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ALCOHOLIC POLYNEUROPATHY - DIAGNOSTIC AND TREATMENT METHODS

Introduction: Alcoholic polyneuropathy is a disease associated with damage to peripheral nerves that develops against the background of prolonged alcohol abuse. It is accompanied by muscle weakness, impaired sensitivity, ataxia, and other symptoms. The main causes include the toxic effects of alcohol, vitamin B deficiency, and eating disorders. In Uzbekistan, as in other countries, the treatment of alcoholic polyneuropathy includes alcohol withdrawal, vitamin therapy, metabolic therapy and physiotherapy. The success of treatment largely depends on timely medical treatment and compliance with the recommendations of doctors.

Keywords: alcoholic polyneuropathy, muscle weakness, sensory impairment, ataxia, B vitamins, treatment, diagnosis.

In relation to other polyneuropathies, the proportion of alcoholic lesions is 36% [4]. According to literature data, AP occurs from 9 to 76% of cases in patients suffering from alcohol dependence for more than 5 years. However, subclinical forms of AP are detected in 97-100% of patients who chronically consume alcohol., by means of electroneuromyography (ENMG). In this regard, some authors consider AP as one of the symptoms of alcoholism [4, 7].

It is believed that AP develops in people who drink alcohol regardless of race, nationality, age and gender. However, it was also noted that women tend to develop alcohol dependence, as well as the incidence of subsequent complications, including polyneuropathy, is higher than in men. Such gender-specific physiological differences in terms of alcohol metabolism are due to a higher absorption rate and, as a result, a higher alcohol level in the blood.

There is more blood in women than in men. AP is a symmetrical sensorimotor neuropathy based on axonal degeneration with secondary demyelination. The main pathogenetic mechanism of axonal injury is generalized damage to the axial cylinders of peripheral nerves. Axonal degeneration develops as a result of mpaired metabolic processes at the neuron level due to a deficiency in the production of ATP molecules in the mitochondria and/or damage to axonal transport [7, 10].

Depending on the course of the disease, there are acute, subacute, and chronic forms of AP. The most common variant is the chronic form of AP, characterized by a gradual (over several years) progression of pathological processes and a gradual development of the main symptoms. Acute and subacute forms are less common, as a rule, against the background of vitamin B1 (thiamine) deficiency, characterized by a more rapid development of symptoms (within a few days / months). Patients with chronic alcoholism also have asymptomatic forms of the disease [4, 6].

Pathogenetic mechanisms underlying AP, they still remain unclear. Currently, two main mechanisms of AP development are being considered. One of them is caused by the direct toxic effect of ethanol and its metabolites, mainly acetaldehyde, on the fibers of the peripheral nervous system. Alcohol enters the bloodstream within 5 minutes after ingestion and reaches its peak after 30-90 minutes. Ethanol and its toxic degradation metabolites affect the metabolism of neurons: they activate glutamate receptors in the spinal cord, which leads to the induction of glutamate neurotoxicity, processes free radical lipid peroxidation, increased production of

proinflammatory cytokines [7]. Free oxygen radicals disrupt the activity of cellular structures, primarily the endothelium, causing endoneural hypoxia and leading to the development of AP. In addition, ethanol reduces synthesis and disrupts the normal configuration of nerve fiber cytoskeleton proteins and slows down axonal transport [4]. Experimental studies have provided data on ethanol activation of spinal microglial cells brain function, increased functional activity of the hypothalamic-pituitary-adrenal and sympathoadrenal systems. These changes in combination with alcohol-induced oxidative stress play a significant role in the formation of central sensitization in the spinal cord and, as a result, in the development of neuropathic pain syndrome in alcoholic polyneuropathy [2]. Another pathogenetic mechanism of AP development (acute and subacute forms) is vitamin deficiency B1 (thiamine). On the one hand, thiamine hypovitaminosis in patients with alcoholism is caused by insufficiency its intake from food due to the consumption of calorie-rich alcoholic beverages with low nutritional value [9]. On the other hand, ethanol reduces the absorption of thiamine in the small intestine, reduces liver reserves of thiamine, and disrupts the processes of thiamine phosphorylation and formation of its active form, thiamine pyrophosphate (TPF). TPF is a coenzyme of the most important multicomponent enzyme complexes: pyruvate dehydrogenase, α-ketoglutarate dehydrogenase and α-ketodehydrogenase complexes. These enzymes are involved in carbohydrate metabolism (the Krebs cycle, the formation of ATP), the biosynthesis of some structural components of the cell, components of the endogenous antioxidant system, and are also involved in the pentose phosphate pathway for the synthesis of nucleic acid precursors and NADFH (pentose). TPF deficiency leads to a decrease in the activity of these enzyme systems, which, in turn, reduces the incorporation of lipids into myelin, disrupts the biosynthesis and metabolism of neurotransmitters, and zones with lactic acidosis and intracellular accumulation form in neurons. calcium, which potentiate the neurotoxic effect alcohol [4]

