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DIFFERENTIATED THERAPY OF PATIENTS WITH INTRACEREBRAL COMPLICATED HEMISPHERIC ISCHEMIC CEREBRAL STROKE WITH SECONDARY BRAINSTEM HEMORRHAGES AGAINST THE BACKGROUND OF HYPERTENSIVE ENCEPHALOPATHY

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Abstract.

The purpose of the study is to assessment of the risk of secondary brainstem hemorrhages against the background of hypertensive encephalopathy in patients with intracerebral complicated hemispheric ischemic cerebral stroke using anticoagulant therapy.

Was conducted a clinical and pathological study of 97 patients with intracerebral complicated hemispheric ischemic cerebral stroke aged 41 to 87 years. Of these, 55 were men (56,7%), average age 72,5±2,4; women 42 (43,3%), average age 76,5±2,1.

Data on survival time and complications in the form of secondary brainstem hemorrhages directly correlated with the results of pathological changes in the brainstem. During autopsy of deceased patients with hemispheric ischemic cerebral stroke complicated by secondary hemorrhages of the brainstem who received anticoagulant therapy, in 12 cases (70,6%) out of 17, secondary massive hemorrhages in the brainstem were found, consisting of multiple hemorrhagic foci merging with each other. In individuals with hemispheric ischemic cerebral stroke who did not receive anticoagulant therapy, pathomorphologically, secondary massive hemorrhages in the brainstem were noted in only 12 (25,5%) of 47 deceased, while in 35 observations (74,5%), hemorrhages were determined in the form of individual hemorrhagic foci of small size or individual small-point hemorrhages, sometimes detected during macroscopic examination.

Data on the presence of hypertensive encephalopathy in the pre-stroke anamnesis directly correlated with the results of secondary pathological changes in the brainstem. At autopsy, hypertensive encephalopathy was detected in 92,2% of deceased patients with secondary hemorrhages in the brainstem, while with ischemic nature of brainstem changes only in 42,4%.

The above proves the need to take into account differentiated therapy depending not only on the nature of the damage to the hemispheric structures, but also on the pathomorphological type of secondary changes in the brainstem.

In patients with hemispheric ischemic infarction who are predisposed to complicated hemorrhagic secondary brainstem syndrome, especially those with a history of hypertensive encephalopathy, the use of anticoagulant, thrombolytic, and dual antiplatelet therapy is not recommended due to the risk of developing secondary hemorrhagic stem syndrome as a consequence of secondary changes in microvessels, which always change under the influence of high blood pressure.

Key words. Ischemic cerebral stroke, secondary brainstem hemorrhages, hypertensive encephalopathy, anticoagulant therapy.

Introduction.

Each year, about 795000 people suffer a new or recurrent stroke, of which 87% are ischemic. The number of strokes is expected to more than double between 2010 and 2050, especially among older adults and people from underrepresented racial and ethnic groups, even though stroke death rates have declined slightly over the past few decades due to advances in prevention, diagnosis, and treatment [1].

The development of clear criteria for diagnosis and tactics of therapy of patients with intracerebral complicated hemispheric ischemic cerebral stroke (ICS) is a significant task of angioneurology. In the system of urgent medical care for ICS, there are currently quite definite ideas about the effectiveness of pharmacological correction affecting the coagulating functions of the blood. In this case, preference is given to anticoagulant drugs [2-4].

However, the high percentage of hemorrhagic complications in ICS, especially of a stem nature, despite modern approaches to cases and consequences of the use of thrombolytic, anticoagulant, dual antiplatelet therapy, forms new approaches to the differentiated use of these drugs [5-8]. It should be taken into account that against the background of cerebrovascular disease, especially with respect to the severity and duration of chronic cerebral ischemia caused by arterial hypertension, hypertensive encephalopathy may be observed.

Inadequately controlled primary hypertension is the most common cause of hypertensive encephalopathy. Secondary causes of hypertension, such as kidney disorders and adrenal tumors, can also predispose to this condition. Autoregulatory mechanisms normally enable the brain to maintain adequate cerebral perfusion pressure, altering arterial and arteriolar resistance in response to physiological changes. Steep blood pressure elevation can overwhelm these mechanisms, leading to vascular wall damage, blood-brain barrier disruption, and plasma, red blood cell, and macromolecule exudation.

