AJPMHS GLOBAL RESEARCH NETWORK

AMERICAN Journal of Pediatric Medicine and Health Sciences
Volume 2, Issue 5, 2024 ISSN (E): 2993-2149

Pathogenetic Factors and Mechanisms of Development of Acute Ischemic Type Cerebral Circulation in Young People

Kim O. A.
Samarkand State Medical University, Uzbekistan

Abstract: The article analyzes the literature sources covering the results of the study of causative factors and pathogenetic mechanisms of the development of ischemic stroke in young people. Cerebral factors, the influence of homocysteine and neurotrophins on the course, clinical manifestations and outcome of the disease were studied. Knowledge of all macro- and microstructural cerebral factors will make it possible to determine the criteria for choosing the most optimal treatment, prevent the development of possible complications, and develop an algorithm for rehabilitation measures.

Keywords: ischemic stroke, young age, cerebral factors, homocysteine, neurotrophins.

Currently, determining the role of macro- and microstructural cerebral factors, among which a special place is given to hypoperfusion, is becoming of great importance in the study of the development and course of ischemic stroke. A complete understanding of this problem is given to us by studying the brain when conducting neuroimaging research methods, as evidenced by numerous studies [1,2].

There is a concept of “neuroimaging phenomenon”, consisting of such neuroimaging indicators as acute lacunar infarctions, lacunar lesions, white matter hyperintensity, expansion of perivascular spaces and the presence of hemorrhagic components, which are microstructural markers of ischemic brain damage. [2,3].

The size and localization of the ischemic focus are considered as macrostructural indicators. Thus, according to a number of authors, in approximately 50% of all registered cases of acute ischemic stroke, the focus of the infarction is located in the parietal lobe, in 20% - in the occipital lobe, in 10-15% - in the temporal lobe, in 5-10% - in the trunk , in 7% - the frontal lobe, 3% - in the cerebellum [4,5,6]. At the same time, the frequency of damage to the left and right hemispheres does not have significant differences, but differs by age and gender [5,6]. When studying lesions of the vascular area, most often the focus of ischemia was located in the area of the middle cerebral artery.

Also of great importance are biochemical markers of cerebral circulation and hemostasis, in particular the antioxidant system, which results in endothelial dysfunction and endogenous intoxication. The endothelium, being in constant contact with blood, continuously receives “information” about the state of blood flow, tissue metabolism, changes in the living conditions of cells, transforming it into “response” signals [7,8]. But, unfortunately, the functional state of the vascular endothelium in this pathology has been little studied.

The discovery of the successive stages of ischemic brain damage led to a deepening of ideas about the complexity, dynamism, interconnection and cascade nature of the biochemical reactions underlying it [2,9].

As is known, the degree of damaging effect of ischemia is determined, first of all, by the depth and duration of the decrease in cerebral blood flow. According to various studies, the formation of most of the heart attack ends within 3-6 hours from the moment the first symptoms appear [1,3,10]. In response to ischemic damage to brain tissue, polymorphonuclear leukocytes begin to adhere to the vascular endothelium, and local inflammation develops, causing obstruction of small vessels. The anticoagulant surface of the vascular endothelium is transformed into a procoagulant one. The fibrinolytic activity of the blood is inhibited, the zone of the infarct core expands, and new areas of ischemic penumbra are formed. At the same time, free radical oxidation and acidosis aggravate disturbances in the mechanisms of autoregulation of cerebral circulation, which leads to the development of reactive hyperemia in the ischemic penumbra and the formation of vasogenic cerebral edema.. Activation of lipid peroxidation (LPO) and NO synthesis with depletion of the endogenous antioxidant defense system leads to the development of oxidative stress [1,4,7].

Oxidative stress is accompanied by various biochemical disorders and is an important cause of the progression of atherosclerosis, hypertension, diabetes and other diseases. Oxidative stress causes a variety of damage to the structural components of the cell: lipids, proteins and nucleic acids. Free radicals initiate reactions of proteins with other cell components, causing fragmentation of protein molecules and disruption of their functions [1,3,10,11].

Oxidative stress is a universal response of the body to pathological processes, and its severity largely determines the course and outcome of diseases. Studies aimed at identifying markers of oxidative stress in ischemic stroke indicate a direct connection between the presence of oxidized metabolites in the blood and worsening prognosis in various subtypes of IS, as well as the high diagnostic significance of such markers [11,12].

