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EFFICIENCY OF TREATMENT IN DISEASE OF MEGALOBLAST ANEMIA

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✓ ***Resume,***

Anemia associated with a violation of the synthesis of DNA and RNA is a large group of both hereditary and acquired diseases. These anemias combine presence in Bone marrow of megaloblasts - peculiar large cells of a red row with a delicate structure and an unusual arrangement of chromatin in the nucleus.

Synthesis of DNA is disrupted with a deficiency of vitamin B12, folic acid, and some rare hereditary diseases.

Key words: anemia, bone marrow, cells megaloblast, DNA and RNA.

МЕГАЛОБЛАСТ АНЕМИЯЛАРНИ ДАВОЛАШ САМАРАДОРЛИГИ

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✓ ***Резюме,***

ДНК ва РНК синтезининг бузилиши билан боғлиқ бўлган анемиялар ирсий ва орттирилган касалликларнинг катта гурухини ташкил қилади. Бу анемиялар тўғридан тўғри суяк кўмиги патологияси билан бирлашади. Мегалобластлар - ўзига хос тузилишга ва қизил ядро хроматинида ажойиб жойлашиши билан ажралиб турувчи катта ҳужайралар ҳисобланади.

Калит сўзлар: анемия, суяк кўмиги, ҳужайра,мегалобласт, ДНК ва РНК.

ЭФФЕКТИВНОСТИ ЛЕЧЕНИЯ ПРИ БОЛЕЗНИ МЕГАЛОБЛАСТНОЙ АНЕМИИ

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✓ ***Резюме,***

Анемии, связанные с нарушением синтеза ДНК и РНК, - большая группа как наследственных, так и приобретенных заболеваний. Эти анемии объединяет присутствие в

костном мозге мегалобластов - своеобразных больших клеток красного ряда с нежной структурой и необычным расположением хроматина в ядре.

Синтез ДНК нарушается при дефиците витамина B12, фолиевой кислоты, некоторых редких наследственных заболеваниях.

Ключевые слова: анемия, костный мозг,клетка, мегалобласт, ДНК и РНК.

Relevance

Anemia is a clinical and hematological syndrome, characterized by a decrease in the number of red blood cells and hemoglobin in the blood. A variety of pathological processes can serve as the basis for the development of anemic conditions, and therefore anemia should be considered as one of the symptoms of the underlying disease. The prevalence of anemia varies considerably in the range from 0.7 to 6.9%. The cause of anemia can be one of three factors or a combination of them: blood loss, insufficient red blood cell formation or increased destruction (hemolysis).

Among the various anemic conditions, iron deficiency anemia are the most common and constitute about 80% of all anemias.

Iron deficiency anemia is a hypochromic microcytic anemia that develops as a result of an absolute decrease in iron reserves in the body. Iron deficiency anemia occurs, as a rule, in chronic blood loss or inadequate intake of iron in the body.

According to the World Health Organization, every 3rd woman

Iron is an indispensable biometal that plays an important role in the functioning of the cells of many body systems. The biological value of iron is determined by its ability to reversibly oxidize and regenerate. This property ensures the participation of iron in the processes of tissue respiration. Iron makes up only 0.0065% of body weight. The body of a man weighing 70 kg contains about 3.5 g (50 mg / kg body weight) of iron. The iron content in the body of a woman weighing 60 kg is about 2.1 g (35 mg / kg body weight). Iron compounds have a different structure, have characteristic only for them functional activity and play an important biological role. The most important iron-containing compounds include: hemoproteins, which is a structural component of heme (hemoglobin, myoglobin, cytochromes, catalase, peroxidase), enzymes nonheme group (succinate dehydrogenase, acetyl-CoA-dehydrogenase, xanthine oxidase), ferritin, hemosiderin, transferrin. Iron is part of the complex compounds and is distributed in the body as follows:

— heme iron — 70%;

— iron depot — 18% (intracellular accumulation in the form of ferritin and hemosiderin);

— functioning iron — 12% (myoglobin and iron-containing enzymes);

— transported iron — 0.1% (iron associated with transferrin).

There are two types of iron: heme and non-heme. Heme iron is a part of hemoglobin. It is contained only in

a small part of the food ration (meat products), is well absorbed (by 20-30%), other components of food practically do not affect its absorption. Non-heme iron is in the free ionic form - bivalent (Fe II) or ferric iron (Fe III). Most of the dietary iron is non-heme (mainly found in vegetables). The degree of its absorption is lower than that of heme, and depends on a number of factors. Only divalent non-heme iron is absorbed from food products. In order to "turn" trivalent iron into bivalent, a reducing agent is necessary, the role of which in most cases is played by ascorbic acid (vitamin C). In the process of absorption in the cells of the intestinal mucosa, ferrous iron Fe2 + turns into oxide Fe3 + and binds to a special carrier protein, transferrin, which transports iron to hematopoietic tissues and iron deposition sites.

