EXPERIENCE IN THE USE OF THIAMINE (VITAMIN B1) MEGADOSE IN THE TREATMENT OF KORSAKOV-TYPE ALCOHOLIC ENCEPHALOPATHY

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Abstract. *Treatment of alcoholic encephalopathies is predictive. In many ways, their result depends on the time and quality of the start of the healing process. Most often, alcoholic encephalopathies are formed in the last (encephalopathic) stage of alcohol dependence, but it can also occur in the former, in the latter. In these cases, the development of alcoholic encephalopathies often precedes the severe course of acute alcoholic psychoses, in particular delirium.*

Keywords: *alcoholic encephalopathy, Korsakov psychosis, treatment, thiamine, delirium.*

Introduction. In cases where delirium lasts more than a week (transmitted delirium) we are usually talking about alcoholic encephalopathies. The result of such delirium can be temporary Korsakov syndrome (psychosis) or permanent amnestic syndrome (Korsakov psychosis) with a tendency to relative recovery. As a rule, the mental component of the syndrome is accompanied by polyneuropathy. For effective treatment, it is necessary to take into account the pathogenetic mechanisms of the development of alcoholic encephalopathies [1, 2]. Thiamine deficiency plays an important role in the development of alcoholic encephalopathies, which is due to its insufficient intake with food and a decrease in intestinal absorption. In addition, ethanol inhibits the phosphorylation of thiamine and the formation of its metabolite, thiamine pyrophosphate, which is involved in maintaining normal metabolism of nerve tissue. Therefore, the use of thiamine is an almost mandatory component of the treatment of alcoholic encephalopathies and related diseases of the peripheral nervous system [3-5].

Alcohol abuse is one of the most important social and medical problems in the world. There is a steady increase in the number of people addicted to alcohol. The negative impact of alcohol on the physical and mental health of a person and the human gene pool in general is indisputable. According to the World Health Organization, alcohol consumption in our country leads to an early, preventable death of about 0.5 million people every year [6-8]. Chronic alcohol intoxication is based on the development of alcohol disease, which is considered as a complex of mental, neurological and somatic diseases associated with regular alcohol consumption [9]. To objectively assess the alcohol content in consumed drinks, the concept of a standard dose – the amount of an alcoholic beverage containing ethanol equal to 10 g of pure alcohol-was introduced [10].

Consuming more than 2-3 doses per day or 14 doses per week for women, 3-4 doses per day for men, or 21 doses per week is considered dangerous to health [11]. Currently, alcohol abuse

has been proven to damage almost all vital organs and systems of the body: liver and gastrointestinal tract (gastrointestinal tract), cardiovascular and nervous system, endocrine, respiratory system, reproductive function and disorders of the mental sphere [12].

Both acute and chronic alcohol intoxication is associated with various pathological effects on the central (CNS) and peripheral nervous system [13]. The pathogenesis of damage to various parts of the nervous system during alcohol poisoning is complex and has not yet been fully studied [14].

Eating disorders that develop with chronic alcoholic intoxication, malabsorption syndrome and other lesions of the gastrointestinal tract lead to a lack of many nutrients and mainly vitamin B1 (thiamine). Thiamine deficiency plays a leading role in the pathogenesis of alcohol-related neurological disorders. Ethanol and its metabolite acetaldehyde have neurotoxic dose-dependent effects on the structures of the central nervous system and peripheral nervous system [15]. In particular, ethanol leads to decreased synthesis and disruption of the normal configuration (misfolding) of the cytoskeletal proteins of the nerve fiber, and slowed axonal transport. Acetaldehyde forms complexes with the normal proteins of the cell, converting them into cytotoxic substances, which in turn affect the neurons of the central nervous system, as well as myocytes, hepatocytes, which leads to the development of cirrhosis of the liver and myopathy. The toxic effects of ethanol and its metabolites on neurons are predicted by activating glutamate receptors in the spinal cord and inducing glutamate neurotoxicity, enhancing free radical lipid peroxidation processes, and increasing the production of anti-inflammatory cytokines [16-18].

The effect of ethanol on the central nervous system, including the formation of alcohol dependence, is caused by a violation of the balance between inhibitory and excitatory neurotransmitters [19]. Alcohol activates inhibitory GABA-Ergic systems; in addition, its compounds with biogenic monoamines (norepinephrine, adrenaline, serotonin) have morphine-like properties, which play an important role in the formation of alcohol dependence and withdrawal syndrome [20]. In addition to the degree of damage to the nervous system, alcohol content and duration of its consumption as a result of the action of acetaldehyde, genetic factors are also determined by the activity of the enzymes alcohol dehydrogenase and acetaldehyde dehydrogenase. The combination of high activity of alcohol dehydrogenase and low activity of acetaldehyde dehydrogenase is predictably unfavorable, leading to the accumulation of acetaldehyde in tissues [21].