Hypertensive encephalopathy shares many clinical features with other syndromes giving rise to cerebral edema, such as posterior reversible encephalopathy syndrome, hypertensive brainstem encephalopathy, and eclampsia. Evaluation for underlying causes like renal disease, sympathomimetic (e.g., amphetamines and cocaine) consumption, adverse effects of drugs like immunosuppressive agents, and pregnancy-induced hypertensive states should be considered if a patient is not known to have primary hypertension [9-11].

At the same time, one of the complications of hemispheric ICS is secondary hemorrhage of the brainstem, which triggers a whole chain of pathophysiological shifts that affect the outcome

of the process. The latter can be either hemorrhagic or secondary ischemic syndromes.

The Monro-Kellie doctrine determines the balance of the three main volumes of the intracranial cavity, such as cerebrospinal fluid, brain tissue and vascular bed. Due to the rigidity of the cranial cavity, an increase in one volume causes a compensatory decrease in another [12].

The increase in the volume of the brain due to the development of a pathological focus and perifocal edema leads to a disruption of cerebrospinal fluid circulation and venous outflow from the cranial cavity. The compensatory capabilities of redistribution of cerebrospinal fluid in reserve spaces – subarachnoid, cisterns and ventricles of the brain are gradually depleted. With slow development of the pathological focus, signs of displacement (dislocation) are often observed over a long period due to intracranial reserve spaces. At the same time, with rapid expansion of the focus, a stormy clinical picture occurs, and the compensatory capabilities of the reserve spaces also quickly exhaust themselves, and ICS, as a rule, ends fatally. Even before the introduction of computed tomography into clinical medicine, numerous autopsy studies showed, according to which dislocation syndrome is the main cause of death in patients with massive ICS [13].

According to the clinical and radiological classification of dislocation syndromes, the following stages are distinguished:

Stage 1: Hypertensive-discirculatory syndrome (general condition of moderate severity, displacement of the septum pellucidum does not exceed 4 mm);

Stage 2: Hypertension-dislocation hemispheric syndrome (general condition is severe, displacement of the septum pellucidum is 4-9 mm);

Stage 3: Hypertension-dislocation brainstem syndrome (general condition is extremely severe, displacement of the septum pellucidum exceeds 10 mm) [14].

In this regard, new approaches are needed to optimize differentiated drug correction taking into account the nature of the secondary stem complication in the acute period of hemispheric ICS [15-18].

The purpose of the study is to assessment of the risk of secondary brainstem hemorrhages against the background of hypertensive encephalopathy in patients with intracerebral complicated hemispheric ischemic cerebral stroke using anticoagulant therapy.

Materials and Methods.

To achieve the set goal, we conducted a prospective-retrospective multicenter study of 97 patients with intracerebrally complicated hemispheric ICS aged from 41 to 87 years, who were treated in the neurology department and the intensive care unit of the Municipal Non-profit Enterprise "City Hospital № 6" of Zaporizhzhya City Council. There were 55 were men (56,7%), average age 72,5±2,4; women 42 (43,3%), average age 76,5±2,1.

The study lasted for 3 years and was completed by February 2022.

There were no differences in racial characteristics.

Depending on the nature of the intracerebrally complicated hemispheric ICS against the background of hypertensive encephalopathy, the patients were divided into 2 groups.

Group 1 consisted of 64 patients with ICS complicated by secondary hemorrhage of the brainstem.

Group 2 consisted of 33 patients with ICS complicated by secondary ischemic syndrome.

Inclusion criteria.

Patients with intracerebral complicated hemispheric ICS.

Exclusion criteria.

Patients with ICS not complicated by secondary brainstem hemorrhages;

Patients with ICS without concomitant hypertensive encephalopathy.

Written consent to conduct the study was obtained from each patient or his relative, in accordance with the recommendations of ethical committees on biomedical research, Ukrainian legislation on health protection and the 2000 Declaration of Helsinki, European Society Directive 86/609 on participation people in biomedical research.

Statistical processing of the study results was carried out using descriptive statistics methods using the Microsoft Excel 2010 software package. The reliability of the values was assessed according to Student's t-test. The results obtained were considered significant at a significance level of $p < 0,05$.

Results and Discussion.

