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PATHOPHYSIOLOGICAL ANGIONEUROLOGICAL CEREBROVASCULAR CHANGES IN THE ACUTE STAGES OF ISCHEMIC STROKE

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The aim of our research *is to study pathophysiological (pathomorphological) angioneurological cerebrovascular changes in the acute phase of the rehabilitation process of patients with ischemic stroke.*

Research methods*. We used the following research methods: theoretical methods: study, processing and systematization of theoretical material; formal-logical methods: inductive, deductive ones, methods of analytical inferences; substantive-theoretical methods – methods of analysis and synthesis; empirical methods: method of observation, analysis of existing practice, conducting experimental research.*

The results of the research. *It was shown, that neurological symptoms of patients with chronic cerebrovascular diseases, as well as patients with initial manifestations of cerebral circulatory insufficiency complicated by dyscirculatory encephalopathy, occured against the background of a concomitant physiological abnormality of metabolic genesis, which led to ischemic stroke in a case of these patients, were also more pronounced than in patients without metabolic syndrome, and they were characterized by the relative “malignancy” of the onset and course of ischemic stroke.*

Conclusions. *We have proven that the implementation of a unified treatment regimen of patients with and without metabolic syndrome during three weeks of the acute phase or acute period of ischemic stroke was accompanied by a more significant, more significant regression of neurological symptoms of patients without metabolic syndrome, while in a case of patients with ischemic stroke with metabolic syndrome this process was more prolonged and less pronounced than in a case of patients without metabolic syndrome. Neurological symptoms of patients with chronic cerebrovascular diseases, as well as patients with initial manifestations of cerebral circulatory insufficiency complicated by dyscirculatory encephalopathy, occur against the background of a concomitant physiological abnormality of metabolic genesis, which led to ischemic stroke in a case of these patients, are also more pronounced than in patients without metabolic syndrome, and they are characterized by the relative "malignancy" of the onset and course of ischemic stroke.*

Key words: *ischemic stroke, physical therapy instruments, rehabilitation process, acute recovery stages, blood pressure, antihypertensive drugs, lifelong antiplatelet therapy, cardiological diseases, a deep depressive state.*

Наталія Михальчук, Євген Харченко, Едуард Івашкевич, Ернест Івашкевич, Наталія Хупавцева. Патофізіологічні ангіоневрологічні цереброваскулярні зміни при гострих змінах у пацієнтів з ішемічним інсультом

Метою нашого дослідження *є вивчення патофізіологічних (патоморфологічних) ангіоневрологічних цереброваскулярних змін при гострих змінах реабілітаційного процесу пацієнтів з ішемічним інсультом.*

Методи дослідження. *Ми використовували такі методи дослідження: теоретичні методи: вивчення, обробка та систематизація теоретичного матеріалу; формально-логічні методи: індуктивний, дедуктивний, методи формулювання аналітичних висновків; змістово-теоретичні методи – методи аналізу та синтезу; емпіричні методи: метод спостереження, аналіз існуючої практики, проведення експериментальних досліджень.*

Результати дослідження. *Було продемонстровано, що неврологічна симптоматика у хворих з хронічними цереброваскулярними захворюваннями також, як і у хворих із початковими проявами недостатності мозкового кругообігу, ускладненого дисциркуляторної енцефалопатії, протікають на тлі супутньої фізіологічної аномалії метаболічного генезу, що призвело у цих хворих до ішемічного інсульту, також є більшою мірою вираженою, ніж у пацієнтів без метаболічного синдрому, та характеризується відносною «злоякісністю» виникнення та перебігу ішемічного інсульту.*

Висновки. *Нами доведено, що впровадження єдиного режиму лікування пацієнтів з метаболічним синдромом та без нього протягом трьох тижнів гострого періоду ішемічного інсульту супроводжувалося більш значущим, вираженим регресом неврологічної симптоматики у пацієнтів без метаболічного синдрому, тоді як у випадку пацієнтів з ішемічним інсультом з метаболічним синдромом цей процес був більш тривалим та меншою мірою вираженим, ніж у випадку пацієнтів без метаболічного синдрому. Неврологічна симптоматика у пацієнтів із хронічними цереброваскулярними захворюваннями, а також у пацієнтів з початковими проявами недостатності мозкового кровообігу, ускладненої дисциркуляторною енцефалопатією, виникає на тлі супутньої фізіологічної аномалії метаболічного генезу, яка призвела до ішемічного інсульту у цих пацієнтів, і також є більшою мірою вираженою, ніж у пацієнтів без метаболічного синдрому, та характеризується відносною «злоякісністю» початку та перебігу ішемічного інсульту.*

