
MODERN IDEAS ABOUT THE PATHOGENESIS OF CEREBRAL ISCHEMIA

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ABSTRACT: - The high mortality and disability of patients with vascular diseases of the brain makes research devoted to this problem particularly relevant (1,3). Patients with vascular diseases of the brain account for up to 20% of all patients with pathology of the nervous system. Of these, 23% are cerebral stroke. Persistent disability due to stroke is 3.2 per 10,000 population, 20.2% of previously employed patients return to work. High rates of disability among working age people give the problem of stroke a social character (2,5,6).

KEY WORDS: - Pathophysiological disorders, glutamate, aspartate, ischemic penumbra, aminacidergic neurotransmitters.

INTRODUCTION

It is known that the cause of stroke can be diseases of the cardiovascular system, kidneys, hematopoietic system, etc. in this regard, strokes can be classified as multidisciplinary problems, i.e. studied at the intersection of several medical sciences. The pathogenesis of ischemic stroke is based on a complex pathobiochemical process, including a cascade of pathophysiological disorders, both in the focal zone and in the surrounding zone of hypoxic-ischemic disorders - the "penumbra". The size of the penumbra depends on many factors: the severity of the development of the process, the state of the collateral bed, the underlying disease that led to the development of acute ischemia, etc., and the volume of the penumbra itself largely determines the degree of neurological defect and the time of the rehabilitation period (2,8).

THE MAIN FINDINGS AND RESULTS

In the early 80s of the XX century. the concept of ischemic penumbra (penumbra) was formed, i.e. brain tissue (in and around the central zone of a severely ischemic area of the brain and non-excitabile but viable cells, based on the concept of threshold ischemic blood flow. When blood flow levels decrease below 55 ml/100 g/min, protein synthesis is primarily inhibited, but neuronal function is still preserved This is followed by stimulation of anaerobic glycolysis (at 35 ml/100 g/min), release of certain neurotransmitters (glutamate, aspartate), disruption of energy metabolism. When cerebral blood flow approaches 20 ml/100 g/min, the oxygen extraction fraction becomes maximum and this degree of ischemia is considered the upper threshold of ischemia, i.e. the threshold for the loss of electrical function of a neuron with preservation of their membrane potential. A further decrease in cerebral blood flow (less than 15 ml/100g/min) causes

the disappearance of the evoked potential, i.e. anoxic depolarization, but the structural organization of cells is preserved.(2,6,9) The critical threshold of cerebral circulation for the development of irreversible cell damage is 10 ml/100 g/min. At this stage, the lack of oxygen stops metabolism in mitochondria and activates the anaerobic pathway for the breakdown of glucose, causing a decrease in pH due to the accumulation of pyruvate, lactate and the development of acidosis. The energy-dependent functions of membranes are disrupted, as a result of which K⁻ ions leave the cell, and Ca²⁺, Na⁺ and water ions enter the cell, causing cytotoxicity. This degree of ischemia represents the threshold for loss of cellular ion homeostasis (ie, membrane failure). These thresholds indicate the upper and lower limits of blood flow in the ischemic penumbra.

Neuronal damage in acute ischemic stroke is provoked by cytotoxic free radicals. One of these aggressive radicals is the NO radical, which promotes neurochemical damage to cells in the area of the ischemic focus. An important role in the development of ischemic brain damage has been established for excitotoxicity (from the English *excite* - to excite), caused by an imbalance between excitatory and inhibitory neurotransmitter systems (2,6,9). The channels that conduct incoming calcium current when exposed to neurotransmitters include glutamate (N-methyl-D-aspartate) activated NMDA receptors. It is this type of glutamate receptor that is known to predominate in the central nervous system (CNS) of vertebrates. NMDA receptors not only control the transmission of excitatory nerve impulses from cell to cell, but are also responsible for profound changes in the structure and properties of synapses. It is known that under normal conditions there is a stable balance between the activity of the glutamatergic and GABAergic neurotransmitter systems. The separation in the dynamics of changes in the level of excitatory and inhibitory aminacidergic neurotransmitters revealed in acute ischemic stroke indicates that not only the phenomenon of “excitotoxicity” takes part in the development of acute cerebral ischemia, but also the formation of an imbalance between excitatory and inhibitory mechanisms with signs of insufficiency of protective inhibition in the first stroke hours (2.4). These data are consistent with experimental data on a decrease in intracellular glutamate concentration with increasing global and focal cerebral ischemia.

CONCLUSION

The gray and white matter of the brain are highly sensitive to hypoxic-ischemic injury, and NMDA receptor antagonists play a critical role in protecting them from injury, which represents degeneration of not only the cerebral cortex, but also the white matter structures of the myelin and axon. The degree of imbalance between excitatory and inhibitory neurotransmitter systems, assessed by the level of corresponding amino acids in the cerebrospinal fluid, largely determines the severity of the clinical manifestations of ischemic stroke and the possibility of the recovery process.

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