In order to determine the proportion of secondary brainstem hemorrhage, the mortality structure of another 83 deceased with hemispheric ICS and hemorrhagic hemispheric ICS complicated by secondary brainstem syndrome was additionally analyzed. Of the 36 deceased with intracerebrally complicated hemispheric ICS with secondary brainstem syndromes, 11 patients had brainstem hemorrhages. Of the 47 patients with cerebral hemisphere hemorrhage, 15 patients had a secondary hemorrhagic brainstem component. Thus, in a third of deceased patients, regardless of the type of primary hemispheric lesion, secondary stem manifestations were manifested by hemorrhages in the brainstem.

However, in order to optimize differentiated treatment of ischemic infarction, further analysis of the outcomes of ICS with secondary brainstem hemorrhage and with secondary ischemic syndrome was performed depending on the use of thrombolytic, anticoagulant, dual antiplatelet therapy and the presence of hypertensive encephalopathy in the pre-stroke history.

The role of secondary hemorrhagic stem complications in the outcome of ICS is convincingly demonstrated by the data in Table 1, which demonstrates the dependence of their prognosis on the pathomorphological nature of the stem lesion in patients with hemispheric ischemic strokes.

Table 1. *Dependence of life expectancy and duration of secondary brainstem complication on its nature in patients with hemispheric ischemic cerebral strokes (M±m).*

Secondary complications of the brainstem	**Number of patients**	**Duration**	
		Secondary Brainstem Syndrome (days)	Life after illness (days)
Ischemic	33	7,67+0,71*	8,98+0,73*
Hemorrhagic	64	3,34+0,43*	4,18+0,45*

Note: **-$p < 0,05$ compared to baseline values.*

The above results show that the survival time after the disease and the survival time with hemorrhages in the brainstem are reduced by two or more times compared to secondary brainstem syndrome, not complicated by secondary brainstem hemorrhages in the brainstem, regardless of the primary hemispheric focus. In addition, the nature of secondary changes in the brainstem is more significant than primary hemispheric changes for prognosis.

Thus, every third patient with developed severe secondary brainstem syndrome may have secondary hemorrhage in the brainstem, which largely determines the resulting cerebral vascular catastrophe. Therefore, the approach to the treatment of secondary brainstem syndrome complicated by a hemorrhagic component in conditions of ICS of the hemispheres is of particular relevance. This is due to the fact that patients with primary hemorrhagic hemispheric stroke usually undergo hemostatic therapy. In case of complications with a secondary stem hemorrhagic component, the basic principles of therapy remain the same. In the conditions of intracerebrally complicated hemispheric ICS, when the nature of the latter is absolutely proven by computer and clinical data, the doctor chooses differentiated therapy, among which thrombolytic, anticoagulant and antithrombotic drugs are in one of the first places [3,6-8,17,19].

In connection with the above, the results of drug therapy of 64 patients with hemispheric ICS complicated by secondary stem hemorrhages were retrospectively analyzed.

Of the 64 patients with ICS complicated by secondary brainstem hemorrhage, 17 patients received anticoagulant therapy (before the occurrence of secondary brainstem hemorrhages) according to the generally accepted regimen against the background of basic treatment (Group 1). Moreover, patients with systolic blood pressure not exceeding 180 mm Hg and not in a comatose state at the onset of secondary stem syndrome, which was a contraindication to the administration of anticoagulants, were selected [19]. In 33 patients, only basic therapy was used in the complex treatment of complicated ICS (Group 2).

The initial data of the hemostasis system, studied in the dynamics of the acute period of ICS, characterizing simultaneously the state of the coagulation, fibrinolytic and anticoagulant systems of the blood, showed the identity of the results of these two groups of patients.

The dependence of life expectancy and duration of secondary stem complication on its nature and the use of anticoagulants in patients with hemispheric ICS is presented in Table 2.

The above results show that in patients of the 1st group, the life expectancy from the onset of the disease was 2,87+0,61 ($p < 0,05$) days, and in the 2nd group it was 4,87+0,31 ($p < 0,05$) days. In addition, the time from the onset of secondary stem syndrome to death in patients receiving anticoagulant therapy was 1,89+0,69 ($p < 0,05$) days, and in patients receiving only basic therapy 3,99+0,36 ($p < 0,05$) days. As can be seen, patients who received anticoagulant therapy had a life expectancy and duration of secondary stem syndrome almost 2 times shorter than those of individuals who did not receive this treatment ($p < 0,05$).