Immunological diseases also play a role in the pathogenesis of chronic alcoholism. People who suffer from alcoholism have autoantibodies to neurotransmitters, which are mediators and modulators of mechanisms for the development of alcohol dependence. There is an inverse relationship between the titers of autoantibodies and the level of alcohol consumption. With a favorable course of alcohol disease characterized by long-term (up to 4-6 years) remission after treatment, high titers of autoantibodies to serotonin, glutamate and catecholamines are often detected [22]. Over time, the risk of developing neurological complications increases in the presence of comorbid pathology of the liver and other internal organs of alcohol Genesis. Treatment of diseases of the nervous system caused by alcohol abuse is a complex problem and often requires the participation of doctors of various specialties due to damage to the liver, gastrointestinal tract in combination with the development of malabsorption syndrome. The main task and key to the success of therapy is to give up alcohol to the patient and restore a fully balanced diet. However, due to the complexity of the mechanisms of the pathogenesis of alcohol-induced

injury, the central nervous system and peripheral nervous system are not enough to consume only alcohol and detoxify. Pathogenetic therapy, as well as symptomatic treatment, is important to reduce the severity of various symptoms of the disease and improve the quality of life of patients [23].

Symptomatic therapy includes stopping neuropathic pain with APNS, treating various manifestations of peripheral autonomic insufficiency, "restless legs syndrome", stopping epileptic seizures, correcting psycho-emotional disorders. Physical and psychological rehabilitation of patients is also important.

Given the role of activating free radical lipid peroxidation processes in the pathogenesis of the neurotoxic action of ethanol, a-lipoic acid (ala) preparations have been demonstrated as pathogenetic therapy. Experimental studies have shown that a-lipoic acid increases the activity of endogenous antioxidants (glutathione, vitamin E), inhibits free radical peroxide oxidation of lipids, increases k+-Na+ -Atpase activity, normalizes the NAD: NADH ratio, improves endoneural blood flow. In addition, there is evidence of direct detoxification effects of a-lipoic acid in ethanol-related neurotoxicity in vivo [24].

Drugs with metabolic effects, as well as improving microcirculation, are very widely used, but their effectiveness has not been proven in controlled clinical studies. In the treatment of chronic am, possible therapeutic effects of leucine-containing amino acid mixtures and glutathione precursor amino acids are discussed [25].

At the same time, taking into account the leading role of thiamine deficiency in the development of most clinical forms of alcoholic damage to the central nervous system and peripheral nerves, B vitamins are the basis of pathogenetic therapy, currently a decrease in the concentration of thiamine in the blood is noted in 40-80% of people with chronic alcohol poisoning. The active form of thiamine-the oxidative decarboxylation of thiamine diphosphate-keto acids, essential for the synthesis of acetylcholine, is involved in carbohydrate metabolism and other types of metabolism, providing axonal transport that determines the renewal of nerve tissue. In addition, thiamine (Vitamin B1) increases intracellular reserves of magnesium, which plays an important role in energy processes in the nervous system. As a result of vitamin B1 deficiency, the addition of lipids to myelin is reduced, the biosynthesis and metabolism of neurotransmitters, glucose is disrupted, zones are formed in neurons with lactate acidosis and intracellular accumulation of calcium, which enhances the neurotoxic effect of alcohol [25, 26].

The phosphorylated form of pyridoxine (vitamin B6) serves as a cofactor of more than 100 enzymes, is involved in the synthesis of various mediators: catecholamines, histamine and y-aminobutyric acid, enhances the action of antinocytic mediators (norepinephrine and serotonin). Vitamin B12 is involved in the synthesis of protein and lipid structures of the myelin sheath of nerve fibers, in the production of methionine, is necessary for normal blood formation and erythrocyte maturation, promotes cell proliferation and growth in coenzymes, its analgesic properties have been proven [21-24].

In general, B vitamins and their coenzymes are involved in biochemical processes that ensure the normal functional activity of the structures of the central nervous system and the peripheral nervous system, which makes it possible to consider them as neurotrophic drugs, the use of which is pathogenetically different both in polydeficitic cases of etiology and in the absence of absolute vitamin deficiency [25, 26].

Clinical studies have proven that it is advisable to use B vitamins in patients with chronic alcohol poisoning in the presence of polyneuropathy, regardless of the leading pathogenetic mechanism – toxic or deficiency, since in most cases there is a combination of both factors [27, 28].

The purpose of our study: was to assess the clinical effectiveness of thiamine megadoses in the treatment of Korsakov syndrome (psychosis), which developed at the stage of resolving heavy alcoholic delirium.

Materials and methods. The work was based on the son men's admissions unit. 47 men (average age) were included in the study 44,3 +/- 4,5 with 2 Confirmed Stages of alcoholism, he was admitted to the hospital in the emergency room. The duration of the disease was from 9 to 18 years. According to the ICD-10 criteria, all patients were diagnosed with f 10.4 "delirium alcohol withdrawal syndrome".