Iron is stored in proteins ferritin and hemosiderin. If necessary, iron can be actively released from ferritin and used for erythropoiesis. Hemosiderin is a ferritin derivative with a higher iron content. From hemosiderin, iron is released slowly.The incipient (pre-absent) iron deficiency can be determined by a reduced ferritin concentration even before the iron reserves are exhausted, while the serum levels of iron and transferrin remain normal.

Megaloblastic anemia is a heterogeneous group of disorders with common morphological features. Megaloblastosis is a universal concept, a violation of the nucleation of the nucleus is observed in all rapidly dividing cells of the body, for example, cells of the gastrointestinal mucosa or uterine mucosa [2].

The etiology of megaloblastic anemia is diverse. The most common causes are folate and cobalamin deficiencies (vitamin B12). Of the causes of cobalamin deficiency, the most frequent are pernicious anemia (PA), impaired cobalamin absorption in the terminal ileum, and the effect of drugs (cytostatics). Folate deficiency is more common due to malnutrition (lack of raw vegetables in the diet), during pregnancy and the use of drugs with antifolate action (methotrexate, 6-mercaptopurine, antiretroviral drugs, etc.). Myeloproliferative diseases and viral infections (for example, HIV), disrupting DNA synthesis, can also lead to megalo-blastosis. Many chemotherapeutic, protivosudorozhennye drugs (phenytoin), contraceptives can cause megaloblastosis.

The molecular basis of megaloblastosis is a violation of the synthesis and assembly of DNA. Despite all the available information, biochemical pathways are not fully understood. This is especially true for cobalamin-associated neuropathy, which can exist independently of hematological changes. Recent studies have shown that folic acid deficiency can also cause neurological damage [3].

A sign of megaloblastic anemia is ineffective erythropoiesis, as evidenced by erythroid hyperplasia in the bone marrow, a decrease in reticulocytes at the periphery, an increase in LDH and indirect bilirubin.These laboratory parameters are a consequence of the internal destruction of brittle and improperly formed erythroid precursors.

People cannot synthesize cobalamin and folic acid, so they depend on the intake of these substances from food. Cobalamin is associated with internal factor (HF), and absorbed in the terminal ileum. After absorption, cobalamin joins another protein, transcobalamin II, and is transported to storage sites. Violations at any stage of transport can lead to shortages. The body contains a significant amount of cobalamin; this explains why the years go by before the deficit develops [3].

Although the absorption and transport of folic acid is difficult, violations rarely occur at these stages, most often the deficit is caused by a dietary deficiency. The amount of folate in the body is small, so the deficit may develop within a few months after stopping folate intake with food. Folic acid deficiency can occur in patients with celiac disease, Crohn's disease, small intestinal lymphoma, amyloidosis, and small intestinal lesions in systemic scleroderma.

Recently began to allocate food-related malabsorption of cobalamin (SPMK). In this condition, cobalamin in sufficient quantities comes from food into the stomach, but its separation from food and absorption do not occur. It should be noted that, according to literary data, SPMK is much more common than it is diagnosed. The reason for the low diagnosis in the absence of a sensitive and specific test for this pathology. Until 2003, the Schilling test was practiced in the United States, but due to the high cost and the failure of insurance companies to pay for it, this test was refused.

In the Schilling test, cobalamin was first taken alone on an empty stomach,

then cobalamin along with HF, and if SPICA was required to be removed, everything was mixed with food. Lack of absorption before adding HF means pernicious anemia (PA), absorption problems after adding HF - diseases of the small intestine, lack of absorption of cobalamin mixed with food - SPMK.

With SPMK, clinical manifestations of cobaminamin deficiency develop much more slowly than with perinitic anemia, since cobalamin absorption from bile is maintained.

A number of authors point to positive clinical dynamics of SPMK after treatment with antibiotics directed against H. ru ^ n [4]. This type of SPHM is considered to be associated with H. ru-yy-associated gastritis, but one should not forget that the majority of patients infected with H. ru ^ n have no clinical and biochemical manifestations of cobalt deficiency. The data requires further study [5].

The frequency of PA - 0.25-0.5 cases per 1000 people over 60 years. Other forms of megaloblastosis are rare. The people of the white race suffer from PA several times more often than people of the Asian and African American races.