Ключові слова: *ішемічний інсульт, інструменти фізіотерапії, процес реабілітації, гострі стадії відновлення, артеріальний тиск, антигіпертензивні препарати, довічна антитромбоцитарна терапія, кардіологічні захворювання, глибокий депресивний стан.*

Introduction. Stroke (from the Latin Insulto – I jump, leap) is a kind of cerebral stroke. Stroke is a group of diseases caused by acute vascular pathology of the person's brain, characterized by sudden disappearance or impairment of brain functions, lasting more than 12-24 hours or even leading to the death of the patient. When the first signs of stroke appear, the first minutes and hours of the disease are most important, because it is during this period of time that medical care can be the most effective [1; 8]. One of the most important problems of Modern Neurology is the diagnosis and treatment of cerebral stroke, which is due to their wide prevalence and high mortality rate. About 88% of those patients who survived a cerebral stroke become disabled, some of these people need constant care from relatives of working age, so this problem is not only and not so much medical, but it is also socio-economic one. Achieving the necessary level of self-care of the patient, his/her social, psychological and motor adaptation in the post-stroke period, restoration of working capacity are the main goals of physical rehabilitation, which determine the choice by the specialist of rehabilitation of the features of use of physical therapy for ischemic stroke in the acute recovery stage of rehabilitation [3].

Restoration of impaired neurological functions in the process of physical rehabilitation of patients, features of the use of physical therapy in ischemic stroke in the acute recovery stage of rehabilitation depends on the timing of the start of physical therapy and its duration. The level of true, or more correctly, full recovery, when the impaired function due to ischemic stroke returns to its original state, is possible only in the specific case when there is no complete death of nerve endings, nerve cells and nerve formations in the human brain, and the pathological focus

of the nerves consists mainly of inactivated elements (due to edema, hypoxia, changes in the conduction of nerve impulses). Thus, physical rehabilitation in the acute period of ischemic stroke is a necessary and pathogenetically justified process. So, the problem of use of physical therapy instruments in the acute recovery stages of rehabilitation of patients is quite actual [2].

The object of our research: the use of different ways of restoration of impaired neurological functions in the process of acute recovery stages of patients with ischemic stroke.

The aim of our research is to study pathophysiological (pathomorphological) angioneurological cerebrovascular changes in the acute phase of the rehabilitation process of patients with ischemic stroke.

Methods of the research

To write the research, we used the following research methods:

– *theoretical methods*: study, processing and systematization of theoretical material; formal-logical methods: inductive, deductive ones, methods of analytical inferences; substantive-theoretical methods – methods of analysis and synthesis;

– *empirical methods*: method of observation, analysis of existing practice, conducting experimental research.

In this, the second section of our article, we will describe the features of the treatment of ischemic stroke of patients in the clinic, which we did during our internship in November-December 2025, while practicing in the neurological department of the Rivne City Hospital. We treated 5 patients who were admitted to this department with a diagnosis of "acute ischemic stroke". In our research there were participated such patients (2 men and 3 women) were 55–65 years old.

These 5 patients were included into the experimental group E1. We also selected 5 patients with ischemic stroke who were treated in the same hospital to the control group C1. We did not conduct our research with these patients, did not implement physical rehabilitation measures planned according to our experimental method.

Results and their discussion

Etiology of ischemic stroke: ischemic stroke most often occurs as a result of significant atherosclerotic damage to the main vessels, often against the background of arterial hypertension and diabetes mellitus. Less often, the cause of ischemic stroke is rheumatism, vasculitis of other etiology (nodular periarteritis, Takayasu disease, etc.). Mental and physical overstrain play a provocative role. Mortality in a case of ischemic stroke is 40–50% [5].

Pathogenesis of ischemic stroke: the circulatory system in the human body has, as it is known, three basic components: the heart (a kind of pump in a human body), which ensures the rhythmic supply of blood to the vessels, the vessels themselves and the blood. Disruption of the functioning of each or at least one of these components can cause ischemic disorders of cerebral circulation [6].

Leading among these ischemic disorders of cerebral circulation are: atherosclerotic vascular damage, which is significantly complicated by spasm and thrombosis, disorders of the rheological properties of blood and disorders of its microcirculation, changes in systemic hemodynamics. All these disorders are caused by heart pathology [7]. That is, ischemic stroke can be developed as a result of blockage of a vessel by a thrombus or embolus (in 60% of cases) or vascular cerebral insufficiency, which occurs in the basin of a stenosed cerebral vessel and is aggravated as a result of disorders of systemic hemodynamics [4].