Several additional pathogenetic mechanisms are also being considered. These include activation of the spinal cord and microglia during chronic alcohol consumption, activation of mGlu5 receptors in the spinal cord, oxidative stress leading to damage to peripheral nerves by free radicals, release of proinflammatory cytokines from nerve endings together with activation of protein kinase C, involvement of the opioidergic and hypothalamic-pituitary-adrenal systems .

In clinical practice, sensory, motor, and mixed forms of AP are most common [8].

The sensory form of polyneuropathies is characterized by the development of various kinds of sensory phenomena, mainly in the distal extremities. There may be numbness, a feeling of chilliness or, conversely, burning in the hands and feet, paresthesias in the feet and legs, painful spasms of the muscles of the legs, as well as varying degrees of pain in the distal extremities (more often the lower ones), usually with a neuropathic component. Examination reveals the phenomena of hyperalgesia, hyperpathy, dysesthesia. Touching the skin dramatically increases the pain (allodynia). The diagnosed ones sensitivity disorders (hypo- or hyperesthesia of pain and temperature sensitivity) are usually symmetrical in the palms and feet by the type of gloves and socks, with further extension to the proximal extremities by the type of high gloves, golf, stockings. Dissociated sensitivity disorders are possible [5]. Sensory disorders are often combined with vegetative-vascular changes: impaired pupillary reactions, hyperhidrosis, acrocyanosis, marbling, cyanosis, puffiness and hyperpigmentation of the skin of the palms and feet, dystrophic changes in the nails. Menstrual cycle disorders and impotence are possible. There is an inhibition of tendon and periosteal reflexes. At the preclinical stage, Achilles reflexes disappear first.

When the fibers of deep sensitivity are involved, sensitive ataxia develops. There is also an atactic form of AP (peripheral pseudotabes), in which impaired gait and coordination of

movements are accompanied by numbness and hypesthesia of the distal extremities, lack of Achilles and knee reflexes, and pain on palpation in the area of nerve trunks.

The motor form of AP is characterized by the development of peripheral paresis of varying severity, which are combined with minor sensory disorders. The lower extremities are more often affected. It is characterized by a predominant lesion of the tibial and fibular nerves with the appearance of symmetrical flaccid paresis. When the tibial nerve is affected, plantar flexion is disrupted. feet and fingers, turning the foot inwards, it is impossible to walk on your toes. Fibular nerve damage is characterized by impaired function of the extensors of the toes. The foot is hanging down and turned inwards, patients raise their legs high when walking so as not to touch the floor with their fingers (peroneal gait). Weakness and atrophy the muscles develop, as a rule, with a prolonged course of the disease. Upon examination, hypotension and hypo- or atrophy of the muscles of the legs and feet are detected in the form of sinking of the interosseous spaces – "clawed foot". Sometimes the atrophy extends to the thigh muscles. Often hypermobility and deformity of the ankle joints are detected. Achilles reflexes symmetrically fall out or are reduced, knee reflexes can be increased with the expansion of reflexogenic zones.

The mixed form of AP is characterized by a combination of motor and sensory impairments. The upper and lower extremities are diffusely affected. The development of symmetrical flaccid tetraparesis is characteristic; when the lower extremities are affected separately, the clinical picture is similar to that of the motor form of the disease, and when only the upper extremities are affected, mostly extensors. Various polyneuritic sensitivity disorders are also found in the area of paresis [8].

The main diagnostic method for AP is ENMG, which makes it possible to objectify the level, nature and degree of damage to peripheral nerves. At ENMG Patients with various AP variants show signs of axonal damage. Needle electromyography shows signs of denervation and reinnervation of muscles, especially of the lower extremities. The amplitude of the M-response and the action potentials of the sensory the fibers are reduced mainly from the legs. With thiamine deficiency polyneuropathy, there is usually a more pronounced decrease in the amplitude of the M-response than with ethanol damage, which is accompanied by more pronounced muscle weakness. There may be a slight or moderate slowing of conduction along motor or sensory fibers and a slight increase in distal latency, which is a sign of secondary demyelination [10].

It should be noted that the absence of pathological changes according to the ENMG data does not mean the absence of peripheral nerve damage. According to the ENMG data, it is possible to assess only the condition of thick myelinated fibers. And in the chronic toxic form of AP, thin, weakly myelinated or unmyelinated fibers are mainly affected, therefore, in these cases, ENMG indicators remain within the normal range.