Complaints with megaloblastic anemia, which are rarely paid attention to:

- pain in the tongue and mouth;
- change of gait, loss of memory, paresthesia in the fingers and, above all, the legs;
- visual impairment;
- appeals to a psychiatrist;
- diarrhea.

Nutritional features and previous treatment require detailing in the collection of anamnesis. Dietary deficiency is the most common cause of folate deficiency [6]. A typical patient is an elderly person whose diet is poor in raw vegetables and fruits, or who prepares food in large quantities of water with excessive heat. It is also important to register all the drugs the patient is taking (methotrexate, 6-mercaptopurine, antiretroviral drugs).

PA is an autoimmune disease that can be combined with other autoimmune diseases (autoimmune

thyroiditis, type I diabetes, Addison's disease, hypoparathyroidism, autoimmune hemolytic anemia).

The operated stomach or small intestine predisposes to the development of a deficiency of cobalamin. With a total gastrectomy of 3-5 years, with partial gastrectomy approximately 12 years pass before the development of a deficiency of cobalamin. After surgery, blind loop syndrome may develop.

Zollinger-Ellison syndrome can cause megaloblastosis, because an excess of hydrochloric acid makes it impossible to activate pancreatic enzymes, the action of which is necessary for the cobalamin to be released from its association with the r-factor (contained in saliva) before it is combined with HF. Cutting and / or eating raw fish in the past requires eliminating invasion with tapeworm (wide tapeworm).

In patients with psoriasis and ecfoliative dermatitis, folate is further required due to increased exfoliation of epidermal cells. With full parenteral nutrition and hemodialysis, folate deficiency develops because folate is lost in dialysate fluid. It is known that megaloblastosis occurs in people with alcoholism due to folate deficiency due to the competition of alcohol dehydrogenase with folate. Folate deficiency develops in infants when fed with goat milk (low folate content) and some synthetic mixtures.

Objective data. In addition to the symptoms related to the anemic syndrome (shortness of breath, tachycardia, weakness, etc.), symptoms characteristic only of megaloblastic anemias can be observed. Pale skin with a lemon-yellow tint due to a combination of lower hemoglobin with an increase in indirect bilirubin, skin hyperpigmentation and depigmentation of the hair due to increased melanin synthesis is possible.

Characterized by a smooth tongue due to smoothing papillae, the appearance of glossitis. A number of patients have hepatolienal syndrome.

Neuropsychiatric signs of cobalamin deficiency: peripheral neuropathy, irregular gait, loss of balance, loss of proprioception and vibration, blindness due to optic nerve atrophy, loss of memory, mental disorders (depression). Neuropsychiatric complications of folate deficiency are usually limited to irritability.

Patients with PA may have signs of other autoimmune disorders (autoimmune thyroiditis, type I diabetes, Addison's disease, hypoparathyroidism, autoimmune hemolytic anemia).

Erythrocytes are larger in size, oval and have a larger nucleus in relation to the cytoplasm compared to normal erythrocytes. Neutrophils are hypersegmented (b and more lobules in the nucleus); in the megaloblasts of the bone marrow, the maturation of the nucleus is lagging behind the normally maturing cytoplasm. Macrocytic anemia, thrombocytopenia, decrease in reticulocytes are usually observed. The average volume of the erythrocyte is from 100-150 fL and more.

Macrocytosis may be masked by the presence of thalasemia or iron deficiency (anemia will become normocytic). However, neutrophil hypersegmentation may persist.

LDH is a very convenient test for determining hemolysis, a decrease in LDH indicates a positive dynamic and effect of therapy. The ratio of LDH 1 (LDH1) and

LDH 2 (LDH2) increased, with LDH1 / LDH2> 1. It is imperative to investigate serum iron and ferritin, since the treatment of megaloblastic anemia will slow down due to iron deficiency.

Blood cobalamin should be tested as early as possible; if this is not possible for technical reasons, the serum should be frozen until the time of the test. Falsely elevated levels of cobalamin can occur in myeloproliferative diseases, congenital anomalies of cobalamin metabolism, after using nitrous oxide. Falsely low values of cobalamin occur with folate or iron deficiency, with vegetarians, with high doses of ascorbic acid, with pregnant women, with congenital tra-crapalamine deficiency I.

You also need to determine the level of folic acid, as a low level of folate reduces the level of cobalamin. Serum levels of methylmalonic acid and homocysteine in serum increase with cobalamin deficiency, falsely high values of these indicators appear in renal failure.

Antibodies to parietal cells of the stomach are rarely determined, the test is positive in 90% of patients with PA. However, this test is positive for other autoimmune disorders (a test with good specificity but low sensitivity).

