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# Clinical-Pharmacological Approach to the Rational Treatment of Anemia Syndrome

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Anemia is a pathological disorder of the structure of blood cells, in which the concentration of hemoglobin is reduced. At the same time, the number of red blood cells decreases. Anemia is characterized as a secondary disease and is a symptom of other ailments. Let us examine in detail what anemia is, what are the causes and symptoms of its occurrence, and how anemia can be cured.

## Anemia: symptoms, how to treat

The disease has a second name - anemia. This is a clinical-hematological syndrome that occurs when there is a lack of iron in the body. Anemia itself does not develop, but accompanies many diseases, ranging from viral and infectious diseases to cancer. Therefore, if you experience symptoms indicating the presence of anemia, you should immediately consult a doctor. During the examination, the doctor will be able to understand the causes of the pathology, determine the condition of the blood and prescribe treatment.

## Signs of anemia

Some people call anemia iron deficiency. These concepts can be considered related, but they are not identical. Approximately 17% of men have a deficiency of a component such as iron, 50% of women suffer from manifestations of deficiency. But iron deficiency anemia does not affect everyone. The doctor makes this diagnosis if the level of hemoglobin in the blood is less than 120 g/l. At the same time, the content of red blood cells in the blood should also be reduced to 3.8 million/µl.

It is worth noting that such anemia is considered quite advanced. After all, the blood reacts to iron deficiency last; first, the organs and tissues lack the components. This means that negative processes have already begun in the body. Therefore, it is important to detect signs of anemia in time and begin to fight the disease. The main features are:

the occurrence of muscle weakness. This condition is often attributed to fatigue, but if you notice poor health and weakness regularly, this may indicate anemia;

hair loss and brittle nails indicate the presence of a disease;

the skin becomes yellowish-pale;

there is a burning sensation on the tongue, as if it had been scalded. Altered taste buds are also a sign of the presence of the disease;

Women may experience changes in their menstrual cycle due to blood loss.

The presence of these signs indicates the active development of anemia. You should urgently improve your blood quality, contact a doctor who will help solve problems with anemia. We will tell you below which doctor to contact if you have anemia.

#### Anemia in adults and children

According to WHO, about 2 billion people suffer from anemia worldwide. Among them, the majority of patients are children. 47.4% of preschool children have a similar diagnosis in one form or another, 25.4% of children are susceptible to the disease at school age. Anemia is also common in adults. For whom is it more dangerous? It is difficult to judge, because children are at greater risk, but in adults the treatment period is slightly longer.

One of the reasons for the occurrence of pathology in childhood is rapid growth. The body requires more nutrients; the mechanisms of hematopoiesis have not yet been fully adjusted. That is why some experts consider this pathology safe in childhood. But this is not true, because with a deficiency of components such as iron, appetite is lost and the immune system suffers. This leads to frequent illnesses of a different nature, slow weight gain, and inactivity. Iron deficiency anemia makes the child whiny and irritable.

An adult with iron deficiency anemia may develop a hypoxic coma. With large blood loss, it leads to death. It is important to treat the disease in time. As soon as symptoms of anemia are detected, you should immediately consult a doctor. The doctor will make a diagnosis, improve your overall health, and identify and eliminate hidden threats.

#### Symptoms of anemia

Iron deficiency anemia is not difficult to notice, but most patients consult a doctor in the later stages of the disease. This is due to the fact that anemia does not make itself felt for some time or the symptoms are not particularly bothersome. But, as we have already said, blood damage occurs last, tissues and organs suffer first. Therefore, if symptoms are detected, we strongly recommend that you contact a specialist, undergo an examination and eliminate the disease. Symptoms of anemia include the following:

**Pathogenesis.** The total amount of iron in the body is 4–4.5 g. Iron is involved in the functioning of all biological systems, being an obligatory and indispensable component of various proteins and enzymes that provide the necessary level of systemic and cellular aerobic metabolism, as well as redox homeostasis in the body as a whole. Iron plays an important role in maintaining a high level of immune resistance; its adequate content in the body contributes to the full functioning of nonspecific defense factors, cellular and local immunity. Normal iron content is necessary for complete phagocytosis, synthesis of lysozyme, interferon, ensures high activity of natural killer cells and the bactericidal ability of serum.

