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Use of Glycine in pediatrics

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This review contains the results of an analysis of literature and studies on the use of Glycine in pediatric practice. Examples of preventive medication of children, starting from the newborn period, are described. Adaptation to children's day-care services, prevention of excessive physical fatigue of young athletes and emotional fatigue of schoolchildren under increased psychological stress are examples of situation when Glycine had positive effects. The experience of using Glycine for various diseases of children and adolescents, such as epilepsy, bladder dysfunction, vegetative-vascular disorders, speech disorders and deviant behavior, is also described.

Key words: *Glycine, pediatrics, preventive medication, treatment.*

Glycine is one of many widely used drugs which administrates in pediatric premedication. This drug based on aminoacetic acid which is nonessential amino acid in the man's body. Aminoacetic acid extensively consists in fibrillary proteins and in a free or derivative form also consists in different tissues and biological liquids. The biological meaning of Glycine is driving by its contribution to synthesis of proteins and many other physiologically active compounds [1]. Glycine plays an important role as neurotransmitter in central nervous system [2]. Many evidences have been collected that Glycine is also an effective anti-inflammatory, immunomodulatory and cytoprotective drug [3].

Data of clinical administration of pharmaceutical preparation Glycine in pediatrics are collected in this paper.

Glycine administration in early age

Due to different properties of glycine (tranquilizer, cell membrane stabilizer and vegetal tonus adjuster) the drug has been included to optimization scheme of adaptation process of newborns from the mothers with recurrent miscarriage. Administration of 10-days Glycine courses during the pregnancy resulted in

decreasing of aborning stress reactions – decreasing of cortisol level, improvement of thyroid function particularly in women with cervical incompetence and neurocirculatory dystonia. Glycine administration in new born babies in early adaptation period increased blood leucocytes enzyme activity resulting in stabilisation of cell population formation versus control. Clinically Glycine administration in newborns caused falling of neonatal bilioussness frequency by a factor of 5 versus group without correction, and by a factor of 2 versus group with Glycine administered only by pregnant women. The frequency of hyperexcitability syndrome is also decreased up to 40% versus 85% in control group [4].

A group of 60 children with risk of frequent long-lasting disease rate was picking out to establish a new approach to preventive medication of early age children with aftereffects of perinatal CNS damage. Two courses of Glycine administration by 28 days with a month break was added to traditional therapy in the main group. Decreasing in amount of acute diseases cases accompanied by complications was identified. The amount of children having normal findings in saliva lysozyme level, skin auto-microflora and immunoglobulin A and J in blood serum reliably increased. Decreasing in tension quotient of regulatory body systems in cardiointervalography examining was shown [5-7].

Glycine administration by premature born children with minimal cerebral dysfunction (MCD) resulted in psychophysiological functions improovement [8]. Prescription of Glycine to monthling babies with perinatal brain damage in the presence of syndrome of heightened nervous-reflectory irritability and delayed motor and mental development shown positive results in 73% of cases.

Glycine administration in epilepsy

Integrated medical, electrophysiological and psychological investigations of Glycine administration was conducted in patients in age from 6 to 30 years old affected by various forms of epilepsy. The drug was prescribed for 3-10 tablets per day based on condition of patient. In the first group Glycine was prescribed along with standard anticonvulsant and barbituates therapy, in the second group – along with therapy phasing out, and in the third group – all along. According to EEG results the action was evident in as little as 20 minutes after the drug administration. Under further Glycine administration (throughout a year monitoring) positive dynamic was observed – paroxysmal activity reducing and alpha rhythm normalization, in which case functional load didn't give pathologic features on EEG. The drug significantly decreased intoxication associated with anticonvulsant administration in the first group and allowed for anticonvulsant therapy phasing out completely in the second group. Self-sustainable Glycine

administration decreased anxiety-depressive disorders and increased task performance particularly to earlier administrated base therapy drugs patients [9, 10].

