

## **IRON DEFICIENCY ANEMIA: CURRENT ASPECTS OF DIAGNOSTICS AND TREATMENT**

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**Abstract.** Anemia is a group of diseases characterized by a decrease in the number of circulating erythrocytes and/or hemoglobin per unit of blood volume below normal for a given age and gender. Chronic iron deficiency anemia (IDA) occurs more often (80–95% of all anemias) in real clinical practice. IDA is often found in the practice of a gastroenterologist and in patients of surgical departments. This review discusses the most significant aspects of the diagnosis and treatment of IDA in the practice of a gastroenterologist and surgeon. Parenteral iron preparations are indicated in cases where there are contraindications to the use of oral preparations or they are ineffective. In surgical practice (if it is necessary to quickly replenish iron in the body) and in gastroenterology (peptic ulcer and duodenal ulcer, a history of surgical interventions in the gastrointestinal tract, Crohn's disease, ulcerative colitis, malabsorption syndrome), parenteral iron preparations are considered as drugs of choice. The results of numerous international and Russian studies indicate the efficacy and safety of iron (III) hydroxide oligoisomaltosate as the drug of choice for the treatment of absolute or functional iron deficiency states in the absence of the effectiveness of oral iron preparations and, if necessary, rapid iron replacement.

**Keywords:** iron deficiency anemia, gastroenterology, surgery, diagnostics, treatment, iron preparations, iron (III) hydroxide oligoisomaltosate, Monofer.

### **Introduction**

Anemias are a group of diseases characterized by a decrease in the number of circulating red blood cells and / or hemoglobin (Hb) per unit of blood volume below normal for a given age and gender.

In accordance with the recommendations of the World Health Organization (WHO), the criterion for anemia is a decrease in Hb concentration to less than 110 g / l for children, less than 120 g / l for women (during pregnancy - less than 110 g / l), less than 130 g / l - for men. According to the severity, anemia is distinguished between mild (blood Hb level above 90 g / l), moderate (Hb 70–89 g / l) and severe (Hb <70 g / l) [1-3].

In clinical practice, the most common chronic iron deficiency anemia - IDA (80–95% of all cases of anemia) - is a painful condition caused by impaired Hb synthesis due to iron deficiency (ID). In the International Classification of Diseases, it corresponds to heading D50 - Iron deficiency anemia.

According to the WHO, more than 2 billion people worldwide have IDA, most of whom are women and children. In developed countries of Europe and on the territory of Russia, about 12% of women of fertile age suffer from IDA, and latent ID is observed in almost 1/2 of this category of women [1, 3–7]. Children get sick less often than adults [8].

The most common problems with IDA are encountered in outpatient practice by a therapist, general practitioner (family doctor), hematologist, and obstetrician-gynecologist at the antenatal clinic [9].

Often, IDA is also found in the practice of a gastroenterologist, since almost any lesion of the gastrointestinal tract (GIT) that causes a defect in the mucous membrane can bleed enough to cause latent bleeding, respectively, cause chronic blood loss and ultimately lead to the development of IDA [ 10, 11]. Endoscopic evaluation of patients with IDA shows that almost 2/3 of patients have gastrointestinal lesions, which are believed to cause occult bleeding [12].

In a hospital, IDA is often found in patients of surgical departments. Thus, in a meta-analysis of 18 large observational studies covering more than 650 thousand surgical patients, it was shown that the average prevalence of preoperative anemia is about 35%, ranging from 10.5 to 47.9% [13]. The incidence of IDA was higher than

in the general population, and there were marked differences in the prevalence of preoperative anemia depending on the type and profile of surgery and patient populations.

Often, when discussing various aspects of the diagnosis and treatment of IDA, one may come across the position that “everything has been well known about IDA for a long time”. This point of view is usually found only in relation to arterial hypertension. However, the problem of arterial hypertension is still relevant. And with regard to IDA in real clinical practice, for various reasons, possible "pitfalls, reefs and shoals" are not taken into account, the underestimation of which can introduce certain difficulties in diagnosis and treatment.

diagnostics of ID and IDA

Currently, there is a predisposition (in the presence of risk factors) and three stages of ID: prelate, latent and IDA [22].

Prelate deficiency is characterized by a decrease in tissue iron stores without a decrease in its consumption for erythropoiesis; it can be assumed if the patient has factors that contribute to an insufficient intake of iron into the body or its increased consumption. This stage has no clinical manifestations. The only laboratory criterion for this stage is a decrease in serum ferritin levels ( $<20 \mu\text{g} / \text{L}$ ).