The daily requirement for iron is 10 mg for men, 18 mg for women (during pregnancy -38 mg, lactation -33 mg). The need for iron is also increased in active donors. In children and adolescents, due to the increased needs of the growing body and insufficient intake of iron from food, the iron balance is often disturbed.

The main source of iron for humans is food products of animal origin, which contain iron in the most digestible form (as heme). The absorption of iron from foods decreases after heat treatment, freezing, and long-term storage.

Iron, entering the body with food, is absorbed in the intestine (most intensively in the duodenum and the initial part of the jejunum). Iron absorption depends on the nature of the food, the calorie content of the diet and the absorption capacity of the small intestine. Iron in heme is absorbed much better. People who eat meat get more heme iron (in myoglobin) than vegetarians. Strict vegetarians may develop iron deficiency over time because vegetables and grains contain substances that interfere with iron absorption, particularly phosphates. Fructose, hydrochloric,

ascorbic, succinic, pyruvic acids, cysteine, sorbitol and alcohol enhance iron resorption. Ferrous inorganic iron is absorbed much better than oxide iron contained in meat products.

From the gastrointestinal tract (GIT), iron is absorbed only in the divalent state, the conversion to which is ensured by organic acids, in particular ascorbic acid. The main share of absorbed iron in the transport protein, transferrin, is transferred to the bone marrow, where it is used for the synthesis of heme-containing compounds (hemoglobin, myoglobin, enzymes), non-heme enzymes (for example, NADH dehydrogenase), and metalloproteins. In tissues, iron is deposited in the form of ferritin and hemosiderin, with predominant deposition in the liver, spleen and muscles. Iron deficiency in the body develops when iron losses exceed 2 mg/day. .

However, not every iron deficiency is accompanied by anemia; prelatent and latent iron deficiency are also distinguished [2,5]. Prelatent deficiency develops when the intake of iron from food does not meet physiological needs (body growth, menstruation, pregnancy), but the insufficient intake of iron is covered by its reserves. At the same time, iron reserves are depleted. Latent deficiency is the next stage at which the supply of iron to the cells of the erythroid germ is reduced and the production of red blood cells is limited. IDA with hypochromia and microcytosis develops as a result of a long-term negative iron balance, when hemoglobin synthesis decreases.

Diagnostics. To diagnose iron deficiency in the body, indicators characterizing various funds of iron metabolism are determined: transport, functional, reserve and iron regulatory (Table 2). Laboratory signs that allow one to suspect and verify IDA are a low color index, a decrease in the MSI index (below 27 pg, normally 27-35 pg), hypochromia and microcytosis of erythrocytes, a decrease in serum iron levels, an increase in the TI value, a decrease in serum ferritin levels.

**Differential diagnosis** for IDA is also carried out with anemia in chronic diseases, megaloblastic anemia associated with deficiency of vitamin B12 or folic acid, hemolytic and aplastic anemia (possible, among other things, due to the toxic effects of various classes of drugs, occupational hazards, such as lead, benzene) [ 12]. The differential diagnosis of IDA and anemia in chronic diseases is presented in Table 3.

The most common causes of anemia in chronic diseases are chronic infections (diseases of the respiratory system, urinary tract, osteomyelitis), chronic non-infectious diseases (diffuse connective tissue diseases, rheumatic fever), malignant tumors (cancer, lymphogranulomatosis, non-Hodgkin lymphoma, leukemia).

**Treatment.** In accordance with the etiological and pathogenetic factors of IDA, treatment should be comprehensive, aimed at eliminating the cause that caused the disease, and include adequate intake of microelements, vitamins, proteins and correction of iron deficiency.

Iron is absorbed most effectively from foods in which it is contained in the form of heme, when it is actively captured and absorbed by the cells of the intestinal mucosa in unchanged form (beef tongue, rabbit, turkey, chicken, beef). The processes of heme absorption in the intestine do not depend on the acidity of the environment and inhibitory nutrients. As already mentioned, in cereals, fruits and vegetables, iron is in non-heme form, and absorption from them is much worse. The presence of oxalates, phosphates, tannin and other ferroabsorption inhibitors also contributes to a decrease in absorption (Table 4). It should be borne in mind that a diet that is complete and balanced in terms of the main ingredients can only "cover" the body's physiological need for iron, but does not eliminate its deficiency, and should be considered as one of the auxiliary components of therapy.

