

# APPLICATION OF GLYCINE IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER

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*The article reflects the peculiarities of treatment of children with attention deficit/hyperactivity disorder. Data on the application of glycine and its effectiveness are presented.*

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Attention deficit hyperactivity disorder (ADHD) is one of the most common psychoneurological disorders in childhood. ADHD has become more important in recent years [1]. In developed European countries, it is recorded in at least 2—18% of schoolchildren. In the Russian Federation, the syndrome is diagnosed in 7—28% of younger schoolchildren and is often registered in preschool age. This dispersion is due to the lack of uniform methodological approaches and criteria for diagnosis of this disorder [2].

The symptom complex of ADHD includes inattentiveness, hyperactivity, impulsivity, learning difficulties, and interpersonal relationships. It should be noted that children with ADHD did not find serious disorders, changes in muscle tone and disorders of motor reflexes [3].

According to neuropsychological studies, in children with ADHD detected impairment of the executive functions of the brain responsible for targeted organization of activities [4, 5]. In this disease, cortical relationships are disrupted, presumably. There is also evidence of hereditary predisposition to the disease. The causes of ADHD include hypoxic conditions of the child during the perinatal period, traumatic brain injuries, stress situations leading to disruption of adaptive mechanisms. According to literary data, in the formation of ADHD early damage to the central nervous system (CNS) during pregnancy and childbirth mattered in 84% of cases, genetic mechanisms in 57%.

At the same time, in 41% of cases, the formation of the syndrome was determined by the combined influence of these factors [6, 7]. It is suggested that one mechanism for ADHD development is neurotransmitter failure in the metabolism of dopamine and noradrenaline (CNS neurotransmitters). Catecholamine regulation affects the main centers of higher nervous activity — center of control and inhibition of motor and emotional activity, activity programming, attention system and RAM, so there is a need to correct cholinergic deficiency.

Symptoms of impaired attention and hyperactivity have been treated for several decades by psychostimulants, which are antagonists of catecholamines and alter the balance of catecholamines in the body. In the US in the 1990s, 90% of children suffering from ADHD were prescribed psychostimulants [4]. These drugs are supposed to increase the availability of catecholamines at synapse levels by stimulating their synthesis and inhibiting reverse capture in the presynaptic nerve endings. Although drug treatment is effective in about 75—80% of cases, it is necessary to consider that its effect, although pronounced, is still symptomatic.

Many of the drugs of this group are capable of causing narcotic addictions and addictions, and find limited use in medicine in Western countries [9]. Given the importance of the preservation of the intellectual sphere, which does not imply aggressive drug impact, as well as imperfection of the endocrine system in children, apply strong substances shall be followed with great care [10, 11].

In this situation, nootropic drugs are most appropriate — drugs that have an effective effect on the higher integrative functions of the brain [12]. Nootrops represent a group of drugs that affect memory, mental activity, as well as contribute to increasing the brain's resistance to adverse effects from the external environment. Their action is aimed at improving the adaptive capabilities of the

brain, cognitive functions, harmonizing arousal and inhibition in the brain. The effect of a number of nootropic agents is mediated through neurotransmitter systems of the brain, one of which is the glutamatergic system (e.g., the amino acid glycine acting through glycine and NMDA-receptors). In modern pharmacology, great emphasis is placed on amino acids as a structural basis for the creation of novel psychotropic agents that have an impact on brain cognitive functions. One of the representatives of this class of compounds is glycine — an amino acid regulating the metabolism of nerve cells, the processes of excitation and inhibition of the vegetative nervous system of the human body. which helps to relieve nervous tension, improves sleep, reduces hyperactivity, increases mental performance. Being substituted with an amino acid and possessing a short-chain molecule, glycine is involved in many metabolic processes (so, for example, through serine in tryptophan synthesis).

Glycine refers to drugs that improve metabolic processes in brain cells; possesses glycin- and GABAergic,  $\alpha$ 1-adrenoblocking, antioxidant, antitoxic action; regulates glutamate (NMDA) receptor activity. Glycine receptors are present in many areas of the brain and spinal cord. By binding to receptors (which are encoded by the *GLRA1*, *GLRA2*, *GLRA3* and *GLRB* genes), glycine causes “inhibiting” effects on neurons, reduces secretion from neurons of “excitatory” amino acids such as glutamic acid, increasing the release of GABA. In the spinal cord, glycine leads to motor neurons inhibition, which is especially important in the treatment of ADHD.

Nootropic drugs in the treatment of children should meet the following requirements: minimal side effects, pronounced therapeutic effect, possibility of integrated use with other drugs, ease of use, good taste. These criteria are allowed to determine the effectiveness of glycine use in children with ADHD.

The purpose of this study was to assess the effectiveness of the drug Glycine, sublingual tablets 100 mg (OOO “MNPK “BIOTIKI”), in children with ADHD. The study was carried out in “Academy of Health “Edelweiss” LLC (Krasnoyarsk).

Copying from medical documentation - electronic version of the outpatient card (software “Ariadna”) was performed. A total of 86 outpatient maps of children diagnosed with ADHD were analyzed. Diagnosis was established on the basis of an ADHD questionnaire (ICD-10 criteria; children between the ages of 6 and 13). The survey was conducted among parents whose children showed symptoms of these disorders (attention function, increased activity, impulsivity) observed during  $\geq 6$  months.

The choice of diagnostic studies was determined, based on data of history, examination, complaints.

Additional examinations were carried out to exclude organic brain lesion: cerebral CT scans in 27% of patients; neurosonography transtemporally (closed Acoustic window, this study allows to diagnose children up to 6—7 years) — in 19%; duplex scanning of head and neck vessels — in 76%; routine electroencephalography — in 100%; examination of the fundus — in 44%.

