficiency of therapy and safety, which has the prospect of improving the statistics of pneumonia treatment.
5. Among the symptoms and syndromes that dominate the clinical picture of POST-COVID syndrome, there are salient signs of asthenization, increased fatigue, excessive exhaustion in normal daily activities, which form an asthenic syndrome. A combination of pathogenetically substantiated drugs is proposed for treatment of the POST-COVID asthenic syndrome: edaravone, combination of L-arginine and L-carnitine and xylitol solution. In order to test the effectiveness of this combination, a special pilot study was carried out, based on the results of which there was a definite decrease in the weakness and fatigue of patients in the main group on the 7th day of treatment. The study concluded with an improvement in the physical condition of patients and physical fitness for work. The proposed scheme was well carried by patients, complications and side effects were not observed during the infusion therapy.
6. Experience has shown that 50 per cent of patients in the POST-COVID period show signs of endotheliitis, microcirculation disorders and deterioration of cardiovascular diseases. Focus on ischemic heart disease.
That's why the heart is in great danger. To ensure pump function of the heart, the myocardium needs adequate blood supply and oxygen delivery, and any inflammatory process can lead to increased ischemia and fatal complications.
For example, if a patient after COVID-19 has a cardiac complaint, then with a high probability it will be a sign of myocarditis, which is a consequence of the complications of a course of ischaemic heart disease. Combination of L-carnitine and L-arginine reduces cardiac muscle ischemia and provides myocardium with an adequate amount of oxygen under hypoxia conditions. It is important to remember that one-time use of meldonium and fixed combination of L-carnitine and L-arginine leads to accumulation of fatty acids in myocardium, which causes arrhythmias and myocardial infarction. The course of treatment with the combination L-carnitine and L-arginine is 14 days, 100 ml once a day intravenously. A full course of vascular therapy is a prerequisite for a full recovery of the endothelial system – 28 days with L-arginine oral solution (Tivortin aspartate).

7. During POST-COVID period 60% of patients have signs of:

- endotheliitis
- «systemic smouldering inflammation»

which, in its turn, is the reason for development of micro-circulatory disorders in those endothelial areas that were damaged by the cytokine acute phase fire of COVID-19. There is a high risk of parietal blood clots, reduced elasticity of blood corpuscles results in sludge phenomenon. A complex solution of Ringer's lactate with pentoxifylline is used to prevent such complications. Lactate enhances pentoxifylline and suppresses additional inflammation, and pentoxifylline in its turn prevents adhesion and helps to restore the elasticity of blood corpuscles. Thus, tissue perfusion improves. Of particular note is the fact that the active substance is evenly distributed throughout the solution under production conditions, reducing the probability of side effects in several times.

8. SARS-CoV-2 virus is characterized by high affinity to pancreas gland cells. Cell disruption results in organ dysfunction and increase of blood glucose level in more than 50 per cent of patients after COVID-19. Those patients who had significant damages of the pancreas gland acquired diabetes mellitus right in POST-COVID period. The main tasks of the general practitioner are: to reduce pressure on the pancreas and to normalize blood glucose level. Increased glucose level and insulin resistance require a substance that can penetrate the cell without insulin and provide the necessary energy in the amount of 837 kJ. This substance is xylitol, which is contained in a balanced hyperosmolar solution. It freely penetrates the cell and gives 837 kJ of energy. The course of treatment is 7-14 days, 200 ml a day.
9. Most of women in the transition period are concerned about deterioration of their health, which is reflected in the increased risk of hypertension, atherosclerosis, diabetes mellitus. The basis for this is the reduction of estradiol level with the formation of insulin resistance, which promotes further disruption of carbohydrate metabolism, synthesis of proinflammatory cytokines and dislipidemy. Xylitol, as an insulin-independent source of energy, restores normal carbohydrate metabolism. L-arginine, an indispensable substrate for nitrogen oxide synthesis, prevents endothelial dysfunction and development of atherosclerotic plaques. The results of clinical observations show an improvement in the quality of life and a decrease in the clinical manifestations of menopause in women over 45 years when xylitol and L-arginine are used in comprehensive therapy in the form of Xylat-Tivortin course. The treatment and prevention strategy with application of Xylat-Tivortin course Anti-aging postpones aging results.
10. The key direction of pathogenesis of severe and critical COVID-19 is a cytokine storm which initiates an extensive endothelial damage and coagulopathy that result in organ dysfunction and death. The most important areas of COVID-19 intensive care are timely and effective anti-inflammatory therapy and anticoagulation. Hypovolemia and low heart emission have an adverse effect on the flow of COVID-19 in patients of intensive care unit. To prevent hypovolemia, balanced crystalloid solutions with hyperosmolar effects, for example, containing sorbitol, should be used. Pulmonary hypertension, which is a consequence of pulmonary thrombovasculitis, requires correction with the combination of L-arginine and L-carnitine, which certainly lowers the pressure by an average of 10 mm of mercury. The course of treatment is 100 ml/day, 14 days.
11. In 2020 125,000 strokes were registered in Ukraine. Since the beginning of the program of medical guarantees, the number of thrombolysis has been 1.3-1.4 per cent. 98.6 per cent of patients do not receive proper treatment and this situation leads to disability and hospital mortality. Patients with acute ischemic stroke require penumbra protection and medical assistance in the form of edaravone, which inhibits lipid peroxidation, oxidative stress, endothelial injury and neuronal death. Edaravone is a powerful acceptor of free radicals and a blocking agent for ischemic cascade. In the form of a solution for intravenous infusion, the preparation is used in the first 72 hours after stroke, contributing to the

