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FEATURES OF THE COURSE AND MEASURES OF CORRECTION OF THE NEUROLOGICAL SYNDROME IN VITAMIN B12 DEFICIENCY ANEMIA ASSOCIATED WITH H. PYLORI

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ABSTRACT

Today's article provides a theoretical perspective on vitamin B-12 and the changes in the human nervous system caused by vitamin B-12 deficiency.
Vitamin B-12 or Cobalamin is the most necessary and important vitamin complex for humans. While even a small deficiency of vitamin B-12 can cause anemia, fatigue, obsessive-compulsive disorder, and depression, a long-term deficiency of this vitamin can have negative effects on your brain and central nervous system.

KEYWORDS: *Vitamin B-12, Deficiency, Nervous System, Memory, Chronic Fatigue, Depression, Restlessness, Metabolism, "Cobalamin - R".*

INTRODUCTION

Vitamin B-12 is mainly found naturally, in animal products, and in synthetic forms. There is no harm in taking more vitamin B-12 than you need, the liver stores a 1-year supply and uses it when needed.

Lack of vitamin B-12 mainly causes anemia, frequent mood disorders, has a negative effect on the nervous system, and impairs memory.

Also, vitamin B-12 deficiency can cause shortness of breath, chronic fatigue, depression, restlessness, indigestion, dizziness, drowsiness, liver swelling, eye problems, hallucinations,

headaches, tongue infection, balance problems. It can also cause memory loss, nervous breakdowns, heart attacks, anemia, tinnitus, constipation, and weight loss.

Vitamin B12 is a water-soluble vitamin that is naturally produced by microorganisms, but is not synthesized in the human body. The average daily requirement for vitamin B12 is 2.4 mg for men and non-pregnant women, 2.6 mg for pregnant women and 2.8 mg for lactating women [2].

In foods, B12 is usually found in the form of the coenzyme deoxyadenosylcobalamin or methylcobalamin and is associated with proteins. The first step in vitamin B12 metabolism is its proteolysis in the stomach at low pH, whereby it is released from dietary protein and binds to the R protein of gastric juice. The parietal cells of the stomach produce the internal factor of Castle – a glycoprotein, which, together with the protein complex "cobalamin - R", enters the duodenum. The complex of intrinsic factor Castle and cobalamin in the ileum binds to intrinsic factor cobalamin receptors located on the microvilli of the mucosal cells of the ileum. At neutral pH and in the presence of calcium ions, the “cobalamin-Castle factor” complex decomposes, cobalamin enters the enterocyte, is transferred to transcobalamin II (holotranscobalamin) and, in combination with it, enters the bloodstream. In the presence of a large amount of vitamin B12, about 1% can penetrate into the blood due to passive diffusion [2, 2].

The pathogenetic mechanism of damage to the central and peripheral nervous system in vitamin B12 deficiency remains unclear. A decrease in S-adenosylmethionine (SAM) or an increase in the level of homocysteine and methylmalonic acid (MMA) due to vitamin B12 deficiency can cause a violation of the synthesis of myelin phospholipids with the development of myelopathy and encephalopathy. In addition, SAM affects the synthesis of serotonin, norepinephrine and dopamine, which are related to mental status. Another possible cause of neurological disorders is associated with the role of the metabolically active form of cobalamin (adenosylcobalamin) - a mitochondrial cofactor - in the conversion of L-methylmalonyl-CoA to succinyl-CoA. B12 deficiency leads to an increase in L-methylmalonyl-CoA, which is converted to D-methylmalonyl-CoA and hydrolyzed into MMA. An increase in MMA and branched-chain fatty acids leads to a violation of myelin.

Recent research suggests the following paradigms. B12 deficiency affects the neurotrophic and neurotoxic effects of cytokinins and growth factors such as tumor necrosis factor alpha (TNF), nerve growth factor (NGF), IL-6, and epidermal growth factor (EGF). In experimental studies of blood serum and cerebrospinal fluid in humans and rodents, along with a decrease in the level of vitamin B12, the level of EGF decreases. At the same time, the level of TNF-alpha increases simultaneously with the increase in the level of homocysteine, which leads to a decrease in glial fibrous acidic protein and myelin basic protein. These observations suggest that the clinical and histological changes in vitamin B12 deficiency may result from activation of the neurotoxic effects of cytokines and decreased regulation of neurotrophic factors.

Destruction of myelin in vitamin B12 deficiency occurs in the white matter of the brain. In this case, there are various clinical manifestations of encephalopathy.

In many cases, vitamin B12 deficiency debuts with psychoemotional disorders (fatigue, drowsiness, apathy, depression, emotional lability, aggressiveness, visual and auditory hallucinations, acute psychotic reactions). Focal changes in white matter, usually found in the frontal and parietal lobes of the brain, corpus callosum, can lead to memory loss and impairment

of higher brain functions up to the development of dementia [10, 11]. Cognitive impairment reaching the degree of dementia occurs in 4–16% of patients with pernicious anemia [9].

Among the scientific works of recent years, one can find many publications devoted to the study of dementia and the potential role of homocysteine, folic acid and vitamin B12 in its pathogenesis.

Dementia due to vitamin B12 deficiency has no specific clinical manifestations. In most cases, there is a rapid progression of cognitive impairment with transient episodes of confusion, dementia is accompanied by emotional disturbances, mainly depression. Stem and cerebellar disorders are rarely recorded [9, 13].

Data on the possible reversibility of cognitive impairment associated with vitamin B12 deficiency vary. The literature describes cases of almost complete recovery of cognitive functions and regression of emotional disorders (depression) with mild severity of the defect and the duration of the disease for no more than a year. However, in some cases, even the normalization of the level of vitamin B12 in the blood does not improve cognitive functions. As a rule, this is observed with a significant duration of the disease, the presence of a neurodegenerative disease (Alzheimer's disease, etc.) [9, 15].