Currently, the indications for parenteral use of iron preparations have been narrowed: they are used in the presence of intestinal pathology with malabsorption (various enteritis, malabsorption syndrome, resection of the small intestine, Billroth II gastric resection with the formation of a "blind loop"). Parenteral iron supplements may be the treatment of choice if oral iron supplements are poorly tolerated.

Currently, in the treatment of IDA, the oral use of combination drugs (containing both iron salts and other components), the leading of which is Ferro-Folgamma, seems promising.

Ferro-Folgamma (Wörwag Pharma, Germany) is a multifactorial hematopoietic that includes all the necessary components (1 capsule contains 112.6 mg of iron sulfate (equivalent to 37 mg of iron ion), 5 mg of folic acid, 0.010 mg of cyanocobalamin), providing stimulation of the structural synthesis of Hb and increasing the reproduction of red blood cells by the red sprout of the bone marrow. The drug also contains ascorbic acid.

Ferro-Folgamma is prescribed 1 capsule 3 times a day. The best effect is obtained by using the drug after meals. For mild anemia, it is recommended to take 1 capsule 3 times a day, within 3-4 weeks; for moderate forms – 1 capsule 3 times a day, within 8–12 weeks; in severe cases - 1 capsule 3 times a day. within 16 weeks. and more.

The good clinical effect of the drug is confirmed by data from numerous clinical studies. Thus, in the studies of A.L. Vertkina et al. [14] have proven the high effectiveness of the drug Ferro-Folgamma (compared to other ferrodrugs) in the treatment of IDA. The authors observed 83 people (22 men and 61 women) aged from 17 to 92 years (average age – 57.7±1.4 years). In the group, the average hemoglobin level was reduced to 87.8±0.4 g/l, the average duration of anemia was 1.5±0.1 years. The causes of anemia were: acute or chronic blood loss - in 54.3% of cases, malabsorption - in 28.3%, other or combined causes - in 17.3% of cases. When using the drug Ferro-Folgamma, more pronounced positive dynamics of both clinical and laboratory parameters were observed compared with other ferrocontaining drugs [14] (Tables 5 and 6).

The use of Ferro-Folgamma in the correction of IDA in chronic heart failure (CHF) has also been proven to be highly effective [15]. The authors selected for examination and treatment 42 patients with CHF combined with IDA (in the whole group Hb =  $97.1 \pm 3.7$  g/l; serum Fe = 5.84 $\pm 0.51$  mmol/l): in II FC HF – Hb =  $102.3\pm 3.6$  g/l, with FC III HF – Hb =  $97.6\pm 3.3$  g/l, with FC IV HF – Hb =  $84.4\pm3.5$  g/ l. During the treatment of CHF (ACE inhibitors, cardiac glycosides, diuretics), relief of anemic syndrome was carried out by prescribing Ferro-Folgamma (a complex of 100 mg of anhydrous Fe sulfate with 5 mg of folic acid, 10 µg of cyanocobalamin and 100 mg of ascorbic acid) in the total dose for the whole group  $-137.75\pm7.5$  mg Fe.

The clinical effectiveness of the drug Ferro-Folgamma has been most fully studied, which has been successfully used for the treatment of latent iron deficiency (LDI) and manifest iron deficiency (MID) in obstetric and gynecological patients, both alone and in combination with recombinant erythropoietin preparations. The results obtained showed that the unique ratio between the optimal content of ferrous iron, folic acid and cyanocobalamin in one Ferro-Folgamma capsule allows one to achieve excellent results in the treatment of pregnant women, postpartum women and gynecological patients with not only mild, but also moderate and severe MID. The presence of folic acid and cyanocobalamin in the Ferro-Folgamma preparation is its additional advantage, since with MID in pregnant women there is often a deficiency of many vitamins, especially those involved in hematopoiesis. According to the data obtained, if there are indications for the use of recombinant erythropoietin, the optimal oral iron preparation for the combined treatment of MAD in women outside and during pregnancy, as well as after childbirth, is currently Ferro-Folgamma.

Scientific and practical experience convinces us of the feasibility and high efficiency of using Ferro-Folgamma in therapeutic, hematological, obstetric and gynecological practice in the treatment of iron deficiency conditions as a drug with proven effectiveness and safety, with an optimal cost-effectiveness ratio.

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