At the same time, atherosclerotic plaques that form on the walls of the vessels of the brain of a sick person are much more often determined by the main vessels of the skull. In this case, the source of cerebral embolism is often the products of the decay of atherosclerotic plaques and platelet aggregates [9]. About 20-25% of embolisms are of cardiogenic etiology (endocarditis, heart defects, myocardial infarctions, atrial fibrillation). In the case of operations on the heart, the vessels of the skull, the so-called air embolism occurs. Gas embolism also occurs during decompression. Fat embolism also occurs in the case of fractures of the tubular bones.

According to clinical and angiographic studies, scientists have described ischemia caused by retrograde blood flow due to the so-called cerebral vascular theft syndrome:

1. Carotid-carotid ischemia, which implies blood flow through the anterior communicating artery from an unaffected artery or vessel.

2. Vascular theft syndrome under conditions of occlusion of the common carotid artery due to a sharp decrease in pressure in the external carotid artery, the so-called "siphon" effect.

3. Carotid-vertebral ischemia.

4. Vertebral-carotid ischemia.

5. Cerebral vascular theft syndrome due to cortical anastomoses [10].

As for cerebral vasospasm, to date there has been no convincing empirical evidence that such cerebral vasospasm can lead to cerebral ischemia. The excep-

tion is ischemia in the setting of subarachnoid hemorrhage.

Studying the personal data of patients recorded in their medical history who were admitted to the Rivne City Hospital with a diagnosis of "acute ischemic stroke", we came to the conclusion that the extreme urgency of the increase in cerebrovascular morbidity, in particular the occurrence of ischemic strokes, necessitates the development and implementation of effective methods of prevention and treatment of this group of diseases, in particular the prevention and prophylaxis of ischemic stroke of the brain. In general, if we analyze the current state of angioneurology, it should be noted that it is characterized by a significant "rejuvenation" of the main causes of cerebrovascular diseases, which often lead to ischemic stroke: arterial hypertension and atherosclerosis of cerebral vessels. Chronic, constant psycho-emotional stress, eating disorders and a chaotic, carefree lifestyle, as well as largely unfavorable environmental factors often contribute to the development of metabolic syndrome and, in turn, lead to the occurrence of ischemic stroke.

Thus, the combination of various physiological abnormalities of metabolic origin increases the risk of developing vascular diseases. Currently, the prevalence of metabolic syndrome in the general population of Ukraine is from 30 to 45%, and in the next 30 years an increase in the rate of growth of the incidence of ischemic stroke and a shift towards its significant increase in a case of young people (we mean people under 40-45 years old) is expected. Provoked and/or enhanced physiological abnormalities of metabolic origin, in particular morphological and functional changes in cerebral vessels, changes in heart vessels, blood vessels contribute to the development of ischemia manifestations, including an increase in the risk of ischemic stroke among the population of Ukraine by 3-4 times.

Studying the personal data of patients recorded in the medical history of patients who were admitted to the Rivne City Hospital with a diagnosis of "acute ischemic stroke", we came to the conclusion that there is a direct dependence of the physiological abnormality of metabolic genesis on the ischemic stroke that occurred: in a case of people with 1-3 components of physiological abnormalities of metabolic genesis, new episodes of manifestations of cardiovascular diseases are noted in 22,3% after 4-5 years of observation, and in a case of people with 4 or more components – in 44,6% of cases during the same observation period. Moreover, cases of the development of cerebral pathology, occurrence of ischemic stroke of the brain prevail 3-6 times over cases of manifestation of cardiac pathology, which leads to myocardial infarction.

In a case of all five patients, we observed them in the hospital, who were admitted to the hospital with a diagnosis of "acute ischemic stroke", the presence of physiological abnormalities of metabolic genesis with their classic pathobiochemistry hyperlipidemia, hyperglycemia and in a case of one patient it is accompanied by insulin resistance was observed. All these signs contributed to the disruption of metabolism in the vascular wall, including the transport of lipoproteins in it. Excessive intake of already oxidized, active forms of low and very low density lipoproteins, their accessibility to the subendothelial layer does not allow to fully, in general, achieve even at least a positive effect for their utilization and neutralization by tissue macrophages. This, in turn, led to the gradual transformation of the latter into foam cells with simultaneous hyperproduction of a number of biologically active substances (interleukins, cytokines, growth factors, etc.), which would contribute to the development of an inflammatory reaction in the subendothelial layer of the cerebral vessels.