Antibodies to HF are extremely rare. Measurement of gastrin and pepsinogen I is used (a test with good sensitivity, but low specificity).

The study of bone marrow is best carried out in the early stages of diagnosis to exclude myelo-dysplasia, and before the appointment of treatment, since the bone marrow changes within 24 hours from the start of treatment. Bone marrow is hypercellular. An increase in the erythroid sprout is manifested by a change in the myeloid-erythroid ratio. Erythroid progenitors with megaloblastic hematopoiesis are larger in size and have a nucleus lagging behind in maturation. Cytoplasmic maturation is normal; Howell-Jolly bodies can be observed in the cytoplasm [7].

Cobalamin deficiency rarely requires immediate treatment and allows for diagnostic testing within a few days. For a long time, for months, existing anemia leads to the development of compensatory mechanisms. Even elderly patients with hemoglobin 50 g / l do not tolerate this condition. Immediate cobalamin parenteral administration requires severe neurological disorders (marked sensory deficiency and gait disturbances), since irreversible changes are possible. An immediate red blood cell transfusion is required only for symptoms of myocardial ischemia, brain, or the threat of heart failure. Unreasonable erythrocyte mass transfusion can enhance hemolysis, so often seen in B12-deficient anemia.

American sources recommend the following: in severe forms, cyanocobalamin (1000 μg) is administered parenterally daily for 2 weeks, then 1 time per week until hematocrit normalizes, then 1 time per month for life. This dose is large, but it is justified in most cases, because 250 mg is deposited in the depot. Patients with neurological complications should receive cyanocobalamin in a dose of 1000 mcg (sometimes more) every day for 2 weeks, then once every 2 weeks for 6 months, and monthly for a lifetime.

Materials and methods

To solve the tasks, we examined 101 patients diagnosed with IDA in the clinic of the Medical Institute.

The results of the study

The oral form of cobalamin (1000 xg) can be prescribed to patients with hemophilia. You can begin treatment with parenteral cobalamin with the transition to oral.

Cobalamin therapy is sometimes required in patients

with a serum cobalamin borderline value and minor neurological impairment. These patients need 50 xg of oral cyanocobalamin daily. When using injectable forms of cobalamin, allergic reactions are more common, requiring the use of anti-histamine or steroid preparations.

A number of authors recommend the administration of potassium preparations during treatment with cobalamin, since potassium is consumed by newly formed red blood cells and the development of hypokalemia is possible. Transfusion of liquids should be limited during the administration of cobalamin.

The currently recommended folic acid supplements for pregnant women and the elderly have reduced folic acid deficiency. A prophylactic dose of folate (1 mg / day) is recommended to be prescribed during pregnancy and the perinatal period, in case of chronic hemolysis.

Currently, folic acid supplementation is recommended for the prevention of atherosclerosis and thromboembolic events, since folic acid reduces blood homocysteine levels. The effect of folic acid on female and male reproductive function has also been proven. Folate (1-5 mg) is prescribed orally.

In no case is it recommended to prescribe a therapeutic dose (1-5 mg / day) of folic acid, if the cause of megaloblastosis is not clear. It is proposed to prescribe a physiological dose of folate 100-400 mcg, since cobalamin deficiency does not respond to such a dose, but it will lead to positive symptoms in patients with folate deficiency.

Consultation specialists. Consultation with a hematologist - if the cause of macrocytosis is unclear, if there is no response to therapy, if there are neurological complications. Consultation of a neurologist - in the presence of neurological complications. Consultation with a gastroenterologist - to exclude PA, blind loop syndrome. The diagnosis of pernicious anemia requires periodic oncological examination of the patient due to the increased risk of developing stomach tumors.

Conclusions

1. Despite the appearance of a surge of strength in the first 24 hours after the administration of cobalamin, hematological changes begin to disappear only a few days later and the first objective criterion is an increase in the level of reticulocytes within 3-5 days with a peak after 4-10 days. In the absence of an increase in reticulocyte levels, an incorrect diagnosis or a concomitant iron deficiency must be assumed.

2. Elevated levels of LDH and indirect bilirubin decrease rapidly. Hemoglobin levels should increase by approximately 1 g / l / week. If hemoglobin does not increase at approximately this rate and does not reach normal numbers within 2 months, there is another reason for anemia.

Leukocytes and platelets are usually restored within days of several days from the start of therapy, and hypersegmented neutrophils may persist for 10-14 days.

3. Reduction of LDH and reticulocytosis are excellent parameters of the effectiveness of therapy in the early stages. The final criterion for the effectiveness of treatment is the normalization of the average red blood cell volume (MCV) by the 8th week of treatment.

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