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ЄВРАЗІЙСЬКИЙ ТЕЛЕМІСТ  
«ІV МІЖДИСЦИПЛІНАРНИЙ КОЛЕГІУМ  
З НЕВРОЛОГІЧНИХ ЗАХВОРЮВАНЬ»



# **RESOLUTION**

## **of Euro-Asian Online-Teleconference**

### **«IV Interdisciplinary Collegium of Neurological Diseases»**

#### **June 2, 2022**

Almost 6 000 health care specialists from Ukraine, Uzbekistan, Tadjikistan, Kazakhstan, Azerbaijan, Georgia, Moldova and other countries have registered to participate in the Euro-Asian Online-Teleconference «IV Interdisciplinary Collegium of Neurological Diseases».

Interdisciplinary format of the Teleconference was assured by involvement of speakers from different special fields, such as: neurologists, anesthesiologists, and general practitioners.

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

- Management of acute and chronic cerebrovascular diseases.
- Pathogenic role of oxidative cascade blocker in management of acute ischemic stroke.
- Intensive therapy of cerebral edema in case of traumatic brain injury (TBI).
- Rational approaches to diagnostics and treatment of chronic cerebral ischemia (CCI).
- Secondary prevention of ischemic stroke.
- Dorsopathies: treatment principles.

#### **Conclusions and decisions based on discussion of reports:**

1. Acute cerebral stroke, despite significant progress in prevention and treatment, remains one of the leading causes of death worldwide. The persistence of high levels of mortality and disability due to stroke requires that modern medicine should adopt an early and multimodal approach to its treatment. This approach is a comprehensive treatment that is based on a strategy to protect the neurovascular unit, as not only neurons, but the entire neurovascular unit, are damaged during cerebral ischemia. Neurovascular unit is a structurally (that is, anatomically) and functionally related complex consisting of microcirculatory link (endothelial cells, basal membrane endothelium, pericytes) and nerve tissue (astrocytes and neurons). And the ultimate goal of the therapeutic route is to protect the entire neurovascular unit in the penumbra.
2. The pathogenesis of acute ischemic stroke consists of a sequential cascade of reactions in the brain, which, in addition to ischemia, are responsible for further damage to the brain tissue and slow down the development of compensatory and regenerative mechanisms. Ischemia by itself or ischemia followed by reperfusion increases the production of free radicals that attack cell membranes by oxidizing unsaturated fatty acids in phospholipids into peroxide compounds. The resulting chain reaction leads to ischemic damage to the brain, manifesting as edema, a cerebral infarction. Therefore, protecting a neurovascular unit from attacks by free radicals is considered an important therapeutic target in the acute stroke phase. Edaravone has excellent neutralizing activity against a wide range of aggressive free radicals and inhibits the chain reaction of peroxidation of lipids by absorbing the peroxy radicals that cause this reaction. As a blocker of ischemic cascade, edaravone inhibits the NMDA receptor, reduces glutamate excitotoxicity, inhibits NMDA receptors, reduces the intake of  $\text{Ca}^{2+}$  into the cell, prevents the risk of development

of cerebral edema, reduces BBB damage, neutralizes oxidative and nitrite stress, suppresses secondary inflammation and prevents cell apoptosis.