It has now been established that B12 deficiency can be considered one of the risk factors for the development of acute cerebrovascular and cardiovascular pathology of atherothrombotic origin. The metabolism of vitamin B12 is closely related to the metabolism of the amino acid homocysteine. Deficiency of B12 and folic acid is the main risk factor for the development of acquired hyperhomocysteinemia [4].

In recent years, many studies have been conducted, the results of which confirmed that hyperhomocysteinemia is an independent risk factor for venous thrombosis and is associated with faster progression of atherosclerotic lesions of large arteries, and therefore with an increased risk of ischemic stroke [1, 18].

When conducting magnetic resonance imaging (MRI) of the brain in patients with elevated levels of homocysteine in the blood serum, more significant cerebral atrophy and atrophy of the hippocampus are detected [9, 14].

A number of studies have shown that hyperhomocysteinemia increases the risk of developing both vascular dementia and Alzheimer's disease, which may indicate common pathogenetic mechanisms of these diseases.

The development of cognitive impairment in hyperhomocysteinemia is based on several pathological processes: cerebral microangiopathy, endothelial dysfunction, oxidative stress, increased beta-amyloid neurotoxicity, and apoptosis [9].

The literature also discusses the role of deficiency of B vitamins, folic acid, and hyperhomocysteinemia in the pathogenesis of the most common motion sickness, Parkinson's disease.

According to the results of the LiangShen study, the level of vitamin B12 in patients with Parkinson's disease is significantly lower than in the control group. However, there is no evidence that eating supplements containing vitamin B12 and folic acid can reduce the risk of

developing Parkinson's disease. Contrasting information exists for vitamin B6: Eating higher concentrations of vitamin B6 may be associated with a reduced risk of developing Parkinson's disease. It is assumed that vitamin B6 reduces this risk not by influencing homocysteine metabolism, but by reducing oxidative stress. Meanwhile, to test this hypothesis and clarify the pathogenetic mechanisms of the protective effect of vitamin B6 in relation to the risk of developing Parkinson's disease, additional studies are required.

A number of studies have shown that B12 inhibits alpha-synuclein fibrillogenesis and modulates the enzyme kinase 2 (LRRK2), which is involved in the pathogenesis of Parkinson's disease [6].

In addition to damage to the brain and spinal cord, vitamin B12 deficiency is often accompanied by damage to the peripheral nervous system, which is usually manifested by distal sensory polyneuropathy. Polyneuropathy is mixed (axonopathy and myelinopathy). The clinical picture of B12-deficient polyneuropathy is nonspecific: one of the first to occur is paresthesia in the extremities (usually in the legs), then a violation of pain and temperature sensitivity of the "gloves and socks" type, weakening of vibration sensitivity, loss of Achilles reflexes, instability when walking. Often B12-deficient polyneuropathy is combined with funicular myelosis.

In about 5% of cases with vitamin B12 deficiency, atrophy of the optic nerves is observed with the appearance of central scotomas and a decrease in visual acuity. Miosis with preserved pupillary reactions is rare. Sometimes there are violations of taste and smell. In some cases, the autonomic nervous system is affected, which is accompanied by orthostatic hypotension and fainting, impotence, fecal and urinary incontinence, and increased urge to urinate.

In most cases, damage to the peripheral nervous system is characterized by a slowly progressing course over weeks or months [9, 21].

Neurological disorders in B12 deficiency, including dementia and other psychiatric disorders, and classic signs of vitamin B12 deficiency such as funicular myelosis and polyneuropathy. In most cases, the initial (minimal) signs of damage to the nervous system in a B12-deficient state last for weeks or months before the onset of pronounced clinical signs. It should be noted that approximately 15% of patients can proceed without characteristic hematological changes (B12-deficient - macrocytic - anemia).

For the treatment of psycho-neurological manifestations of vitamin B12 deficiency, vitamin B12 is prescribed intramuscularly at a daily dose of 1000 mcg for 5 days, then 1000 mcg once a month. Sometimes at the beginning of the course of therapy, there may be some transient deterioration in the condition of patients, the genesis of which remains unclear. Recent randomized trials have shown that, regardless of the etiology of vitamin B12 deficiency, oral administration of this vitamin (ie, cyanocobalamin) is as effective as parenteral administration. Therefore, taking large doses of vitamin B12 (cobalamin) by mouth (orally) is an alternative, as 1% is absorbed by passive diffusion, and 1000 mcg per day gives a daily absorption of 10 mcg, which exceeds the two-microgram recommended daily allowance (in malnourished and malabsorption is prescribed orally 1 mg per day for a month to saturate the vitamin depot, then 125-250 mcg per day as maintenance therapy). To date, the question of preventive vitamin therapy remains open. Some experts recommend that a maintenance dose of vitamin B12 be given to all persons over 60 years of age due to the high prevalence of hypovitaminosis.

Information on the potential reversibility of dementia due to vitamin B12 deficiency is contradictory and based on small studies, however, in some cases, especially with mild cognitive impairment (non-dementia cognitive disorders), complete or significant recovery is possible. There is also evidence that the use of cyanocobalamin reduces the severity of cognitive impairment and depression in patients who have had lacunar infarction. In general, it is believed that if disorders caused by vitamin B12 deficiency exist for more than a year, then their regression, even with adequate therapy, is unlikely (this distinguishes the course of hypovitaminosis B12 in the elderly from that in young people and children who "catch up" with their peers in development and cognitive abilities after the restoration of B12 depot in the body). One reason for the lack of effect of therapy may be the conditionality of cognitive impairment both vitamin B12 deficiency and Alzheimer's disease in the same patient.

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