When taken, a severe course of alcoholic delirium was observed in all patients, corresponding to the muscitative option, which by 8-10 days turned into Korsakov-type alcoholic encephalopathy.

Research results and discussion. Treatment began immediately after hospitalization. All patients underwent detoxification therapy, at the same time the use of glucose Solutions was excluded and carbohydrate intake was restricted to the body, as their metabolism requires increased thiamine intake. Also, all patients received tranquilizer therapy: up to 30 mg of diazepam per day. Parenteral for 7-10 days, then oral phenazepam up to 2 mg per day. In 2-3 weeks.

Against the background of this therapy, 23 people (Group 1) were parenterally administered thiamine (Vitamin B1) at a dose of 1500 mg per day. dripping for a week, then switching to Per OS at a dose of 400 mg IV 3 times a day for 2 weeks, then 200 mg 3 times a day for a month.

From the first day, 24 people (2 groups) underwent complex therapy, including drip 200 mg of B1 vitamins per day., B6 200 mg / day., piracetam 1.5 g / day., Mexidol is 200 mg / day., geptrala 800 mg / day., neuromidine 100 mg / day. for the first week, then for 2 weeks, the drugs were administered in the same doses i/m, and then for a month for us.

The average duration of the inpatient therapy phase ranged from 4 to 6 weeks. The criterion for completing inpatient treatment in both groups was to reduce the psychopathological symptoms of Korsakov syndrome to the level of Asthenic Syndrome (asthenic variant of Psycho-organic syndrome).

Evaluation of the effectiveness of therapy was carried out using the praise-17 scale 0, 7, 14, 21, 28, 35 and 42 days of therapy and the general clinical impression scale (CGI) before and after the start of therapy.

Group 1 (23 people) observed positive dynamics of the clinical condition from the 14th to the 16th day of therapy: mental state gradually reduced episodes of confusion and put Memory Disorders first in current events, pseudo-minisences, confabulations were observed. There was a slight slowdown in thinking, a narrowing of the circle of associations. At the same time, the emotional background rose, euphoria was noted. When trying to get out of bed, patients experienced dizziness, a violation of coordination of movements was noted, they could only walk with support.

By the 21st to 28th day of therapy, memory impairment was mainly manifested in the direction of memory impairment, especially since everyday events were not strictly maintained

and repeated. The emotional background was labile, periods of tactless moods were replaced by irritability. Neurological condition improved coordination of movements, decreased paresthesias, patients tried to act independently.

By 35-42 days, the positive dynamics in the mental and neurological state remained. Patients were fully focused. The emotional background was equalized. The memory of current events has improved. There was partial awareness of the disease.

Almost the opposite development of polyneuropathy was observed. Asthenic symptoms came to the fore: phenomena of mental and physical weakness, rapid fatigue, difficulties in concentration were noted. A significant and very significant effect was observed in 5 (20,8%), less pronounced in 6 (23,1%).

Thus, in the first group, in the results of severe delirium, a short period of Korsakov syndrome (up to 10 days) was recorded in almost half; in 12 people (52,1%), the duration of Korsakov syndrome was more than 10 days, which later switched to asthenic. At the same time, the phenomena of polyneuropathy decreased almost completely.

In Group 2 (24 patients), the positive dynamics in the condition of patients began a little later, on the 18-21 day of therapy. At the same time, the mental state observed periods of confusion and amnestic disorientation, confabulation and pseudoremeniscence flows. Externally, the patients were confused, they could not determine where they were. Both motor and ideator inhibition were characteristic. Neurological symptoms turned out to be more resistant, patients lay in bed, complaining of calf pain, general weakness.

By the 28th-35th day of therapy, a gradual decrease in psychopathological symptoms was noted in a mental state. Recall of current events decreased, inertia and a decrease in the level of associations were noted. At the same time, there was no critical assessment of their insolvency. Polyneuropathy events decreased slightly, but patients complained of weakness in the leg muscles, discomfort, impaired coordination of movements.

By the 42nd day of therapy, the positive dynamics became more pronounced. The weakening of memory was manifested in the difficulty of repeating the sequence and chronology of events in an arbitrary presentation. There was a general decrease in the pace of mental activity, increased fatigue, weakening of active attention function. The neurological condition maintained positive dynamics, with a gradual decrease in polyneuropatic disorders. A significant and very significant effect was observed in 3 (12.5%), with a lower effect in 5 (21.7%), while Korsakov syndrome was prolonged in 15 (62.5%).

Conclusion. Thus, the decrease in Korsakov syndrome (psychosis) in the treatment with megadoses of vitamin B1 occurred 7-10 days faster than in complex therapy with moderate therapeutic doses of thiamine. A reduction in the time of condemnation of consciousness was noted, Korsakov syndrome acquired a temporary character in almost half. At the same time, a clearer Dynamics was observed in terms of the decrease in polyneuropatic diseases, which confirms the view of the main role of thiamine in the violation of metabolic processes in Korsakov-type alcoholic encephalopathy.

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