In order to verify damage to the thin fibers of peripheral nerves, such research methods as quantitative sensory testing, laser evoked potentials, evoked potentials for thermal stimulation, and the study of intraepidermal nerve fibers are used [7].

In some cases, histological examination of nerve fiber biopsies is possible for the differential diagnosis of AP with polyneuropathy of a different nature, as well as to establish the form of AP. Examination of the drugs reveals signs of axonal degeneration with secondary demyelination. In case of toxic. The form often involves thin myelinated and unmyelinated fibers, and in thiamine-deficient polyneuropathy– predominantly thick myelinated fibers.

The alcoholic genesis of polyneuropathy may also be supported by other manifestations of alcoholic damage to the nervous system, such as Korsakov's amnestic syndrome, cerebellar degeneration, as well as systemic manifestations (skin changes, signs of liver dysfunction, increased levels of gammaglutamyltranspeptidase).

Considering the multifactorial mechanisms of pathogenesis However, the treatment of this condition requires an integrated approach. A necessary component of successful treatment is abstinence from alcohol and a balanced diet with sufficient vitamins and protein, as well as physical rehabilitation of the patient. Taking into account the mechanisms of AP development, when developing therapy tactics, it is of great importance pathogenetic and symptomatic treatment aimed at reducing the severity of the disease. Despite the lack of a significant evidence base, drugs with metabolic and neurotrophic effects, as well as those that improve regional microcirculation, are widely used [4, 8].

Given the developing multivitamin deficiency in AP, it is advisable to prescribe primarily B vitamin preparations, especially thiamine. In patients with AP, the replenishment of the vitamin deficiency restores activity It helps to stop the progression of the disease and promotes a more complete and rapid restoration of functions [9]. Due to the fact that patients with alcoholism have impaired absorption of nutrients in the small intestine, in severe cases, they begin with parenteral administration of thiamine (2-3 ml of 5% solution i.m.) followed by oral administration. The use of a special fat-soluble form of thiamine (benfotiamine) increases the effectiveness of treatment due to better absorption in the intestine and better penetration through the blood-brain barrier, thereby creating. This results in a higher intracellular concentration of active metabolites. It is also possible to prescribe combined preparations of B vitamins – B1 (thiamine), B6 (pyridoxine), B12 (cyanocobalamin) in combination with folic acid or as part of multivitamins [9].

Preparations of thioctic (α-lipoic) acid are similar in biochemical mechanism of action to B vitamins. Being an endogenous antioxidant, thioctic acid performs the function of a coenzyme in the reactions of oxidative phosphorylation of pyruvic acid and alpha-keto acids. Thus, protects the neuron from the toxic effects of free radicals, and also helps to increase the concentration of the endogenous antioxidant glutathione, which ultimately leads to a decrease in the severity of the symptoms of polyneuropathy.

Thioctic acid is synthesized in animals and humans, but when exogenous, it is well absorbed by oral administration and quickly transforms into its reduced form, dihydrolipoic acid, in many body tissues. The daily need of a healthy adult for alpha-lipoic acid is 1-2 mg. Thioctic acid is excreted by the kidneys, mainly in the form of oxidized or conjugated metabolites. Thioctic acid is a potential antioxidant that works in both fat–soluble and water-soluble media. Its two forms have antioxidant activity – oxidized and reduced. Thioctic acid also plays a fairly important role in the utilization of carbohydrates and the implementation of normal energy etabolism, improves the energy status of the cell.; induces acidification of the extracellular environment, increasing lactate production; reduces ketogenesis.

One of the drugs containing thioctic acid is Berlithione, whose action is based on a number of effects: Improvement of energy metabolism.

Normalization of axonal transport.

Inhibition of gluconeogenesis and ketogenesis.

Normalization of the breakdown of high molecular weight alcohols.

Free radical binding and inactivation of oxidants.

Inhibition of radical formation.

Membrane repair.

In AP, the role of Berlithione in ensuring he function of the body's antioxidant defense system is very important. The mechanism of the antioxidant effect of the drug is twofold. Berlithione is able to directly inactivate free radicals by acting as a kind of "trap" for them. In addition, it contributes to the normalization of the function of the glutathione system of antiradical protection, acting as a donor of SH groups and replacing reduced glutathione in reactions provided by glutathione peroxidase. This multidimensional mechanism of action of the drug makes it possible to act on several links of the pathogenesis of AP at once and at the same time expect promising positive effects on other organs and systems affected by chronic alcohol intake.