3. Edaravone has an indisputable basis in the treatment of acute ischemic stroke, which includes 4 meta-analyses, a retrospective study of the Japanese national database, the Cochrane Review, according to which, prescription of edaravone in the early stages of acute ischemic stroke reliably provides a significant improvement in the neurological effects of stroke – twice as much as placebo.
4. In stroke, in addition to neuronal death, there is damage to neuroaxonal connections and the transmission of nerve impulses is disrupted. In addition to citicoline, the Neurocitin contains a complex of electrolytes and sodium lactate, which provides balanced volemic support and simultaneous protection of neurovascular unit. To prevent the development of repeated disorders of the cerebral circulation in the early recovery period, vascular rehabilitation is recommended. The levorotatory nitrogen oxide donator (L-arginine hydrochloride) stimulates physiological vasodilation, improves blood flow and reduces the risk of repeated stroke.
5. Traumatic brain injury (TBI) is one of major health and socio-economic problems worldwide: it is the leading cause of death and disability at a young age. Cerebral edema is a formidable and frequent complication of TBI. We have observed clinical efficiency of Sorbilact medicine in treatment of cerebral edema of different genesis. Hyperosmolar solution causes long-term reduction of ICP without clinically significant side effects. The anti-edema effect of the Medicine is not accompanied by the «rebound effect», peculiar to mannitol. In addition, hyperosmolar solution has a beneficial effect on hemodynamics, which is an additional factor in the elimination of cerebral edema and contributes to the stabilization of patient's condition. Edaravone is another medicine that can prevent the risk of development of cerebral edema and reduce it. Studies show that edaravone attenuates cerebral edema, suppresses inflammatory and oxidative reactions caused by TBI. This was evidenced by inhibition of excess production of inflammation mediators in the form of reduction of levels of glutathione peroxidase, interleukin 6, tumor necrosis factor- $\alpha$  and hydrogen peroxide, as well as activation of enzymes of antioxidant protection in the form of increased levels of heme-oxygenase-1 and superoxide dismutase, thereby alleviating neuro-functional deficiency, cell apoptosis, and structural damage. Timely use of edaravone, due to its ability to influence the main links of the neurometabolic cascade at TBI, will reduce secondary damage, reduce or eliminate the long-term and late effects of injury, quickly achieve clinical stabilization, accelerate functional recovery, protect and recover cognitive health and mental well-being.
6. Taking into account the simultaneous involvement of vascular pathology, damage to neurons and glial cells into the pathogenesis of CCI, modern approaches to its treatment are based on the concept of protection of the entire neurovascular unit. One of the main «axis of evil» in the pathophysiology of CCI is endothelial dysfunction and alteration of rheological properties of the blood, which are the basis of strengthening its coagulation activity, which leads to thrombosis and enhances brain ischemia. The use of a levorotatory nitrogen oxide donator (L-arginine hydrochloride) in patients with CCI compensates for NO deficiency, ensures better vasodilation, reduces cerebral ischemia area, and improves brain perfusion, thereby reducing the risk of recurrent stroke. In ischemia, with accompanying neuronal disorder, the synthesis of endogenous 5'-diphosphocholine cytidine is disrupted. The combination of electrolytes and citicoline provides double modulation of nerve impulse transmission, thus restoring cognitive, sensitive and motor functions of the CNS. In CCI, erythrocyte deformity is disturbed, which exacerbates microcirculation in the cerebral vessels. A ready-made solution of electrolytes with pentoxifylline increases erythrocyte elasticity, reduces platelet aggregation and increases cerebral blood flow.
7. One of the most pressing problems of modern neuroscience is back pain, with at least one episode of back pain statistically occurring in 70-80% of people. The most common etiological factors of

dorsopathies are diseases that cause degeneration in the mediated cartilages, facet joints, ligaments, and those resulting in myofascial pain syndrome. The most vulnerable structure of the intervertebral foramen is venous plexus, which is compressed already at the stage of relative stenosis without signs of direct compression of the spine. Venous hyperemia leads to chronic edema with local ischemia, demyelination, and subsequent development of peri- and intraneural fibrosis. Treatment of dorsopathies is mostly conservative. In this case, restoration of microcirculation is considered to be one of the pathogenetically based objectives of the therapy. Complex microcirculatory approach allows to prevent the development of complications in the form of edema and demyelination of spine, and to achieve a stable and long-term remission. This result can be achieved with L-arginine, a balanced hyperosmolar crystalloid solution and a ready-made solution of electrolytes with pentoxifylline. L-arginine, affecting endothelium, exerts endothelium-dependent vasodilation, reduces leukocyte adhesion to the vascular wall and parietal thrombosis. The possibilities of a multifunctional solution containing sorbitol are manifested in the reduction of edema and the opening of precapillary sphincters. And the well-known effects of pentoxifylline are expressed in reduced blood viscosity, improved rheology, vasodilatory action.

8. Among all neurological diseases in adults, acute ischemic stroke is the most frequent and has a disabling effect. After ischemic heart disease, stroke is the second most common cause of death worldwide, claiming more than 5 million lives a year. The main purpose of therapy of patients with stroke is not only to prevent the recurrent episode, but also to level the existing neurological deficit. Many studies suggest that edaravone plays a powerful role as an antioxidant, capturing free oxygen radicals and contributing to the same reduction of inflammation in nerve structures and excessive activation of microglia, as well as the development of atrophy of dysfunctional muscles of the extremities. Edaravone is used successfully in complex therapy of disorders of the cerebral circulation in acute, sub-acute and remote periods, as well as for treatment of degenerative diseases of the nervous system.

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