In the presence of symptoms of cardiovascular damage, ECG (55% of cases) was carried out, and patients with functional disorders of the digestive tract — studies to exclude parasitic pathology.

According to the age criterion, the children were distributed as follows: 6—7 years — 40%; 8—10 years — 33%; 11—13 years — 27%. Thus, ADHD is found to be most common in preschool and early school age children. Despite the fact that, according to literary data, the relative prevalence among boys and girls varies from 3:1 to 9:1, this pattern is not established in this study — boys there were 52%, girls 48%. When addressing the following complaints are noted: increased excitability, absenteeism, violation of attention, inclination to addictions (computer, etc., food addictions), intrusive movements, stereotypes in behavior, poor school performance, forgetfulness, sleep disturbances, fears, tantrums. The autonomic nervous system disorders in children with ADHD showed predominantly in the form of cardiovascular damage (31%) and irritable bowel syndrome (40%).

27 (31%) of children had heart rate changes in the form of tachycardia or bradycardia confirmed for ECG, pulse lability when excited. Functional disorders of the gastrointestinal tract were manifested in the form of pain syndrome, disturbance of evacuation function (constipation,

diarrhea), cyclic vomiting syndrome, pain in the right and left subrib at physical exertion. Vegetative manifestations in the form of skin marbling and sweating were also noted.

Analysis of outpatient maps revealed that in 73% of cases there was fetal hypoxia; 50% of children are in the group of often and long-term patients, 37% of cases noted lymphoproliferative diseases in the form of adenoid vegetations.

Importantly, one or both parents of most children (79%) showed symptoms of ADHD in childhood. All children are prescribed comprehensive treatment: diet with restriction of tonic products, proconvulsants, in 24 (28%) cases — gluten-free diet; therapeutic exercise, massage, physio, swimming; the same type of drug therapy (nootropic drugs, vitamins, sedatives, reducing agents).

To assess the efficacy of glycine in treating children with ADHD, patients were divided into 2 groups. Patients of the 1st group (n=46) as a nootropic drug was prescribed glycine (OOO “MNPK “BIOTIKI”), 2nd (n=40) — nootropi of other groups (gliatiline, cerepro, nootropy1).

Patients of group 1 glycine was prescribed for 1 month in a dose dependent on age: children 6—7 years — 0.05 g 3 times per day; 8—10 years — 0.1 g 2 times per day; 11—13 years — 0.1 g 3 times per day.

In children 6—7 years old, there is a marked effect in the form of improved concentration of attention and memory. The time of attention retention increased from  $12.0 \pm 0.3$  to  $37.0 \pm 0.5$  min, and there was also a positive perception of the educational process. This effect had an accumulative severity starting on the 10th day, and weakened somewhat by the 24—25th day of reception.

In children 9—10 and 10—13 years old, attention retention times increased to  $40.0 \pm 0.2$  min. In addition to improving concentration of attention and memory, there was a decrease in the severity of vegetative manifestations: pulse lability during excitement, severity of skin marbling, 20% of cases bought arrhythmia (which was confirmed with repeated ECG).

Children of this group showed a decrease in severity and frequency of manifestations of functional disorders of the gastrointestinal tract (reduction of pain intensity, control of meteorism, stool normalization).

Positive results were also noted in the analysis of the effectiveness of treatment of children of group 2. Attention retention time in children 6—7 years increased to  $28.0 \pm 0.3$  min, 9—13 years — to  $35.0 \pm 0.3$  min. Vegetative manifestations persisted. After the end of the course of treatment, children of the 1st group are recommended to take glycine repeated courses lasting 30 days on 3-4 courses during the year.

Children of group 2 are also recommended for prolonged treatment with nootropes for 2—3 months.

When observing patients in dynamics (3, 6, 9, 12 months), more pronounced, persistent positive changes were observed in children receiving glycine. The positive effect of the drug on vegetative manifestations is noted — the intensity of functional disorders of the gastrointestinal tract is reduced, which indirectly reduces psycho-emotional tension and reduces symptoms of ADHD manifestations in children.

It should be noted that convenient dosage form, sublingual application, pleasant taste qualities, affordable price allow to prescribe glycine to patients with any level of affluence and at any age that is important in the treatment of children. Other drugs in this range are more commonly released in capsules, making them difficult to use as children.

Adverse actions of glycine during prolonged use of the drug are not detected. Despite the fact that the application instructions contain information about the possibility of hypersensitivity reactions development, these reactions are not registered in this observation. No cases of overdose have been identified.

In the use of other nootropic drugs, the following effects were observed: sleep disorders (intermittent sleep, prolonged sleep, insomnia) — in 43%; dyspepsy disorders — in 24%; headache — in 3%; allergic manifestations (rash, itching) — in 6%; increased excitability — in 32%.

An important link in the psycho-correction of children with ADHD is the change in adult (parent) behavior and adequate treatment of behavioral features. Given that many parents respond acutely to the child's hyperactivity and there are often conflicting relationships in the family, we recommended parents take glycine at the same time as their child. In situations where parents took glycine at the same time as the child, the most positive results and a more stable effect from the therapy were noted.

Thus, based on available data, it can be concluded that glycine is most acceptable in the treatment of children with ADHD. Glycine has effects on pathogenesis and additional factors causing neurological disorders, has minimal side effects, can be used at younger age, prolonged use the drug allows to improve the course of the disease, facilitates social adaptation and, accordingly, the quality of life of patients and their loved ones.