# Glycine importance in acute ischemic stroke therapy

*Yaroslav R., Nartsissov, Elena V. Sheshegova, Elena V.Mashkovtseva, Lyudmila N.Maksimova*
*Institute of Cytochemistry and Molecular Pharmacology*
"Neurological Herold", 2015 — T. XLVII, # 1, УДК: 616.831—005.1—08:615.035.1

**Abstract**

There was shown the prevalence of vascular diseases, including acute cerebrovascular events, reasons of such disorders being multiple systemic changes of neuron metabolism. The correction of imbalance of excitatory and inhibitory neurotransmitter systems is one of the most promising methods of neuroprotection. Much attention is paid to the role of an inhibitory neurotransmitter glycine in the mechanisms of acute cerebral ischemia. Positive effects of glycine on neuronal mitochondrial metabolism have been observed under hypoxic (anoxic) conditions. It was also shown a reduction of events which had been induced by glutamate concentration excess. Along with the effect of direct vasodilation of glycine on arterioles of different tissues it enables to consider glycine as a neuroprotective compound i.e. the medicines which protect against ischemic cascade in therapeutic window.

**Key words:** metabolic therapy, glycine, ischemic stroke.

This is a review of main effects of glycine on the ischemia and its use in the treatment of ischemic stroke.

The problem of early diagnosis and treatment of cerebral strokes is one of the most important in modern medicine [3, 6, 17]. Current therapy for acute ischemic stroke is limited to thrombolysis with plasminogen activators and mechanical recanalization [25].

In the article authors describe development of views on the pathogenesis of stroke and approaches to its therapy. In the 60's there was an opinion that a stroke develops immediately and irreversibly. Now it is known that 80% of changes in the affected area are formed within about 3-6 hours - the so-called therapeutic window [8].

At the molecular and cellular levels, three main pathogenetic mechanisms of stroke can be highlighted – excitotoxicity, oxidative stress, and inflammation [37]. In the first hours, the main mechanism of brain damage is cell necrosis due to an acute energy deficit (deficit of ATP in cells), which triggers the glutamate-calcium cascade of reactions [7, 13, 20, 24, 29, 34]. At the same time, a large number of excitatory neurotransmitters — glutamate and aspartate — are released into the intercellular space [22, 23]. This means that not only excitotoxicity takes place at this time, but also an imbalance is formed between inhibitory and excitatory neurotransmitters with inadequate protective inhibition [8, 18]. Moreover, in animal experiments, impaired glycine metabolism correlates with the formation and size of the ischemic zone [28]. Levels of other amino acids (not neurotransmitters) do not change during ischemia.

Thus, a promising area for the search of effective therapy for ischemic stroke is the correction of levels of neurotransmitters, as well as the protection of cells from low levels of ATP and, as a result, energy deficiency.

One of the directions of this search is the possibility of using glycine for treatment of ischemia [8, 12, 21]. Glycine, firstly, is an important inhibitory neurotransmitter, and secondly, it can bind to the NMDA receptors of excitatory neurotransmitters. Studies have shown the ability of glycine to protect tissues during hypoxia, intoxication or reperfusion [41], and also the effect of glycine on increasing the lifespan of neurons in the cerebral cortex [40].

The anti-ischemic effect of glycine can be associated with improved microcirculation in the brain [31], suppression of the apoptosis process [26], the ability to restore the oxidative phosphorylation system [33], and also to bind various endogenous toxic compounds formed in cascade reactions triggered by ischemia [21].

A randomized, double-blind, placebo-controlled clinical trial of glycine efficacy in ischemia was carried out [2, 3]. The study involved 200 patients in the acute phase of ischemic stroke (0-6 hours from onset). Neurological status, the content of antibodies to NMDA receptors, as well as the concentrations of glutamate, aspartate, glycine, GABA, and lipid peroxidation products in the cerebrospinal fluid were evaluated.

A study was also conducted of the effect of glycine on the concentration of neurotransmitter amino acids in cerebrospinal fluid. The study involved 132 people with acute ischemia. 58 people received 2 g of glycine together with the basic therapy, 74 people received only basic therapy.

The results of the studies confirmed the complex neuroprotective effect of the drug [3], a significant positive effect of glycine on the neurological status, concentration of stimulating neurotransmitters, activation of inhibitory neurotransmission, on the number of cases of disability, and also on patient survival [1, 3, 21]. Glycine also shown the ability to reduce the size of cerebral infarction, to lengthen the period of the “therapeutic window”, to expand the possibilities of thrombolytic therapy, and to protect brain tissue from reperfusion [3].

Thus, the effectiveness of glycine is shown in the first hours after the development of stroke in a dose of 1-2 g and also over the next 5 days. This became the basis for studying its use for the prevention of stroke [4].