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Clinical basis for the development of neuroprotective therapy in acute ischemic stroke

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Abstract---In recent years, the incidence of ischemic stroke has increased everywhere. This fact is explained by the increase in the number of elderly people and the prevalence of risk factors for stroke, such as arterial hypertension, diabetes, obesity, heart disease, etc., more than 80% of survivors are disabled. To date, neuroprotective therapy is the most important treatment in the treatment of this disease, and this article really describes its improving properties.

Keywords---vertebrobasilar bassen, arterial hypertension, neuroprotective therapy, stroke.

Introduction

More than 80% of stroke patients permanently lose their ability to work, and only 10.2% of survivors return to work (1). Stroke deaths are projected to rise to 7.8 million per year globally by 2030 unless strong global action is taken to control the epidemic (2).

Reperfusion via thrombolysis remains the current "gold standard" for the treatment of ischemic stroke. However, the use of thrombolytic therapy has a number of organizational and clinical limitations. So, according to ChangT.S. et al., due to time constraints and side effects of thrombolysis, only about 3% of all stroke patients receive it. An alternative treatment for stroke is neuroprotection.

Experimental studies have shown that neuroprotective drugs can restore up to 80% of the volume of ischemic tissue (3).

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. Rumyantseva, N.G. Benevolskaya, 2006). This motivated the study of the neuroprotective potential of this drug.

Recently, the definition of neuroprotection in ischemic stroke has been developed as a treatment strategy aimed at reducing, interrupting or slowing down the sequence of biochemical or molecular processes that lead to irreversible brain damage (4). Although the effectiveness of many drugs has been demonstrated in experimental studies, cases of proven efficacy of neuroprotective drugs in the clinical setting are rare. This is due to the etiological, pathogenetic and clinical heterogeneity of ischemic stroke, as well as the presence of comorbidities in patients that aggravate the course of stroke and prevent the directed action of neuroprotectors. Thus, the presence of arterial hypertension, diabetes mellitus, heart failure, etc. affects the structure of the blood-brain barrier, collateral circulation, cellular metabolism, and the neuroimmune system. Due to these and a number of other factors, drugs that are effective under experimental conditions do not confirm their effect in the clinic.

An analysis of the dynamics of the deployment of molecular and biochemical mechanisms triggered by acute focal cerebral ischemia established a clear temporal sequence of their "switching on". During the first 3 hours from the moment of acute cerebrovascular accident, the energy deficit is maximal in the ischemic tissue; after 3-6 hours - glutamate-calcium excitotoxicity and lactate acidosis, fading away by the end of the 1st day [5].

Such consequences of ischemia as oxidative stress, local inflammation, secondary microcirculatory disorders in the focus of ischemia, increased permeability of the blood-brain barrier, autoimmune reactions begin to appear at 2-3 hours, reach a maximum after 12-36 hours. The process of apoptosis is maximally expressed by 2-3 days. The consequences of ischemia persist for a long time - for several months, contributing to the progression of dystrophic processes and the development of encephalopathy in the post-stroke period [6].

Each stage of the ischemic cascade is a potential target for therapeutic interventions. The earlier the cascade is interrupted, the greater the effect can be expected from the treatment [7]. Currently, there are several goals in the fight for the survival of brain cells [9]: a decrease in glutamate expression, normalization of ion channels, restoration of phosphatidylcholine levels, and a decrease in the level of arachidonic acid and other inflammatory mediators. The variety of mechanisms for the formation of cerebral infarction allows us to conditionally distinguish two main areas of neuroprotective therapy: primary and secondary neuroprotection [8].

Primary neuroprotection is aimed at interrupting the rapid mechanisms of necrotic cell death - reactions of the glutamate-calcium cascade; it should be applied from the first minutes of ischemia and continue during the first 3 days of stroke [12]. Secondary neuroprotection is aimed at reducing the severity of long-term effects of ischemia, it can be started 3-6 hours after the development of a stroke and continue for at least a week [11]. Magnesium sulfate and glycine are proposed to be used as primary neuroprotectors, and methionyl-glutamyl-histidyl-phenylalanine-prolyl-glycyl-proline, ethylmethylhydroxypyridine succinate, and cytoflavin are used as secondary ones [13].

Subsequent treatment should be aimed at activating regenerative processes. The effects of the neuroprotective action of drugs are manifested in an increase in the resistance of brain cells to hypoxia and ischemia; correction of the level of cellular energy; improvement of blood supply to the brain; increased functional activity of neurons and glial cells; normalization of mediator imbalance [4].