One of these markers is homocysteine, which was first described in 1932 by chemists Butz и Vigneaud as a sulfur-containing amino acid obtained by demythelation of methionine. Normally, the content of homocysteine in the blood, according to various authors, is up to 6-7 μmol/l in women and up to 10 μmol/l in men. Homocysteine levels depend on the processes of remethylation and transsulfuration. The condition for the normal functioning of these processes in the body is a sufficient content of B vitamins and folic acid, which play an important role in these reactions. In case of insufficient intake of B1, B6, B12 and folic acid from food, or with genetically determined defects in enzymes, hyperhomocysteinemia is observed. With an increase in the content of homocysteine in the blood, damage to the tissue structure of the arteries occurs and the release of inflammatory mediators, which leads to endothelial dysfunction, deposition of calcium and cholesterol on the vascular wall, oxidation of low-density lipoproteins with the subsequent formation of atherosclerotic plaques and the development of oxidative stress in endothelial cells, there is a modification of blood coagulation factor V with a subsequent decrease and complete loss of sensitivity to the action of C-protein and, as a consequence, an increase in the coagulation properties of blood [9,10,11].

When analyzing the literature of Kameneva N.N. and Kutashov V.A found that moderate hyperhomocysteinemia is found in 42% of patients with cerebrovascular disorders under the age of 50 years, while in men aged 40-50 years the risk of stroke increases 4.1 times. And severe hyperhomocysteinemia is the cause of more than half of all cases of ischemic stroke in people under 30 years of age [7,10,11].

In turn, Tao Zhang et al. conducted a meta-analysis of 13 studies of 3114 patients and established in 2243 cases the relationship between the pathogenetic subtypes of ischemic stroke and elevated levels of homocysteine in the blood, as well as the connection between homocysteine and the course, severity and prognosis of the disease [12].

At the same time, stimulation of neurotrophic processes occurs. Neurotrophicity is a natural reaction manifested by proliferation, migration, differentiation and survival of cells and characterized by regeneration processes. In these neurotrophic processes, the main role is played

by neurotrophins, which are regulatory proteins of nervous tissue. Neurotrophins determine the plasticity of neuronal tissue and form mechanisms involved in the restoration of impaired neurological functions, being a powerful stimulator of neurogenesis [12,13].

Currently, the greatest interest among all neurotrophins for us is brain-derived neurotrophic factor (BDNF), which is a key mediator of the survival and recovery of neurons. BDNF was first described in 1987 after it was isolated from a brain extract as a factor that supports neurons that are not sensitive to nerve growth factor. BDNF is a protein synthesized in the endoplasmic reticulum as the 32–35 kDa pro-BDNF precursor protein (pro-BDNF), which is edited in the Golgi complex to form biologically active mature BDNF (mBDNF) with a molecular weight of 13 kDa. As is known from numerous literature sources, mature BDNF innervates the tropomyosin tyrosine kinase B receptor (TrkB), which triggers phosphorylation cascades and leads to protein synthesis, axonal growth, dendritic maturation and increased synaptic plasticity [13,14]. BDNF also plays an important role in processes such as protection during acute ischemic injury, stimulation of angiogenesis, neurogenesis, and improvement of repair mechanisms in brain tissue. We should not forget about the participation of BDNF in the processes of learning and memory, the growth and differentiation of new neurons and synapses.

With a decrease in the concentration of circulating BDNF, the development of stroke increases, and a decrease in the level of serum BDNF in the acute period of ischemic stroke is considered a factor of poor prognosis, which is confirmed by studies by Stanne et al. (2016) [15,16].

Some literature sources provide information about the role of gene polymorphism in the prognostic significance of BDNF, namely, the rs6265 or Val66Met mutation, which affects the translation of BDNF mRNA, leading to a decrease in the production and secretion of BDNF in neurons of the central nervous system, which, in turn, causes deterioration of neuronal plasticity and may have a negative impact on the recovery of brain function after stroke [13,17,18].

There is a clear relationship between the level of BDNF concentration and the development of acute ischemic stroke. Therefore, BDNF has not only diagnostic but also prognostic value. Patients with the lowest BDNF values have an increased risk of unfavorable outcome of ischemic stroke and a low level of rehabilitation potential, while increased levels of this marker in the brain contribute to the restoration of lost functions.

Thus, knowledge of all macro- and microstructural cerebral factors will make it possible to determine the criteria for choosing the most optimal treatment, prevent the development of possible complications, and develop an algorithm for rehabilitation measures.