reduction of ischemic damage zone, substantial improvement of remote consequences, decrease of manifestations of neurological symptoms, functional disorders, and disruption of daily activities. The compliance of a concept "time=brain" provides for use of a balanced electrolyte solution with an intensive neuroprotective action. The combination of citicoline, lactate and electrolytes is that very preparation. The drug helps to restore the hypoperfusion and hypoxia zone and improves synaptic transmission while reducing neurological deficiency. Note that in the process of nerve impulse transmission, both along the nerve fibre and in the synapse, electrolytes are involved —Na⁺, K⁺, Ca⁺⁺ and Cl⁻ ions. The Na⁺ ion enters the nerve cells and spreads the signal through the nerve fiber. As a choline donor, citicoline is, in its turn, the precursor of the acetylcholine mediator involved in the transmission of nerve impulses in synapses. Accordingly, the expected outcome of citicoline and electrolyte therapy is improved motor, cognitive and sensory functions.

12. Perfusion disorders or microcirculation disorders result in ischemia, accumulation of metabolic products and excessive thrombus formation.
Pentoxifylline is a derivative of methylxanthine which, if administered at therapeutic doses, improves the rheological properties of blood in a variety of ways. In particular, pentoxifylline reduces plasma and whole blood viscosity due to decreased fibrinogen; increases red blood cell elasticity and inhibits aggregation; inhibits neutrophils activation by facilitating passage through vessels. The cumulative effect of this favorable influence is an improvement of the capillary blood flow. This is why pentoxifylline molecules can be used in the complex treatment of many pathological states. The ampouled forms of pentoxifylline have a number of disadvantages, namely that the heavy molecule quickly sedimentates after dissolution, resulting in a relative overdose of the drug, which results in a number of side effects. Therefore, the use of integrated, ready-to-administer pentoxifylline formulations should eliminate the above-mentioned deficiencies and be widely applied in treatment.
13. Mortality from cardiovascular diseases has increased by almost 8% in the last 29 years and in 2019 was 64% of total deaths. Endothelial dysfunction (ED) is an intermediate stage in the continuum of vascular disease. It is endothelium that is the key link in the pathological process, and deficiency of NO in ischemic tissues requires a separate approach when using a protection strategy.
The main role of L-arginine is to be the main substrate for NO synthase, which catalyzes NO synthesis in endotheliocytes. It counteracts thrombus formation, lowers blood cholesterol, prevents atherosclerosis and significantly improves endothelial function. Through the process of regulating tonus of unstriated muscles, permeability and microcirculation of vessels, arginine reduces arterial tension and accelerates blood flow, which facilitates the delivery of oxygen to the myocardium, brain, extremities and other organs.
14. Imbalance in iron metabolism rapidly occurs with inflammation, as evidenced by a decrease in iron content and an increase in ferritin level, sTfR, hepcidin and IL-6 in plasma. Production of hepcidin in the liver is induced by IL-6 and provokes formation of anemia of chronic inflammation. Furthermore, hepcidin, the main regulator of the tissue level of iron, induces the release of iron from macrophages and the absorption of iron in the intestine. After the past infectious disease with a long-term inflammatory reaction, the first step is the assignment of the hydroxide-sugar complex of iron intravenously in the treatment of anaemia.

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