Data on survival time and complications in the form of secondary brainstem hemorrhages were directly correlated with the results of pathological changes in the brainstem. At autopsy of deceased patients with hemispheric ICS complicated by secondary hemorrhages of the brainstem, who received anticoagulant therapy, in 12 cases (70,6%) out of 17, secondary massive hemorrhages in the brainstem were found, consisting of multiple hemorrhagic foci merging with each other. In individuals with hemispheric ICS who did not receive anticoagulant therapy, pathomorphologically, secondary massive hemorrhages in the brainstem were noted in only 12 (25,5%) of 47 deceased, while in 35 observations (74,5%), hemorrhages were determined in the form of individual hemorrhagic foci of small size or individual small-point hemorrhages, sometimes detected during macroscopic examination.

Of interest was the analysis of the dependence of hemorrhagic stem complications on the presence of a history of hypertensive encephalopathy in patients with hemispheric ICS.

The frequency of hemorrhagic stem complications on the presence of a history of hypertensive encephalopathy in patients with hemispheric ICS is presented in Table 3.

Table 2. *Dependence of life expectancy and duration of secondary stem complication on its nature and use of anticoagulants in patients with hemispheric ischemic cerebral strokes (M±m).*

Secondary complications of the brainstem	**Use of anticoagulants**	**Number of patients**	**Duration**	
			Secondary Brainstem Syndrome (days)	Life after illness (days)
Ischemic	Anticoagulants	12	7,5+0,96	8,7+0,93
	Without anticoagulants	21	6,7+0,72	7,7+0,79
Hemorrhagic	Anticoagulants	17	1,89+0,69*	2,87+0,61*
	Without anticoagulants	47	3,99+0,36*	4,87+0,31*

Note: **-p < 0,05 compared to baseline values.*

Table 3. *Frequency of hemorrhagic stem complications from the presence of a history of hypertensive encephalopathy in patients with hemispheric ischemic cerebral strokes (M±m).*

Secondary complications of the brainstem	**Presence of hypertensive encephalopathy**	**Number of patients**	**Hemorrhagic stem complications**
Ischemic	Hypertensive encephalopathy	14	42,4%
	Without hypertensive encephalopathy	19	57,6%
Hemorrhagic	Hypertensive encephalopathy	59	92,2%*
	Without hypertensive encephalopathy	5	7,8%*

The above data on the presence of hypertensive encephalopathy in the pre-stroke anamnesis directly correlated with the results of secondary pathological changes in the brainstem.

At autopsy, hypertensive encephalopathy was detected in 92,2% of deceased patients with secondary hemorrhages in the brainstem ($p < 0,05$ compared to secondary hemorrhages of the brainstem without hypertensive encephalopathy 7,8%), while with ischemic nature of brainstem changes only in 42,4%. Apparently, the preparedness of the cerebral vessels after arterial hypertension is also important for predicting the consequences of not only the use of anticoagulant therapy, but also for the use of thrombolytic and dual antiplatelet therapy

All secondary hemorrhages into the brainstem were combined with ischemia, pronounced edema and deformation of the brainstem. In this case, under conditions of hypoxic changes in the area of the brainstem focus and around it, diapedesis of leukocytes occurs, and then erythrocytes into the area of the secondary brainstem focus or along its periphery. The necessary prerequisites for hemorrhagic impregnation are a slowdown in blood flow, which occurs with rapid dislocation and compression of arteries, veins and capillaries, and subsequently stasis, anoxia and impaired vascular permeability directly in the area of secondary stem lesions. Secondary massive hemorrhages, mainly of arterial origin, were characterized by the presence of multiple hemorrhagic foci merging with each other, with rupture of arteries in the center of these formations or with severe necrobiotic changes in the walls of arteries and veins. Anticoagulants have a clear ability to trigger these mechanisms or to aggravate existing hemorrhagic secondary manifestations in the brainstem.

Conclusion.

1. Summarizing the above results of differentiated therapy, it can be concluded that, despite the improvement of the condition in the area of the hemispheric ischemia focus due to the optimization of the rheological properties of the blood and its increased inflow, there is a threat of additional complications outside the main focus caused by the use of this therapy. At the same time, in the brainstem, in conditions of dislocation, hemorrhagic complications can be caused, or existing ones can be aggravated.

2. The above proves the need to take into account differentiated therapy depending not only on the nature of the damage to the hemispheric structures, but also on the pathomorphological type of secondary changes in the brainstem.