Clinical study of Glycine administration by 58 children of 10-15 years old with generalize epilepsy or with secondary generalization epilepsy with focal seizures (39 patients), as well as epileptic syndromes (19 patients) was conducted in Vilnius University Pediatric Centre. Decreasing of base anticonvulsant therapy adverse event and improving of intracellular enzyme activity index were elicited as a result of monthly Glycine administration (38 children). Convulsions didn't repeat among 21 children (56%) during the period of monitoring [11]. The Glycine effect on intracellular energetic of blood leukocytes of infected with Herpes Simplex virus (HSV) children with epilepsy was also investigated. The activities of succinate and glutamate dehydrogenases, and alkaline and acid phosphatases as well were examined for 74 children of 10-15 years old. 29 infected with HSV children with epilepsy and durably taking anticonvulsant therapy were included in the first group, 20 uninfected with HSV children with epilepsy – in the second group, and 25 apparently healthy children – in the third group. It has been discovered that activities of succinate and glutamate dehydrogenases and alkaline phosphatase were increased in the first group of children, in the second group of children activity of succinate dehydrogenase was decreased, but activities of glutamate dehydrogenase and alkaline phosphatase were increased. Clinical tests indicated normalization of activities of succinate and glutamate dehydrogenases and alkaline phosphatase by 14th and 30th days of Glycine administration by children of both first and second groups. Thus, Glycine has a positive impact on intracellular energetic of blood leukocytes and promoted hepatotoxins eliminaton [12].

Content of autoantibody to GluR1 receptors of man's brain in blood serum was investigated for 71 children of 1 to 16 years old with idiopathic (12 children), and also symptomatic and cryptogenic (59 children) epilepsy forms. The level of autoantibody indicates extent of postsynaptic neuron membrane damage. As an additional medication the first group (23 children) administrated Glycine, the second group (31 children) – Pantogam, the third group (17 children) – Glycine and Pantogam at the same time. The autoantibody level of children from the first group was reliably lower than this meaning in the second group. Thus, Glycine plays important role in increased glutamate release conditions observed in epilepsy [13].

Glycine administration in bladder dysfunction

The effect of Glycine on children of 3 to 15 years old with neurogenic bladder dysfunction of hyper-reflex type. The active treatment group (37 people) administrated Glycine for 50 mg/kg per day divided by three intakes with a background of base therapy. Reparation of normal urodynamics measures was observed 6 months later. Urinary frequency reduced, urinary bladder sensitivity threshold increased, storage function improved. Glycine was proven to have positive effect on urodynamics on both primary and peripheral level [14]. In another such survey reliable positive dynamics in daily rhythm of spontaneous urination measurements, urofluometry and retrograde cystometry were identified to 72,3% of children by the time of treatment termination. Also, temper, self-rating level, sociability were increased and memory and concentration were improved in 73,5% of patients versus control group [15, 16].

Glycin application in vegetative-vascular disorders

Complex clinical Glycine efficiency study on 98 school-aged children with vegetative-vascular dystonia carried out in Smolensk state medical university. Children administrated 0,1 g of Glycine 3 times per day. Treatment efficiency depended on initial vegetative tonus and vegetative reactivity. Vegetative imbalance decreased in 87.2% of cases for children with sympathicotonia and hyper-sympathicotonia on 5th day, and allclinical implications of vegetative-vascular disorder eliminated on 10th day. The mend of vagotonia with hypersympathicotonic vegetative reactivity and hyperkinetic blood circulation type was also remarkable in 83,3% of cases [17].

During investigation of 82 children of 3-15 years old with vegetative-vascular disorder 40 children administrated standard therapy, 20 children with asympathicotonic vegetative reactivity administrated Semax, and 22 children with hypersympathicotonic vegetative reactivity administrated Glycine. The methabolic therapy response was approved by decreasing of sympatic segment activity of vegetative nervous system and increasing of parasympathetic segment activity after three weeks of therapy. Sympatic segment activity increasing and amplification of cardiac rhythm control centralization were noted according to postexercise echocardiography and cardiointervalography estimates [18].

The Glycine survey on children with biliary dyskinesia which is one of contributors to vegetative-vascular disorder facilitated in Clinical Diagnostic Department of Moscow Research and Clinical Institute for Pediatrics and Pediatric Surgery Ministry of Health of the Russian Federation. 55 children of 7 to 14 years old were under observation. Positive response on 10 days of Glycine administration for one tablet twice a day was identified in 69-76% of children with

both sympathicotonia and vagotonia in terms of decreasing and elimination of vegetative-vascular disorder events as well as of associated with vegetative-vascular disorder biliary dyskinesia symptoms. That is abdominal pains and headaches recover, sleep improving, the most important cardiointervalography estimates normalization came alone [19].

