

## RESOLUTION

## Of Teleconference «5th Interdisciplinary School of Infusion Therapy: Opportunities under the Conditions of Wartime»

## May 19, 2022 Kyiv, Ukraine

Almost 6 800 health care specialists have registered to participate in the Teleconference «5th Interdisciplinary School of Infusion Therapy: Opportunities under the Conditions of Wartime».

The task of the School is to help general medicine physicians to improve their ability to administer infusion therapy in accordance with the latest trends and national and international recommendations.

Eight main reports were offered to the participants for review and discussion and they were dealing with approaches to treatment and rehabilitation of patients with traumatic brain injury (TBI), pain treatment during war, the problem of ketoacidosis in endocrinology and therapy, and problem of capillary leakage, as well as the issue of management of patients with anxiety disorders, acute myocardial infarction and chronic coronary heart disease (CHD).

The chat was operated during «5th Interdisciplinary School of Infusion Therapy: Opportunities under the Conditions of Wartime», so each participant had a chance to ask questions and to get answers from the speakers. And many participants left most heartfelt thanks to the speakers in the chat for their informative reports.

## Conclusions and decisions based on discussion of reports:

- 1. Minor traumatic brain injury (mTBI, also known as brain concussion) caused by explosion in the battle field or blow with blunt instrument is a growing concern in the scientific world. Symptoms remain unidentified, there is no «specific» treatment, and further disability from injury is longer, which contradicts the conventional belief that mTBI is an acute injury and that persistent symptoms (more than 3-6 months) arise in a small minority of people. Pathogenesis of TBI is formed by primary damages to blood vessels and cell membranes or secondary ones (calcium overload, oxidative stress, cerebral edema). Reactive oxygen intermediate (ROI) can further contribute to the release of cytokines and chemokines and affect the further path of lipid peroxidation. This causes mitochondrial stress reactions and mechanisms of cytotoxicity, followed by the release of cytokines and chemokines, which cause the activation of astrocytes and microglia and the involvement of circulating immune cells such as neutrophils, macrophages and lymphocytes. Studies have also demonstrated that TBI may cause various neuropathological changes such as accumulation of  $\alpha$  synuclein, multifocal neurofibrillary tangles and hyper-phosphorylation of tau-protein.
- 2. The symptom complex that characterizes the postconcussional syndrome is completely non-specific, difficult to treat and significantly impairs the quality of life. A promising approach to additional treatment for TBI and its long-term effects is to protect the neurovascular unit, since not only the nerve cells are damaged during ischemia, but also the endothelial junction is damaged. Neurovascular unit is a structurally (that is, anatomically) and functionally interdependent complex that consists of microcirculatory junction (endothelial cells, endothelium basal membrane, pericytes) and nerve tissue (astrocytes and neurons). Neurovascular unit protection is a complex approach to blocking of ischemic cascade, reducing brain edema and recovering from neurotrauma. The pathogenetic approach contains