Some drugs, positioned by their manufacturers as neuroprotective, have not demonstrated convincing benefits in large-scale and well-designed studies: nimodipine, magnesium sulfate, citicoline, piracetam, and many others [5]. However, in the CIS countries, drugs with neuroprotective properties are widely used in the treatment of ischemic stroke (IS), showing their effectiveness in separate studies.

The purpose of the study

To study the effectiveness of the treatment of ischemic stroke in the acute period with a complex of neuroprotective drugs.

Materials and Methods

Clinical observations were carried out in the clinic of neurological diseases of the Bukhara State Medical Institute on the basis of the City Clinical Hospital of Bukhara. Us for the period 2018–2020. 154 patients with IS in the acute period at the age of 41–81 years (mean age 60.56 ± 0.60 years) were examined, of which 101 were men and 53 were women. The average age of the observed men was 60.63 ± 0.77 years, women - 60.42 ± 0.94 years.

Results

By simple randomization, patients were divided into two groups with different treatment regimens. The main characteristics of the patients who participated in the study are presented in Table 1.

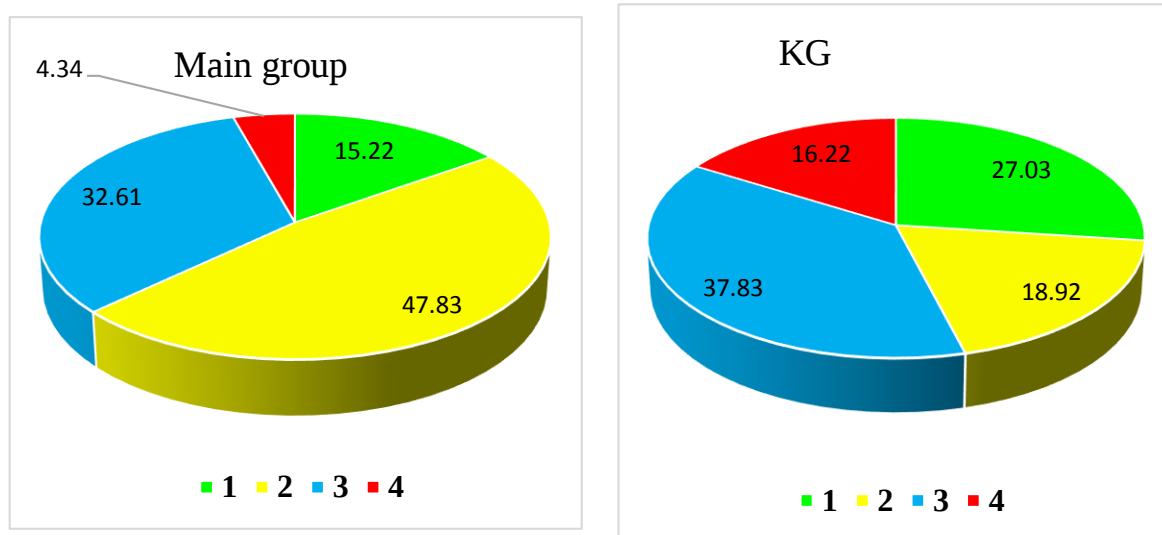
Table 1
Main characteristics of patients participating in the study

Indicator	Main group	Control group
Number of patients, n (%)	85 (55,19%)	69 (44,81%)
Average age, years, (M±δ)	60,15±0,92	60,17±0,88
Men, n(%)	56 (65,88%)	45 (65,22%)
Women, n(%)	29 (34,12%)	24 (34,78%)
Pathogenetic variant of stroke (according to TOAST criteria), n (%)		
atherothrombotic	42 (49,41%)	37 (53,62%)
Cardioembolic	34 (40%)	24 (34,78%)
lacunar	9 (10,59%)	6 (8,70%)
Hemodynamic	0	2 (2,90%)
AI localization:		
Carotid pool, n (%)	68 (80%)	52 (75,36%)
WBB, n (%)	17 (20%)	17 (24,64%)
Admission to the hospital from the moment of stroke, n (%):		
up to 3 hours	22(25,88%)	17(24,64%)
3-6 hours	14 (16,47%)	18(26,09%)
6-12 hours	20(23,53%)	18(26,09%)
12-24 hours	14(16,47%)	6(8,70%)
24-36hours	15(17,65%)	10(14,49%)
Risk factors n(%)		
AG	82(96,47%)	63 (91,30%)
Arrhythmias	43 (50,59%)	28(40,58%)
ischemic heart disease	48(56,47%)	33 (47,83%)
Diabetes	14(16,47%)	7 (10,14%)
Indicators of indices and scales		
Body mass index, Me [25%; 75%]	28,2 [24,9; 31,1]	26,7 [24; 30,8]
Average score of Orgosozo at admission, Me [25%; 75%]	50 [35; 75]	45 [30; 65]
Mean NIHSS score at admission, Me [25%;75%]	10 [8; 14]	10 [7; 14]
Lethal outcome, n (%)	2(2,35%)	6(8,70%)

The patients of both groups were comparable in terms of gender and age. In most cases, the atherothrombotic subtype of stroke occurred, which coincides with the literature data on its predominance among the pathogenetic variants of cerebral infarction [5].

