

Optimization Of Neuroprotective Therapy Of Ischemic Stroke In The Acute Period

Khaydarova Dildora Kadirovna¹, Khodjyeva Dilbar Tadjiyevna², Bobokulov Gulmurod Dilmurodovich³

¹Doctor of Medical Sciences, Department of Neurology, Bukhara State Medical Institute

²Head of the Department of Neurology, Bukhara State Medical Institute, Doctor of Medical Sciences

³Assistant of the Department of Neurology, Bukhara State Medical Institute

Abstract. *The problem of cerebrovascular diseases and stroke is significant not only for clinical neurology, but also for society as a whole. Stroke is the second most common cause of death in many developed countries. In Russia, more than 450 thousand cases of this disease are registered per year, and in the Republic of Uzbekistan there are more than ten thousand cases, the mortality rate in the acute period of stroke in Russia reaches 35%, increasing by another 12-15% by the end of the first year after the stroke. Stroke ranks first among the causes of persistent disability, which necessitates timely drug therapy not only in the acute period of the disease, but also throughout the recovery phase.*

Keywords. *Republic of Uzbekistan, Stroke, neuroprotectors, cytokines, reperfusion.*

1. INTRODUCTION.

The development of acute cerebral ischemia triggers pathobiochemical cascade reactions, the outcome of which is cerebral infarction (MI), which is formed by two mechanisms: necrotic cell death and apoptosis - programmed cell death [2,7]. These modern pathogenetic concepts have made it possible to propose a sequence of stages »Based on their causal relationships. [9] Each stage of the cascade is a target for the therapeutic effect of drugs, primarily with neuroprotective effects. The earlier the cascade is interrupted, the greater the effect can be expected from therapy (Lee R.G., van Donkelaar P., 1995; Lutser H.L., Clark W.M., 1999; Lees K.R., 2000, Skvortsova V.I., 2004).

There are two main areas of neuroprotective therapy. Primary neuroprotection is aimed at interrupting the rapid mechanisms of cell necrosis - the reactions of the calcium glutamate cascade. This type of neuroprotection should begin from the first minutes of ischemia, especially actively in the first 12 hours. Secondary neuroprotection is aimed at reducing the severity of the long-term effects of ischemia: blockade of pro-inflammatory cytokines, inhibition of prooxidant molecules, interruption of apoptosis, is effective in the first 72 hours, when the focus is re-formed. Despite numerous studies, currently, unfortunately, the issue of the effectiveness and absolute evidence of neuroprotection in cerebral ischemia in humans remains controversial. A fairly large number of drugs with different mechanisms of action have been proposed as neuroprotectors. The effectiveness of most of them has been demonstrated experimentally, but has not been confirmed in the clinic. [4]

It is believed that the failure of the clinical application of most neuroprotective agents is due to a number of objective reasons. First, the terms from the beginning of therapy in the clinic, in contrast to the experiment, are mostly outside the "therapeutic window". Also, one of the features of cerebrovascular accident is the contribution of reperfusion both to the

process of cell preservation and to their damage. The absence of reperfusion suggests that the focus will occupy the maximum volume, moreover, in the absence of blood flow, it is difficult or impossible to deliver the drug to the site of the event, and the restoration of blood flow includes new and enhances old damage mechanisms [1]. The drugs proposed for neuroprotection may be far from ideal in their properties - they poorly penetrate the blood-brain barrier, do not enter the penumbra zone, do not develop their effect at the level of the vascular wall [11]. Some neuroprotective agents are not effective in humans, in contrast to animals. In addition, brain damage preceding ischemia could create conditions under which the effect of neuroprotection could be minimal (diabetes mellitus, high arterial hypertension). And finally, ischemic stroke is a heterogeneous state, not only in pathogenesis, but also in localization and size of the lesion, which suggests some difference in the metabolic and hemodynamic conditions created during ischemia. A particular difficulty for assessing the effectiveness of neuroprotective agents in the clinic, in contrast to the experiment, is the standardization of the groups of patients under study and the choice of outcome assessment (Grotta J., 2002).

However, to date, based on an understanding of the pathobiochemistry of ischemia, the study of the neuroprotective effects of drugs that interfere with the mechanisms of excitotoxicity, the development of oxidative stress, as well as drugs with neurotrophic action is considered a promising direction. (5). And, despite the presence of many unresolved problems and contradictions regarding the drug therapy of stroke, an increase in its effectiveness in the appointment of patients with various drugs with different mechanisms of action, points of application and their combination, aimed at correcting pathological processes in stroke, both for theoretical and for practical medicine is an urgent problem. There is a constant search for drugs that can interrupt the pathological processes of ischemia. In this regard, amantadine sulfate is of great interest, the mechanism of action of which is aimed at blocking both dopamine and NMDA receptors, which play an important role in the induction of the ischemic cascade. This provides a theoretical basis for the possibility of a neuroprotective effect of this drug in ischemic brain lesions. And the first pilot studies of amantadine sulfate showed positive results in terms of the effectiveness of the treatment of cerebrovascular accident (CMB) (S.A. Rummyantseva, N.G. Benevolskaya, 2006). This motivated the study of the neuroprotective potential of this drug.