- edaravone, which improves the results of TBI treatment and long-term effects with anti-inflammatory and antioxidant modulation, namely inhibits the excessive production of inflammatory mediators, TBI-induced, activates antioxidant defense enzyme, neutralizes the most aggressive ROI and free radicals, reduces brain edema, inhibits hyper-phosphorylation of tau-protein; balanced solution of electrolytes and citicoline, which accelerates the transmission of nerve impulse with the restoration of CNS functions and corrects the metabolic acidosis due to lactate in the composition; levorotatory nitrogen oxide donator for vascular rehabilitation and universal organ protector with daytime tranquilizer effect to ensure anxiolytic and nootropic treatment effects.
- 3. Anxiety is a normal response when we are in danger or threatened. Constant anxiety can start when we're exhausted and don't feel protected. Arterial hypertension, ischemic heart disease, ulcer disease, thyrotoxicosis, etc. are among the «classical» psychosomatic diseases in the development of which stress plays an important role. Ethylmethylhydroxypyridine succinate in the form of an injection solution is a universal organ protector with a daytime tranquilizer effect. It provides anxiety level decrease by 3 points according to HADS scale on the 8th day of treatment and the effect appears on the 2nd-3rd day. Ethylmethylhydroxypyridine succinate is prescribed in the amount of 5 ml twice a day in order to reduce the level of anxiety. Anxiety disorders are usually accompanied by endothelial dysfunction, which requires appropriate correction with the use of an endothelial protector a levorotatory donator of nitrogen oxide (L-arginine hydrochloride). In case of coronary heart disease, a fixed combination of levocarnitine and L-arginine is recommended.
- 4. Ketoacidosis is an urgent condition that develops, usually against the background of decompensation of diabetes mellitus. But the hyperproduction of the ketone bodies starts much earlier than the patient gets to the intensive care unit. The level of ketone bodies is usually determined by the nitroprusside method, which determines the level of acetoacetic acid. But the severity of the patient's condition is caused primarily by beta-hydroxy-butanoic acid, the level of which increases significantly at the normal level of acetoacetic acid and worsens the patient's condition. Therefore, it is necessary to reduce ketogenesis even before the nitroprusside method shows the presence of ketone bodies in the urine. For this purpose, a balanced crystalloid solution based on xylitol is added to the infusion therapy program. It reduces ketogenesis, corrects metabolic acidosis (due to sodium acetate), restores water-electrolytic balance, and also improves cell nutrition by allowing xylitol to be metabolized without insulin participation.
- 5. In time of war, pain is the most common symptom. It is important to trust the patient's reports of pain and what eases the pain, to perform the intervention in a timely manner. Effective treatment of acute pain requires a multimodal approach. This provides the ability to reduce the dose of analgesics (incl. opioid ones), adequately control pain and reduce the risk of side effects. Dexketoprofen meets the requirements for a modern nonsteroidal anti-inflammatory agent. Injectable Dexketoprofen – is the beginning of therapy for back pain and postconcussional syndrome as far as its effects can be felt within 20 minutes, it doesn't cause risk of development of thromboembolic cardiovascular events, has a high level of safety for gastrointestinal tract and the lowest risk of development of gastrointestinal bleeding, and is safe for simultaneous administration with low molecular heparins. Paracetamol is a basic component of multimodal analgesia, it reduces the intensity of postoperative pain in the first 24 hours and reduces the need for additional opioid analgesics. For lumbar epidural anesthesia, brachial plexus blockages and small nerves, it is recommended to use ropivacaine, which provides a sufficient and lasting level of surgical anesthesia with a high safety profile.
- 6. Drug hypersensitivity reactions account for 15% of all side-effects. Acute toxic-allergic reactions to drugs may be accompanied by the development of capillary leakage syndrome, which manifests itself by the transition of albumin and blood plasma into the interstitial space. The pathogenesis of the capillary leakage is based on a vicious circle: endothelial dysfunction immune reactions inflammation mediators. Tissue hypoxia also plays an important role. The use of a fixed combination of L-carnitine and L-arginine provides antihypoxic action and endothelium protection and thus

reduces the manifestations of capillary leakage. The addition of a hyperosmolar crystalloid solution based on sorbitol helps to eliminate intoxication – the cause of the development of capillary leakage.

- 7. CHD is one of the main reasons of high mortality, loss of productivity and decline in the quality of life of the adult population in Ukraine. According to the recommendations of the European Society of Cardiology, in the case of CHD it is necessary to reduce the level of low-density lipoprotein cholesterol to reduce the risk of cardiovascular disease and death, so statin therapy is very important, but not perfect. Statins can cause side effects, such as damaging of liver, muscles, development of diabetes mellitus type 2, etc. According to a meta-analysis of 55 randomized controlled studies, L-carnitine favorably affects the lipid profile. L-carnitine also lowers the level of hepatic enzymes (ALT, AST, GGT), as confirmed by two meta-analyses. L-arginine also favorably affects lipid profile and improves endothelium function. Therefore, in chronic CHD use of fixed combination of L-carnitine and L-arginine as a part of complex therapy is pathogenetically explained.
- 8. Acute myocardial infarction triggers the development of ischemic cascade in cardiomyocytes. Its main links are overloading of cells with calcium ions, hyperproduction of free oxygen radicals, lipid peroxidation and endothelium damage. Edaravone, an ischemic cascade blocker, may have an impact on these processes. In case of acute myocardial infarction, administration of edaravone is accompanied by reduction of the enzymatic size of the infarction, reduction of the risk of development of reperfusion arrhythmias, relief of reperfusion myocardial lesion, reduction of the apoptosis of cardiomyocytes. In case of an acute myocardial infarction, the first dose of edaravone is administered within 10 minutes before reperfusion, after which 30 mg (1 amp.) are applied twice a day with a course of up to 14 days.