The effectiveness of combined neuroprotective therapy was studied in three subgroups of patients - with moderate IS in CV (National Institutes of Health Stroke Scale) (National Institutes of Health Stroke Scale) and severe IS in CV (15 or more points on the NIHSS scale). NIHSS), and AI in the vertebrobasilar basin. These groups were designated as the main ones. The results of studies in each main group were compared with control groups that were clinically similar and received standard treatment.

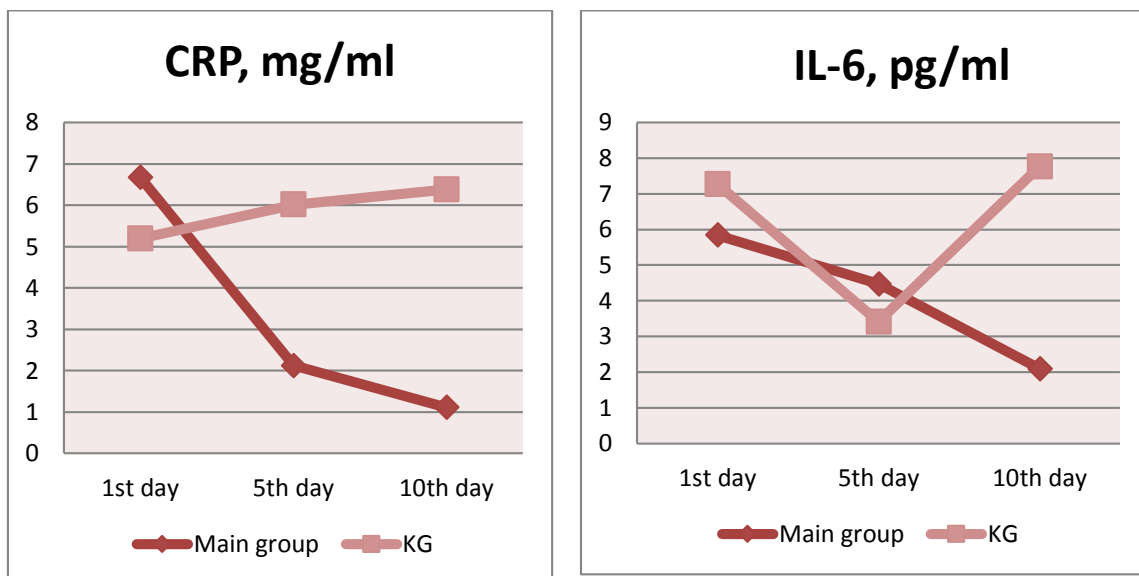
Complete dependence on others in the main group was observed in 2 patients (4.34%), in the CG - in 6 (16.22%). By the time of discharge from the hospital, in the group receiving combined neuroprotective therapy, patients with mild and moderate degrees of dependence prevailed, in the group receiving standard therapy - with severe and complete.



Rice. 1. Distribution of patients (%) according to the degree of dependence on others, according to the Barthel index. Degree of dependence: 1 - mild (91-99 points), 2 - moderate (61-90 points), 3 - severe (21-60 points), 4 - complete (0-20 points).

Figure 2. reflected in the levels of CRP and IL-6 during treatment. On the first day of observation in the main group, an increased level of CRP was noted, which decreased by the 5th day ($p < 0.001$ compared with the CG). In the CG, despite the lower initial level, CRP tended to increase during the observation period. Such dynamics may indicate a positive effect of neuroprotective therapy not only on metabolic, but also on inflammatory processes in IS.

Changes in the pro-inflammatory cytokine IL-6 during treatment in the main group were similar to the direction of the dynamics of CRP - during the first 10 days there was a decrease in the level of IL-6, while in the control group by the 10th day there was an increase in the indicator ($p < 0, 05$ compared to CG). The level of IL-6 at admission was higher in the age group over 65 years - 10.8[8; 12.7] pg/ml, while in patients < 65 years 6.15 [4.35; 7.1] pg/ml, $p = 0.005$.



Rice. Fig. 2. Dynamics of CRP and IL-6 in the main and control groups of IS in the carotid pool of moderate severity

This observation illustrates the combination of high risk factors for brain vascular damage (age, arrhythmia, arterial hypertension, anemia) that preceded the stroke, and severe speech disorders as manifestations of the stroke. Such a status of the patient did not give grounds for a quick recovery of neurological functions. Nevertheless, it was the combined neuroprotective therapy, in our opinion, that caused the active regression of the neurological deficit already in the most acute phase of stroke.

