

CLINICAL LABORATORY DIAGNOSTICS, TREATMENT METHODS AND REHABILITATION OF IRON DEFICIENCY ANEMIA

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Iron deficiency anemia is a clinical hematological disease characterized by a decrease in hemoglobin synthesis due to iron deficiency, dehydration in erythropoiesis, and trophic changes in tissues.

Iron deficiency anemia ranks first among 38 diseases associated with anemia. This pathology is present in 50-60% of women (60% of pregnant women, 30% of children under 2 years old) in Russia, 70% in Japan, and 7-14% in Europe. In our country, iron deficiency is detected in more than half of all children under 3 years old and accounts for approximately 25% of adolescent cases.

The main cause of the development of iron deficiency anemia is the imbalance between the body's need for iron and its utilization. The reasons for this include:

- Blood loss from various localizations (intestinal tract, uterus, nose, stomach, etc.);
- Impaired iron absorption in the small intestine;
- Increased demand for iron (pregnancy, lactation, growth period);
- Impaired iron utilization (various types of hypoproteinemia, transferrin deficiency);
- Digestive system disorders;
- Hemolysis in the blood vessels along with hemoglobinuria;
- Incorrect diet, especially in newborns and children.

The pathogenesis of iron deficiency anemia is based on two main mechanisms:

- A decrease in the amount of hemoglobin leads to hypoxic changes in organs and tissues (this occurs in all types of anemia);
- A decrease in the activity of iron-binding enzymes involved in oxidation-reduction processes in tissues.

The development of iron deficiency anemia can be divided into three stages:

1. In the first stage, iron is mainly used from the body's stores, which leads to a decrease in ferritin levels.
2. The second stage is characterized by hidden iron deficiency. Iron transport and utilization are reduced. The amount of iron in the body decreases, but the level of hemoglobin remains normal. Iron stores (iron in the liver, ferritin) decrease, and compensatory erythropoiesis begins to occur.
3. The third stage is characterized by a decrease in iron levels in the blood and the development of clinical symptoms of iron deficiency anemia.

The clinical manifestations of iron deficiency anemia are not specific and are associated with various degrees of general hypoxic syndrome: general weakness, paleness of the skin, shortness of breath during physical activity, heart palpitations. The following signs of iron deficiency are observed (sideropenic symptoms) in tissues:

- Changes in nails (spoon-shaped, brittle, koilonychia);
- Impaired taste (preference for salty and sour foods) and smell (benzene, acetone-like);
- Muscle weakness;
- Difficulty swallowing dry food;
- Cracking at the corners of the mouth;
- Angular stomatitis;
- Failure to thrive in infants and young children.

The following laboratory changes are observed in iron deficiency anemia according to Table 1.

Table 1. Laboratory changes in iron deficiency anemia.

Laboratory indicators	Reference interval	Changes in iron deficiency anemia
Morphological changes in erythrocytes	Normocytes - 68%; Microcytes - 15.2%; Macrocytes - 16.8%	Anisocytosis, microcytosis, poikilocytosis, and nucleated red blood cells
Hemoglobin composition	Women - at least 120g/l; men - not less than 130g/l	decreases
Mean corpuscular hemoglobin (MCH) in erythrocytes	27(26)–31 pg	less than 26
Mean corpuscular hemoglobin concentration (MCHC) in erythrocytes	31-37%	less than 31%
Mean corpuscular volume (MCV) of erythrocytes	80-100fl	less than 80
Number of reticulocytes	0,2-1,0%	decreased, averaged in blood loss
Serum iron	Women - 12-25 $\mu\text{mol/l}$ Men - 13-30 $\mu\text{mol/l}$	decreased
Total iron-binding capacity	30–85 mkmol/l	average
Transferrin saturation with iron	less than 47 $\mu\text{mol/l}$	decreased
Saturation coefficient of iron transferrin	$\geq 16\%$	decreased
Ferritin level	15–150 mkg/l	decreased.

* The indicator provides information only when there are no signs of a systemic inflammatory reaction (for example, measurements in conjunction with the normal level of C-reactive protein).

Example of a general blood test for iron deficiency anemia: hemoglobin - 70 g/l; erythrocytes - 3.2×10^{12} /l; hematocrit index - 26%; MCV - 64 fl, MCH - 18.5 pg; leukocytes - 7.5×10^9 /l; normal leukocyte formula; platelets - 450×10^9 /l, reticulocytes - 2.6%, ESR - 15 mm/hour. Anisocytosis ++, microcytosis ++, hypochromia.

Diagnostic algorithm for patients with iron deficiency anemia.

List of mandatory medical services in the diagnostic range:

- appointment to a general practitioner (examination, consultation);
- general blood test with platelets and reticulocytes;
- determination of iron deficiency in the blood serum;
- esophagogastroduodenoscopy;
- colonoscopy.

The list of additional medical services is used in case of insufficient information or ineffective treatment in the diagnostic range (a number of tests are carried out in a specialized hematological clinic):

- determination of transferrin level in blood serum;
- determination of ferritin level in blood serum;
- consultation with a gynecologist;
- determination of the ability of blood to bind iron;
- desferal test;
- determination of the lifespan of erythrocytes;
- identification of sideroblasts and siderocytes;
- determination of blood loss volume through the digestive tract using radioactively labeled chromate;
- cytological examination of bone marrow (myelograms);
- histological examination of bone marrow.