3. In patients with hemispheric ischemic infarction who are predisposed to complicated hemorrhagic secondary brainstem syndrome, especially those with a history of hypertensive encephalopathy, the use of anticoagulant, thrombolytic, and dual antiplatelet therapy is not recommended due to the risk of developing secondary hemorrhagic stem syndrome as a consequence of secondary changes in microvessels, which always change under the influence of high blood pressure.

REFERENCES

1. Capirossi C, Laiso A, Renieri L, et al. Epidemiology, organization, diagnosis and treatment of acute ischemic stroke. European Journal of Radiology Open. 2023;11:100527.

2. Zozulya I.S, Volosovets A.O, Parkhomenko B.L. About some diseases and conditions that can cause acute disorders of cerebral blood circulation. Ukrainian Medical Journal. 2023;2:71-73.

3. Safouris A, Psychogios K, Palaiodimou L, et al. Update of Anticoagulation Use in Cardioembolic Stroke with a Special Reference to Endovascular Treatment. Journal of Stroke. 2024;26:13-25.

4. Dariy V, Mishchenko T, Serikov K. Integrative monitoring for intracerebral complications of ischemic stroke. Georgian Medical News. 2019;4:108-113.

5. Mishchenko T.S. Epidemiology of cerebrovascular diseases and organization of medical care for patients with stroke in Ukraine. Ukrains'kyi visnyk psykhonevrolohii. 2017;25:22-24.

6. Levytska OR, Hromovyk BP. Place of anticoagulants in treatment and prevention of ischemic stroke (review of evidence base of use). Pharmaceutical review. 2019;2:94-102.

7. Tirumandyam G, Krishna Mohan G, Addi Palle L, et al. Early Versus Delayed Oral Anticoagulation in Patients with Acute Ischemic Stroke Due to Atrial Fibrillation: A Meta-Analysis. Cureus. 2023;15:e40801.

8. Palaiodimou L, Stefanou MI, Katsanos AH, et al. Early Anticoagulation in Patients with Acute Ischemic Stroke Due to Atrial Fibrillation: A Systematic Review and Meta-Analysis. Journal of Clinical Medicine. 2022;11:4981.

9. Tovazhnyanskaya YeL, Bezuglova IO, Yarosh VA, et al. Hypertensive encephalopathy. The role of antihypertensive therapy in the prevention and treatment. International Neurological Journal. 2014;2:93-99.

10. Miller JB, Suchdev K, Jayaprakash N, et al. New Developments in Hypertensive Encephalopathy. Current Hypertension Reports. 2018;20:13.

11. Darii VI, Bilay IM, Stoyanov AN, et al. Immunological manifestations in patients with cerebral ischemic stroke depend on the presence of hypertensive discirculatory encephalopathy. Men's health, gender and psychosomatic medicine. 2023;1:13-19.

12. Kalisvaart ACJ, Wilkinson CM, Gu S, et al. An update to the Monro–Kellie doctrine to reflect tissue compliance after severe ischemic and hemorrhagic stroke. Scientifc Reports. 2020;10:22013

13. Nikitin AS, Krylov VV, Burov S.A, et al. Dislocation syndrome in patients with severe massive ischemic stroke. S.S. Korsakov Journal of Neurology and Psychiatry. 2015;115:20-26.

14. Dzenis YuL, Sverzickis RJ, Dolgopolova JD. Dislocation syndrome and brainstem herniation (review and first experience surgical treatment for nontraumatical intracerebral haematomas in large hemispheres). Meditsinskie novosti. 2020;7:30-38.

15. Juttukonda MR, Donahue MJ. Neuroimaging of vascular reserve in patients with cerebrovascular diseases. Neuroimage. 2019;187:192-208.

16. Kuznietsov AA. Analysis of diagnostic informative value of the Full Outline of UnResponsiveness Scale in patients with spontaneous supratentorial intracerebral hemorrhage. Zaporozhye medical journal. 2019;21:33-38.

17. Agrawal P, Kushwaha V, Singh SR, et al. Role of Antiplatelet and Anticoagulant Drugs in Stroke Patient – An Overview. International Journal of Pharmaceutical Sciences Review and Research. 2024;11:65-72.

18. Dariy V, Serikov K, Kmyta O, et al. Personification of antihypertensive therapy in ischemic cerebral stroke. Georgian Medical News. 2024;4:75-79.

19. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 Guidelines for the Early Management of Patients with Acute Ischemic Stroke: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. Stroke. 2018;49:46-110.