Further stages of the metabolic cascade with their migration to the area of inflammation of lymphocytes, neutrophils, mast cells will contribute to the progress of endotheliopathy and the growth of atherosclerotic plaque in the vessels of the brain. In addition, metabolic changes will largely contribute to the destabilization of existing atherosclerotic plaques in the vessels of the brain, their rather rapid transition from the "asymptomatic" course of atherosclerotic damage to the arteries of the brain to a symptomatic, with clinical manifestations, acute cerebral circulation disorder, which, in turn, led to ischemic stroke in a case of these patients.

During the analysis of an early marker of the development of atherosclerotic plaque in the vessels of the brain in patients with acute and chronic ischemic strokes complicated by cerebrovascular diseases, with clinical manifestations of acute cerebral circulation disorders. Thus, in patients with ischemic stroke on the background of cerebrovascular diseases, with clinical manifestations of acute cerebral circulation disorders, the value of this indicator was higher than in a case of such a patient without cerebrovascular diseases, with clinical manifestations of acute cerebral circulation disorders (τ=0,5313, ρ<0,05), and directly correlated with the age of patients (τ=0,5651, ρ<0,05), the level of triglycerides (τ=0,5217, ρ<0,05) and glucose (τ=0,5564, ρ<0,05) in the blood serum.

At the same time, the very fact of the implementation of an acute cerebral episode (meaning not only a

stroke, but also clinical manifestations of acute cerebral circulation disorders) also influenced the occurrence of ischemic stroke. Under conditions of acutely increasing brain ischemia associated with dyscirculatory encephalopathy, and in a case of people with ischemic stroke and clinical manifestations, acute cerebral circulation disorders. Thus, increasing brain ischemia associated with dyscirculatory encephalopathy, and in a case of people with ischemic stroke and clinical manifestations, it is an acute cerebral circulation disorder, under which conditions not only its values are higher, but also more cases with the worst values of the intima-media complex.

Morphological study of biopsies of atherosclerotic plaque in the cerebral vessels of the carotid sinus revealed that under conditions of ischemic stroke in a case of patients with cerebrovascular diseases, with clinical manifestations of acute cerebral circulation disorders, regardless of the degree of stenosis, heterogeneous heterogeneous (unstable) atherosclerotic plaques are more often observed, which are more prone to rupture with the development of distal embolism in the cerebral vessels, fibrosis with calcification in the middle layer of the cerebral arteries.

During the study of the relationships between inflammatory markers and progression of atherosclerotic plaque in cerebral vessels, an increase in the content of lipoprotein-associated phospholipase A2 (LP-PLA2) was found in a case of individuals with cerebrovascular diseases on the background of metabolic syndrome compared to its content in patients without concomitant metabolic syndrome: 328 (280; 362) and 305 (251; 359) ng/ml, respectively. Moreover, the former more often had heterogeneity of the structure of atherosclerotic plaque in cerebral vessels with a hypoechoic component, which correlated with an increased content of lipoprotein-associated phospholipase A2 in blood serum (τ=0,6401, ρ<0,05).

In a case of patients with neointimal hyperplasia and restenosis, which more often develop against the background of concomitant metabolic syndrome, a significant increase in the level of lipoprotein-associated phospholipase A2 (375,76±52,3 and 212±51,6 ng/ml; ρ=0,05) and atherosclerotic plaque factor in cerebral vessels (84,13±15,2 and 44,03±14,5 ng/ml; ρ=0,05) was also found in a case of patients with progression of vascular pathology, physiological abnormality of metabolic genesis from ischemic stroke and without metabolic syndrome, respectively. Metabolic disorders have a negative impact on micro- and macrorheological properties of blood, which are of decisive importance in the occurrence, progression and prognosis of cerebrovascular diseases. Various components of the concomitant metabolic syndrome lead to discoordination of the coagulation, anticoagulation, and fibrinolytic properties of the blood. The study found disturbances in all links of the blood coagulation process – from adhesion and aggregation of platelets and erythrocytes to coagulation and fibrinolysis in all patients with concomitant metabolic syndrome (see Table 1).

Assessment of the latent capabilities of the endothelium using a functional “cuff” test revealed a more pronounced dysfunction of the athrombogenic activity of the vascular wall in patients with metabolic syndrome, and the gradual depletion of the antiaggregatory, anticoagulant, procoagulant and fibrinolytic vascular capabilities of the wall is noted in the presence of all cerebrovascular diseases, as well as in the absence of an acute episode, which we consider to be ischemic stroke.A study of the vascular and motor function of the endothelium in the case of an ultrasound “cuff” test, which in healthy people leads to an increase in the diameter of the brachial artery by 10-11% or more, in patients with ischemic stroke with metabolic syndrome revealed a significant decrease in endothelial function in the form of changes in the artery by only 7,7% in the case of chronic cerebrovascular diseases and by 5,0% in a case of patients with acute cerebrovascular diseases.