In severe cases, treatment begins with parenteral administration of the drug for 2-4 weeks, then the patient is transferred to a tablet form at a dosage of 600 mg once a day in the morning 30 minutes before meals for 1.5–2 months [5, 8].

The authors observed the clinical effects of Berlithione in a group of 48 patients (31 men, 17 women) who were treated in the neurological department of the Andijan Regional Narcological Dispensary. Patients received the drug parenterally for 2 weeks, then switched to oral administration. A necessary condition for therapy was complete abolition of alcohol. According to the results of therapy, 89.6% of patients noted an improvement in their general condition. The most active changes were observed in improving walking function, reducing pain and numbness. At the same time, 4 patients (8.3%) had a restoration of surface sensitivity in the lower extremities. In addition, the effectiveness of therapy was assessed according to laboratory examination data: the bilirubin content and lipid profile were studied., alkaline phosphatase. As a result, the majority of patients showed positive clinical dynamics. conditions, a decrease in the severity of biochemical disorders, or even normalization of indicators. Unfortunately, it should be noted that this particular category of patients is particularly difficult for long-term follow-up due to the specific characteristics of their social and clinical statuses.

Thus, it can be concluded that Berlithione is a drug capable of breaking the chain of metabolic disorders that form the basis of the pathogenesis of AP. The multifaceted nature of the drug's action allows it to be recommended not only for the treatment of patients with neurological complications, but also for the purpose of hepatoprotection. Being a universal stabilizer of cell membranes, Berlithione can be used in all pathological conditions based on membrane damage, that is, in almost all chronic complications of alcoholism.

Recently, uridine monophosphate in combination with vitamin B12 and folic acid has been actively used to repair damaged peripheral nerve fibers. It is clinically proven that peripheral nerve damage increases the need for pyrimidines. nucleotides such as uridine monophosphate. In the process of its metabolism, the restoration of important components of the cell membranes of neurons is ensured, as well as the supply of a sufficient number of enzymes to damaged neurons.

Symptomatic therapy is based primarily on the treatment of neuropathic pain syndrome. Neuropathic pain is a frequent and rather painful clinical symptom in AP, in which there is no effect from analgesics and anti-inflammatory drugs. And in this case, analgesics are traditionally used as symptomatic therapy, for example which include antidepressants and anticonvulsants [2, 3]. Among anticonvulsants, carbamazepine is used. The initial dose is 100-200 mg 1-2 times a day, as a rule, a gradual increase in the dose to 400 mg 2-3 times a day is sufficient. The

development of adverse reactions in the form of drowsiness, impaired coordination, dyspepsia, anemia, dry mouth, accommodation disorders, urinary retention, cardiac arrhythmias, and others often limits the possibilities of therapeutic. Therefore, the use of a new generation of anticonvulsants, gabapentin and pregabalin, is promising in pain therapy. The main mechanism of their action is associated with the effect on central sensitization, improvement of neurotransmitter balance towards increased anti-pain GABAERGIC effects and reduction of the effects of glutamate, the main neurotransmitter of pain [2]. Gabapentin It is prescribed at an initial dosage of 300 mg / day with a further increase in the dose to 1800 mg / day. The average duration of treatment is 6 weeks, followed by a slow withdrawal of the drug. In the presence of allodynia, it is recommended to prescribe pregabalin. They start taking 75 mg in the evening for a week, then the dose is gradually increased to 300 mg / day. After the first 3 days of treatment, a positive effect is noted [2, 6].

In some cases, with a long history of pain, antidepressants may also be prescribed. Main The mechanism of their action is aimed at activating antinociceptive systems. Their analgesic effect is due to both direct (increased antinociceptive effects) and indirect (improved mood reduces pain perception) analgesic effects [2]. To date, the main priority is given to dual-acting antidepressants (selective serotonin reuptake inhibitors, SSRIs), since these drugs have pronounced analgesic and antidepressant efficacy and have minimal side effects, unlike tricyclic antidepressants.

In the presence of peripheral paresis, patients with AP are shown physical exercises and therapeutic gymnastics to strengthen muscles and prevent the development of possible contractures. To improve neuromuscular conduction, it is advisable to prescribe anticholinesterase drugs (Proserin, Ipidacrine). Of great importance are the psychological support of patients, explaining to them the causes of the disease, the possibility of a rapid and significant positive effect of treatment if all therapeutic measures are carried out and alcohol consumption is completely eliminated.

Thus, AP is still a common disease. The peculiarities of social status and the variety of clinical manifestations often make the management of patients with AP a difficult therapeutic task, but understanding the mechanisms of pathogenesis and algorithms for the diagnosis and treatment of this disease allows us to hope for a positive prognosis even in this category of patients.

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