Differential diagnosis and additional research are based on the results of a general blood test for iron deficiency anemia. Differential diagnosis is carried out in accordance with the iron deficiency syndrome, excluding the following diseases (the highest risk according to the principle):

- bleeding from the upper and lower gastrointestinal tract;
- two-sided vertical bleeding from the upper and lower gastrointestinal tract with the opening of the diaphragm;
- various etiology of hematuria, helminthic invasion (hookworm disease);
- bleeding during menorrhagia and metrorrhagia;
- natural teleangiectasia with recurrent nasal bleeding;
- iron deficiency in enteritis and digestive system malfunction.

In addition, differential diagnosis of iron deficiency anemia includes anemia caused by impaired hemoglobin synthesis, which is manifested by microcytic anemia

due to porphyrin synthesis disorders (sideroblastic anemia, porphyria, etc.), as well as thalassemia.

Unlike iron deficiency anemia, hypochromic anemia occurs due to the production of excessive iron in the bloodstream and in storage (sideroachresia); in these diseases, signs of iron deficiency anemia may be absent.

Differential diagnosis of anemia caused by impaired porphyrin synthesis is characterized by basophilic punctation of erythrocytes and reticulocytes, an increase in erythropoiesis, and the presence of many sideroblasts in the red bone marrow.

Thalassemia is characterized by similar shape and basophilic punctation of erythrocytes, and

The successful treatment of iron deficiency anemia requires addressing its underlying causes. The basis of pathogenetic therapy for iron deficiency anemia is iron preparations. Therapy can be carried out with iron preparations administered orally or parenterally.

The main guidelines for oral administration of iron preparations are:

1. Determining the appropriate dose of iron preparations, which is 150-200 mg of elemental iron recommended daily for most adults. Higher doses are not logical.

2. Taking iron preparations together with vitamins is not recommended unless specifically indicated. Due to lack of evidence of benefit and possible harm, mono-component preparations should be approved for efficacy and safety before adding vitamins, including group B vitamins (including B12) and folic acid. It is not possible to study drug pharmacokinetics with three or more components.

3. It is not advisable to prescribe iron preparations in cases of malabsorption syndrome.

4. The duration of the therapy should be sufficient (not less than 3 months, and up to 5-6 months).

5. Iron preparations should be continued after the recommended hemoglobin parameters have been achieved.

Table 2. Medications used in the treatment of iron deficiency anemia (pharmacotherapeutic group - iron supplements)

Medicine Group	Drug preparations	Method of Administration	Degree of evidence
Monocomponent preparations of iron			
Iron gluconate	Iron gluconate 300 mg.	Oral administration, 2 tablets 2-3 times a day	II, I, C
Iron sulfate	Iron sulfate 256.3 mg (80 mg iron).	Oral administration 1 tablet twice a day	III, C
	Iron sulfate 325 mg [105 mg iron (II) ions (Fe 2+)].		

Iron fumarate	Iron fumarate 200 tablets, 200 mg (65 mg iron).	Oral administration, 1 tablet 3 times a day	III, C
	Iron fumarate, capsules, 300 mg (100 mg or iron).	Oral administration, 1 capsule 2-4 times a day.	
Iron sulfate + [Ascorbic acid]	Iron sulfate, tablets, 320 mg + ascorbic acid 60 mg	Oral administration, 1 tablet 1-2 times a day	III, C
Iron fumarate + Folic acid	Iron fumarate 163.56 mg (50 mg iron) and folic acid 540 mcg.	Oral administration, 1 capsule twice a day	III, C
Trivalent iron preparations (Fe 3+)			
Iron (III) hydroxide polymaltose	Iron (III) hydroxide polymaltose 400 mg (100 mg elemental iron). Tablets 375 mg (100 mg elemental iron).	Oral administration, 1 chewable tablet 2-3 times a day	II, B

Reasons for therapy failures with iron preparations:

- Inadequate absorption of iron (hypochromic anemia and incorrect identification of iron preparations);
- Insufficient dose of iron preparations;
- Insufficient duration of treatment with iron preparations;
- Patients with malabsorption pathologies related to orally administered iron preparations;
 - Simultaneous use of drugs that interfere with the absorption of iron;
 - The presence of hidden (occult) blood loss, usually from the upper gastrointestinal tract;
- Combination of iron deficiency anemia with other types of anemia syndromes (B12 deficiency, folic acid deficiency).
- Parenteral iron preparations are recommended in hospital settings. Instructions for prescribing parenteral preparations include:
 - Malabsorption in intestinal pathology (enteritis, malabsorption syndrome, resection of the small intestine, resection of the ileum according to the Billroth II method);
 - The negative effect of gastrointestinal side effects cannot be neutralized by other means;
 - Chronic blood loss, which increases the physiological need for iron (e.g., heavy menstrual bleeding, rupture of esophageal varices with the destruction of the venous plexus).

Dispensary monitoring. Patients with iron deficiency anemia should undergo dispensary monitoring with a blood test every 3 months; if the condition worsens,

testing should be performed every month or every 2 months, and monitoring with a stable trend should be conducted once every 6 months. Monitoring of hemoglobin and iron levels should be performed once every 6 months. Iron prophylaxis should be prescribed for all women who have a daily menstrual flow of more than 5 days for several years. A general practitioner should conduct regular check-ups of patients with iron deficiency anemia.

Instructions for hospitalization. The indication for hospitalizing patients with iron deficiency anemia is heart failure with symptoms of moderate or severe severity. Patients with hemoglobin levels above 70 g/L are referred to a district therapist for consultation if hospitalization is necessary.

Iron deficiency testing. The average duration of temporary iron deficiency conditions is 10-14 days for moderate and severe anemia and 10-14 and 15-35 days for moderate and severe anemia, respectively.

Prognosis. The prognosis is good with proper treatment depending on the etiology.

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