In the case of detailing the structural distribution of patients with ischemic stroke as a result of the increase of symptoms of cerebrovascular diseases, a decrease in the number of patients with a normal adequate response to the empirical, clinical studies conducted by us was noted, and the presence of metabolic syndrome significantly influenced this stage of actualization of endothelial function. The above-mentioned changes in the blood and vascular wall may be the basis for the development of clinical manifestations of cerebrovascular diseases. Assessment of the expression of neurological symptoms on various scales indicates that in the presence of concomitant metabolic syndrome the initial neurological deficit is more pronounced than before clinical studies.

A significant difference in the parameters evaluated in the research was diagnosed in a case of patients with ischemic stroke according to the parameters:

– «platelet aggregation» in a case of patients with metabolic syndrome (43,24%) and patients with ischemic stroke without metabolic syndrome (61,07%), τ=0,7109, ρ<0,01;

– «amplitude of erythrocyte aggregation» in a case of patients with metabolic syndrome (14,1 conventional units) and patients with ischemic stroke without metabolic syndrome (9,7 conventional units), τ=0,5005, ρ<0,05;

Table 1

Basic parameters of hemorheology and hemostasisof patients of group E1 with ischemic changes in a case of cerebral vessels and with cerebrovascular diseases (a confirmatory study)

Parameter evaluated in the research	Ischemic stroke of patients with metabolic syndrome	Patients with ischemic stroke without metabolic syndrome	Patients with chronic cerebrovascular diseases with metabolic syndrome	Patients with chronic cerebrovascular diseases without metabolic syndrome
Platelet aggregation, in %	43,24*	61,07* (τ=0,7109, ρ<0,01)	43,54	45,24
Amplitude of erythrocyte aggregation, conventional units	14,1**	9,7** (τ=0,5005, ρ<0,05)	7,7	7,1
Speed of complete disaggregation, s	175*	132* (τ=0,6919, ρ<0,01)	102	104
Erythrocyte deformity, DImax	0,45	0,49	0,46	0,51
Hematocrit, in %	49,04	47,51	43,03	42,10
Fibrinogen, g/l	4,53*	3,01* (τ=0,6512, ρ<0,01)	3,75	3,04
Fibrinolytic activity, in %	8,77**	13,10** (τ=0,5312, ρ<0,05)	14,34	14,76
Antithrombin III, in %	97,40	94,02	93,17	93,10
Antigen, in %	96,12	91,15	93,73**	72,42** (τ=0,5733, ρ<0,05)

Legends:

* – the difference in results between groups of respondents with and without metabolic syndrome is statistically significant, the level of confidence is ρ<0,01;

** – the difference in results between groups of respondents with and without metabolic syndrome is statistically significant, the level of confidence is ρ<0,05.

– «speed of complete disaggregation» in a case of patients with metabolic syndrome (175 s) and patients with ischemic stroke without metabolic syndrome (132 s), τ=0,6919, ρ<0,01;

– «fibrinogen» in a case of patients with metabolic syndrome (4,53 g/l) and patients with ischemic stroke without metabolic syndrome (3,01 g/l), τ=0,6512, ρ<0,01;

– «fibrinolytic activity» in a case of patients with metabolic syndrome (8,77%) and patients with ischemic stroke without metabolic syndrome (13,10%), τ=0,5312, ρ<0,05.

If we compare the group of patients with chronic cerebrovascular diseases with metabolic syndrome and patients with chronic cerebrovascular diseases without metabolic syndrome, we see that only one significant correlation was diagnosed for the “antigen” indicator (93,73% and 72,42%, τ=0,5733, ρ<0,05).

Conclusions. In the course of our clinical empirical study, we have proven that the implementation of a unified treatment regimen of patients with and without metabolic syndrome during three weeks of the acute phase or acute period of ischemic stroke was accompanied by a more significant, more significant regression of neurological symptoms of patients without metabolic syndrome, while in a case of patients with ischemic stroke with metabolic syndrome this process was more prolonged and less pronounced than in a case of patients without metabolic syndrome. Neurological symptoms of patients with chronic cerebrovascular diseases, as well as patients with initial manifestations of cerebral circulatory insufficiency complicated by dyscirculatory encephalopathy, occur against the background of a concomitant physiological abnormality of metabolic genesis, which led to ischemic stroke in a case of these patients, are also more pronounced than in patients without metabolic syndrome, and they are characterized by the relative “malignancy” of the onset and course of ischemic stroke.

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