Glycine application in speech disorders treatment

Positive response on Glycine therapy of children with speech disorders was estimated by time course of sound reproduction, emotive behavior response, results of neuropsychological research and task performance assessment. Different speech abnormality was observed in children of 5-6 years old in forms of dyslalia (30%) and subtle dysarthriac(70%). Glycine administration was divided by three courses of 2 tablets three times per day during 20 days. The most prominent positive response was achieved on cognition interest scale (studies interest, memorizing processes, discipline and attention), improvement was achieved on phobia scale, physical assault and anger reaction and socializing. Logopedic treatment efficiency increased in common. Thus, general tension reducing in children along with nootropic action favored sound reproduction improvement [20].

Young athletes Glycine application

Survey of 137 young athletes (9 – 14 years old) that was going for sport more than one year discovered increased psychoemotional body tension in 85% of cases. Alongside of Glycine application physical efficiency was improved, asthenoneurotic manifestations were reduced [21, 22].

Preventive Glycine application in children and adolescents in child welfare institutions

Glycin was highly praised by VNII hygiene and disease prevention of children, adolescents and youth MH USSR (this institution nowadays is a part of Scientific Center of Children's Health of RAMS) and approved as widespread medical and preventive agent in school age. Glycine administration courses of 15 – 30 days long exert positive action during the school adaptation time in the 1st grade. The drug could be administrated as mental strain and psychoemotional tension prevention during preparation and passing of exams, tests etc. Corrective drug action was revealed in children with compromised neuropsychological status [23].

High drug efficiency was observed while Glycine application in institutions with long-stay facility (health camp, residential school, special needs school, lyceum etc. It's corrective action on children with neurotic and vegetative disorders and

mental retardation was confirmed using medical-teaching observations on neuropsychic health state and scholars learning progress [24-26]. The effect of Glycine on attention, short-term memory and sensomotor reactions of school aged children was also observed. The observations indicated that all schoolchildren registered stressful feelings during special tests performance. The extent of short-term memory increased in 58% of cases on 25% on the average, and in 25,7% of cases didn't change. Drug administration cut short attention switch time and a number of committed mistakes. Fatigue augmentation, performance efficiency decreasing and attention switching time augmentation were admitted in reinvestigation of placebo administrated children in 65% of cases.

95% of scholars mentioned fear vanishing and inner discomfort when Glicine administrated 30 minutes before exam that was also acknowledged by tutor. Moreover, pulse and blood pressure which are mainly reflect neuropsychic condition also remained normal. Significant mistakes decreasing and increasing of works without mistakes was noted in the last half of a week under prolonged drug administration [23, 24].

The part about nonspecific children body resistance was of the main interest in mentioned above investigations. Quantitative lysozyme saliva values of 35 junior flattening school pupils (children with different manifestations of minimal cerebral dysfunction) were measured. Two weeks long Glycine administration (1 tablet 3 times per day) had positive influence on lysozyme content – either on initial quantitative values or on its persistence by the end of learning week [24, 26-28]. The results of complex study of Glycine impact on different substructures psychic area of adolescents with deviant behavior repertoire and having disturbances in mental health made for conclusion that fined during investigation facts evidenced about neurotropic Glycine action focused on homeostasis maintenance. Exhibiting anxiolitic activity the drug facilitates individual mental state harmonization leading to optimal stage of personal responsiveness and behavioral manifestations stabilization. Positive dynamic of electroencephalography data was mentioned ether after single appliance and with two weeks therapy in the background. What is more, based on electroencephalography data it was established that Glycine has nootropic activity and its action directed on optimization of CNS functional condition [23, 24].

The survey of enzymatic state of students' lymphocytes in school year dynamic was conducted. It revealed different energy supplying degree of cells with hypoxia signs but without cell deenergization. The Glycine correction course shone laudable changing in population structure of lymphocytes which revealed in

increasing of mean enzyme activity, stabilization of cell heterogeneity and variety, improvement of numerical cell ratio with high and low activity and content of lymphocytes with typical enzymatic activity. Psychological characteristics (tension, emotional tonus, attentiveness, memory, situational and personal anxiety) were also improved which increase adaptation reserves and optimize learning process [29].

Thus, Glycine has prominent efficiency in different diseases and being a stress protector in pcychoemotional tension in apparently healthy humans. Neuroprotective properties of Glycine and near-complete collateral damage lack provide an opportunity to widely use the drug in pediatrics from neonatal period onwards [30].