Acute disorders of cerebral circulation (ACVA) are the most important medical and social problem. The incidence of stroke is 2.5 - 3 cases per 1000 population per year, mortality - 1 case per 1000 population per year. Mortality in the acute period of stroke in Russia reaches 35%, increasing by 12-15% by the end of the first year after suffering a stroke. Post-stroke disability ranks first among all causes of disability and is 3.2 per 10,000 population. 20% of stroke survivors return to work, while one third of stroke patients are of working age. Thus, in Russia, a stroke develops annually in 400 - 450 thousand people, about 200 thousand of them die. [4,13] There are more than 1 million stroke survivors in the country, 80% of whom are disabled. Despite the fact that primary prevention plays a decisive role in reducing mortality and disability due to stroke, a significant effect in this regard is provided by the optimization of the system of care for ACVA patients, the introduction of therapeutic and diagnostic standards for these patients, including rehabilitation measures and the prevention of recurrent strokes. The Regional Office for Europe of the World Health Organization (WHO) believes that the creation of a modern system of care for patients with stroke will reduce mortality during the first month of the disease to 20% and ensure independence in everyday life 3 months after the onset of the disease at least 70% of surviving patients. [5] The development and implementation of uniform principles of management of patients with acute cerebrovascular accidents should help to optimize the

diagnostic approach and the choice of treatment measures to ensure the best outcome of the disease. [7.8]

Stroke continues to be one of the urgent problems of modern medicine, being the main reason for the disability of the population [10]. In recent years, the number of people with disabilities after a stroke has been steadily increasing. Thus, in Uzbekistan, no more than 3-23% of stroke patients return to work, 85% of patients require constant medical and social support, and 20-30% of patients experience profound disability until the end of their life [8].

As a result of studies carried out in Uzbekistan, it was found that the incidence of stroke is one of the highest among all types of cardiovascular diseases, and mortality from stroke is consistently ranked second in the structure of overall mortality of the population, second only to cardiac pathology. In some regions of Uzbekistan, stroke is more common than myocardial infarction. On average, 60% of stroke patients become disabled, and most of them depend on others or need outside care.

Over the past 5 years, 1.4 million people have died from diseases of the circulatory system in Uzbekistan, of which 18.9% are people of working age [3]. In this regard, the search for optimal and highly effective methods of treating stroke in order to reduce the risk of occurrence and the degree of post-stroke disability is one of the priority tasks of the healthcare system as a whole. [9.12]

Along with the use of specialized treatment technologies in vascular centers, according to the standards, all patients undergo neuroprotective therapy from 1 hour after admission to the intensive care unit in order to reduce the consequences of hypoperfusion in ischemic stroke and perifocal changes in intracerebral hematomas, reperfusion injury when using recanalizing technologies and multiple organ violations. [11] Of the group of drugs recommended by the standards for the treatment of stroke, the most commonly used are those that have a multimodal effect, are safe for all types of stroke, and also improve regenerative-reparative processes with an effect on neuronal plasticity. The drug Mexidol (ethylmethylhydroxypyridine succinate) is widely used in the treatment of ischemic stroke [13].

2. CONCLUSION

it should be noted that neuroprotective therapy for ischemic stroke should begin as early as possible and continue during the recovery period, which will reduce the number of complications, reduce mortality, improve recovery of neurological functions and the quality of life of patients.

3. REFERENCES

- [1] Anatskaya L.N. A cerebral infarction in elderly patients. *Zh Nevrol Psikhiatr Im S S Korsakova*. 2011; (8–2: Stroke): 74–80.
- [2] Kulikov A., Abdrashitova G. Budget Impact Analysis of Cerebrolysin In The Treatment of Acute Ischemic Stroke of Moderate and Severe Degrees of Severity In The Russian Federation. *Value Health*. 2015; 18 (7): A699. PMID: 26533918. DOI: 10.1016/j.jval.2015.09.2612.
- [3] Ziganshina LE, Abakumova T, Vernay L. Cerebrolysin for acute ischaemic stroke. *Cochrane Database Syst Rev*. 2016; 12: CD007026 PMID: 27918088. DOI: 10.1002/14651858.CD007026.pub4.
- [4] *Handbook of Vidal. Medicinal preparations in Russia – 2017*. Moscow: Vidal' Rus Publ., 2017. 1240 p.

- [5] Yasnetsov V.V., Prosvirova E.P., Tsublova E.G., et al. Comparative studies of antihypoxic, neuroprotective and analgesic action of succinatecontaining drugs. *Aviakosmicheskaya i ekologicheskaya meditsina*. 2012; 46 (6):41–45.
- [6] Odinak M.M., Yanishevskiy S.N., Tsygan N.V., et al. The use of succinates for the correction of metabolic disorders in the penumbra in patients with stroke. *Zh Nevrol Psikhiatr Im S S Korsakova*. 2013; 113(12–2: Stroke): 55–60.
- [7] Ivanova GE, Shklovskii VM, Petrova EA. The principles of early rehabilitation of stroke patients. *Kachestvo zhizni. Meditsina*. 2006;2(13):62-70.
- [8] Skvortsova VI. *Snizhenie zaboлеваemosti, smertnosti i invalidnosti ot insul'tov v Rossiiskoi Federatsii*. M.: Litterra; 2008.
- [9] Fedin AI, Tyutyumova EA, Badalyan KR. Ischemic cascade in the acute period of the stroke and methods of its correction. *Farmateka*. 2017;9:99-104.
- [10] Khasanova DR, Gavrilov IA, Prokofeva IuV, Kamalov IR. The introduction of the multilevel system of medical care for stroke patients in the Tatarstan Republic. *Zhurnal nevrologii ipsikhiatrii im. S.S. Korsakova*. 2014;114:8(2):74-79.
- [11] Fedin AI. *Klinicheskie aspekty patogeneticheskoi terapii ishemii go-lovnogo mozga. Minimizatsiya negativnogoprogoza*. M.: OOO «AST»; 2016.
- [12] Voronina TA. The pioneer of antioxidant neuroprotection. 20 years in clinical practice. *RMJ*. 2016;24(7):434-438.
- [13] Shulkin AV. Mexidol influence on the development of the phenomen of neurons excitotoxicity *in vitro*. *Zhurnal nevrologii ipsikhiatrii im. S.S. Korsakova*. 2012;112(2):35-39.