Conclusion

In the study of the effectiveness of neuroprotective therapy, the positive dynamics by the end of the acute period of IS in the carotid pool of moderate severity according to the NIHSS and Orgogozo scales was 4 [2.5; 5] and 15 [10; 27] points, respectively, in the main group, and 2 [1; 4] and 10 [0; 20]. The difference between the main and control groups was statistically significant. Differences were noted in the general course of the pathological process in the studied groups: in the CG, 3 patients died, in 2 patients the neurological deficit grew, in two more focal symptoms remained unchanged.

List of used literature

1. Zalyalova Z.A. Salivation after a stroke // Journal of Neurology and Psychiatry. S.S. Korsakov. - 2017. - T. 117, No. 1. - S. 85-89.
2. Bahodirovna R. G., Shavkatovna G. S. Hemodynamic profile of patients with chronic obstructive pulmonary disease and obstructive sleep apnea syndrome // ACADEMICIA: An International Multidisciplinary Research Journal. - 2021. - T. 11. - №. 12. - C. 587-591.

3. Vishnyakova A.Yu., Malyarova E.Yu., Lelyuk S.E. et al. Cerebrovascular reactivity of the arteries of the vertebrobasal basin with various types of exercise stimulation // *Ultrasonic and functional diagnostics*. - 2012. - No. 6. - S. 56-69.
4. Khaidarov N.K., Gafurov B.G. Nazarova Zh.A. The effectiveness of intranasal use of neuroprotectorcortexin in cognitive impairment in patients with stenosis of the main arteries of the head during surgical treatment. *Scientific and Practical Journal Neurology*. - 2017. - No. 2. - P. 2-5
5. Khodjjeva D.T., Majidova E.N., Khidoyatova D.N., Zhabbarova S.B., Kim O.V. Violation of cerebral circulation in occlusive lesions of the carotid arteries // *Neurology* - 2019. - No. 2 (78). - P.82-85.
6. Khodjjeva D.T., Khaidarov N.K. Khaidarova D.K. Correction of asthenoneurotic syndrome with energy corrector cytoflavin // *Neurology*. - Tashkent, 2013. - No. 3. P.16-19.,
7. Khodjjeva D.T., Khaidarova D.K., Khaidarov N.K., Samadov A.U. Differentiated therapy in the acute period of ischemic stroke // *Neurology* - 2011. - No. 4. - P. 34.
8. Khasanovna M. G. Features of Computer Dependence Comparative Characteristics of Computer-Dependent and Computer-Independent Adolescents by Anthropometric Indicators // *International Journal of Innovative Analyses and Emerging Technology*. - 2021. - T. 1. - №. 6. - C. 213-217.
9. Мухидова Г. X. Comparative Characteristics of morphometric parameters of physical development and anthropo extremities of healthy and computer. Research // *Jet Journal of Analysis and Inventions-RJAI*. - 2021. - T. 2. - №. 9. - C. 14-17.
10. Coutts S.B. Diagnosis and Management of Transient Ischemic Attack // *Continuum (Minneapolis)*. - 2017. - Vol. 23 (1, Cerebrovascular Disease). - P. 82-92.
11. Donnan G.A. New Road Map for Neuroprotection. The 2007 Feinberg Lecture // *Stroke*. - 2008. - Vol.39. - P.242-248
12. Douiri A, McKevitt C, Emmett ES, Rudd AG, Wolfe CD. Long-term effects of secondary prevention on cognitive function in stroke patients. // *Circulation*, - 2013, - №128(12). - p.1341-1348.
13. George M.G., Tong X., Bowman B.A. Prevalence of Cardiovascular Risk Factors and Strokes in Younger Adults // *JAMA Neurology*. 2017. Vol. 74 (6). P. 695-703
14. Khasanovna M. G. Comparative characteristics of morphometric parameters of physical development and anthropometric data of the upper extremities of healthy and computer-dependent children // *ResearchJet Journal of Analysis and Inventions*. - 2021. - T. 2. - №. 09. - C. 14-17.
15. Мухидова, Гулмира Хасановна. "Comparative Characteristics of morphometric parameters of physical development and anthropo extremities of healthy and computer. Research." *Jet Journal of Analysis and Inventions-RJAI* 2.9 (2021): 14-17.
16. Мухидова Г. X. Сравнительная характеристика компьютерно-зависимых компьютерно-независимых подростков по антропометрическим показателям // *Тиббиётда янги кун*. - 2021. - Т. 5. - С. 37