1. Anatolevna K. I. M. O. Clinical and neurological features of ischemic stroke in young with alcohol dependence //Journal of biomedicine and practice. – 2023. – Т. 8. – №. 2.
2. Farkhadovna M. Z. et al. Optimization Of Organization and Conducting of Telerehabilitation of Patients After Stroke //Rivista Italiana di Filosofia Analitica Junior. – 2023. – Т. 14. – №. 2. – С. 653-656.
3. Di Sarsina P.R. Traditional, complementary and alternative medical systems and their contribution to personalisation, prediction and prevention in medicine—person-centred medicine /Alivia M.,Guadagni P. // EPMA J.– 2012. – V.3, №1. – P. 15.
4. Anatolievna K. O. Анализ макро-и микросктруктурных показателей головного мозга больных с ишемическим инсультом на фоне алкогольной зависимости //journal of biomedicine and practice. – 2024. – Т. 9. – №. 1.
5. Donahue M.J. Novel MRI approaches for assessing cerebral hemodynamics in ischemic cerebrovascular disease /Strother M.K., Hendrikse J. // Stroke. – 2012. – V.43, №3. – P. 903-915

6. León Cejas L, Mazziotti J, Zinnerman A, Nofal P, Fernández Pardal M, Bonardo P, Reisin R.Misdiagnosis of acute ischemic stroke in young patients.Medicina (B Aires). 2019;79(2):90-94.
7. Каменева Н.Н., Куташов В.А. Роль гомоцистеина в развитии ишемических инсультов у лиц молодого возраста. //Центральный научный вестник. 2016. Т. 1. № 5 (5). С. 5-6.
8. Pan Y, Zhang H, Yang J, Guo J, Yang Z, Wang J, Song G. Identification and Diagnosis of Cerebral Stroke through Deep Convolutional Neural Network-Based Multimodal MRI Images. Contrast Media Mol Imaging. 2021 Jul 20;2021:7598613 Pan Y, Zhang H, Yang J, Guo J, Yang Z, Wang J, Song G. Identification and Diagnosis of Cerebral Stroke through Deep Convolutional Neural Network-Based Multimodal MRI Images. Contrast Media Mol Imaging.
9. Naess H. et al. C-reactive protein and homocysteine predict long-term mortality in young ischemic stroke patients //Journal of Stroke and Cerebrovascular Diseases. – 2013. – Т. 22. – №. 8. – С. 435-440.
10. Mihai D. et al. Ischemic Stroke in Young Adults: Practical Diagnosis Guide //Ischemic Stroke. – IntechOpen, 2020. – С. 17.
11. Kilmer S. McCully. Chemical Pathology of Homocysteine. IV. Excitotoxicity, Oxidative Stress, Endothelial Dysfunction, and Inflammation / Kilmer S. McCully // Ann Clin. Lab. Sci. — 2009. — Vol. 39, № 3. — P. 219-232
12. Kristensen B. et al. Epidemiology and etiology of ischemic stroke in young adults aged 18 to 44 years in northern Sweden //Stroke. – 1997. – Т. 28. – №. 9. – С. 1702-1709.
13. M'barek L. et al. MTHFR (C677T, A1298C), FV Leiden polymorphisms, and the prothrombin G20210A mutation in arterial ischemic stroke among young tunisian adults //Metabolic Brain Disease. – 2021. – Т. 36. – №. 3. – С. 421-428.
14. Lopaciuk S. et al. Polymorphisms in the factor VII gene and ischemic stroke in young adults //Blood coagulation & fibrinolysis. – 2010. – Т. 21. – №. 5. – С. 442-447.
15. Larrue V. et al. Etiologic investigation of ischemic stroke in young adults //Neurology. – 2011. – Т. 76. – №. 23. – С. 1983-1988.
16. Anatolevna K. O. Relationship of the ischemic stroke risk in young age with the concentration of brain neurotrophic factor //Journal of Modern Educational Achievements. – 2023. – Т. 8. – №. 8. – С. 2-8.
17. Lasek-Bal A. et al. Low concentration of BDNF in the acute phase of ischemic stroke as a factor in poor prognosis in terms of functional status of patients //Medical science monitor: international medical journal of experimental and clinical research. – 2015. – Т. 21. – С. 3900.
18. Anatolevna K. I. M. O. Значение bdnf в развитии ишемического инсульта у лиц молодого возраста //journal of biomedicine and practice. – 2024. – Т. 9. – №. 1.