Latent ID is considered as a functional disorder and accounts for 70% of all iron deficiency states. Latent deficiency is observed with complete depletion of iron stores in the depot, in the absence of clinical signs of anemic syndrome. However, at the same time, different symptoms of hyposiderosis or sideropenic syndrome may already be noted in the clinical picture:

- dry skin, cracks on the surface of the skin of the hands and feet, in the corners of the mouth (angular stomatitis);
- glossitis, accompanied by atrophy of the papillae, soreness and redness of the tongue;

- fragility, thinning, stratification, deformation of nails (koilonychia), which may also have a spoon-like shape;
- hair loss and early graying;
- taste perversion (pica chlorotica): patients eat chalk, coal, clay, ash and / or raw foods - cereals, minced meat, dough;
- addiction to unusual odors: kerosene, fuel oil, gasoline, acetone, shoe polish, naphthalene, exhaust gases of cars - which completely disappears while taking iron preparations;
- dysphagia (difficulty swallowing solid and dry food).

Sideropenic syndrome is caused by tissue ID, which plays an important role as a coenzyme of many metabolic processes in various organs and tissues. moreover, epithelial tissues that need rapid renewal, including the skin and mucous membranes, are particularly affected.

The Hb level with latent ID remains normal, and therefore this condition often remains unrecognized. At the same time, in the general blood test, a decrease in the average content (mean corpuscular hemoglobin - MCH) and average concentration (mean corpuscular hemoglobin concentration - MCHC) Hb in the erythrocyte, a change in the mean corpuscular volume (MCV), their size, shapes and colors (anisocytosis, poikilocytosis, anisochromia). In a biochemical blood test, a decrease in serum ferritin and serum iron, an increase in the total iron-binding capacity of serum are possible.

Thus, it is desirable and possible to diagnose ID at the prelate and latent stages, but this requires a careful history taking and knowledge of diagnostic markers in general and biochemical blood tests.

In accordance with the Federal Clinical Guidelines, screening for anemia from adolescence should be performed in all non-pregnant women every 5-10 years during the entire childbearing age. Women with risk factors for the development of IDA

(profuse blood loss during menstruation or of another nature, insufficient iron intake and a previous IDA diagnosis) are subject to annual screening [23, 24].

When screening in a population with a low prevalence of IDA and in the absence of severe forms of the disease, one should focus not on the data of anamnesis and clinical manifestations (signs of anemia and sideropenia), but on changes in laboratory parameters: Hb, hematocrit, color index, MCV, MCH, MCHS.

Biochemical parameters (serum iron, total iron-binding capacity of serum, serum ferritin, transferrin saturation with iron), as having a high specificity in detecting ID, are recommended to be used only to confirm the diagnosis established on the basis of other tests (for example, hematological) [8, 23, 24].

#### Consequences of prolonged ID

Often at an appointment or a medical examination, when the doctor draws the patient's attention to a decrease in Hb and a decrease in erythrocytes, he hears in response: "Yes, I know ... I've had this for a long time ... I'm already used to it ..." Oral iron supplementation takes a long time period, which reduces the adherence of patients to therapy.

Prolonged uncompensated ID leads to endogenous hemic hypoxia of organs and tissues and, accordingly, deepening of manifestations of secondary immunodeficiency and progression of manifestations of visceral syndrome: disruption of the cardiovascular system; decreased muscle tone, gradual development of muscle atrophy; disorders of the digestive tract; menstrual irregularities in women; the emergence of a threat of miscarriage and premature birth in pregnant women; disruption of the nervous system: a sharp change in mood, anxiety, increased excitability; other visceral pathological conditions.

In patients with ischemic heart disease, anemia is one of the main conditions that provoke ischemia or aggravate its course [15, 16]. In the clinical guidelines for chronic heart failure, anemia is listed among the possible causes of the formation of chronic heart failure [15].

## IDA treatment

The main approaches to the preservation and replenishment of iron in the body, according to the WHO, include [1]:

- diet: eating foods containing bioavailable iron, limiting the use of foods - absorption antagonists;
- fortification - artificial fortification of food with iron and folic acid;
- daily / weekly intake of nutritional supplements containing essential micronutrients;
- Supplementation - saturating drug therapy with iron preparations.

Absorption of iron from food is no more than 2.5 mg / day, while it is absorbed from drugs 15–20 times more. However, for patients with IDA, foods containing sufficient amounts of well-absorbed protein and iron are recommended. Meat products contain iron, which is part of the heme (heme iron), which is absorbed by 25–30%. Iron (liver, eggs, fish), which is part of hemosiderin and ferritin, is absorbed by 10-15%. Iron, which is part of plant products (legumes, soy, spinach, dill, lettuce, apricots, prunes, bread, rice), is absorbed by 3-5%.

Taking a large number of apples, pomegranates, buckwheat is not justified from the point of view of the limited absorption of iron ions from them.

The goals of IDA treatment: it is necessary to eliminate the cause of IDA (identify the source of bleeding or restore the process of iron absorption), replenish the ID in the body, prevent the development of metabolic dystrophic changes in internal organs and maintain their functional capacity in full [1-3].

Drug therapy for IDA is carried out only with iron preparations: trivalent ( $\text{Fe}^{3+}$ ) or bivalent ( $\text{Fe}^{2+}$ ), mainly oral - for a long time, under the control of a detailed blood test. Parenteral (intravenous and intramuscular) iron preparations are indicated in cases where there are contraindications to the use of oral preparations or they are ineffective.

In accordance with the Federal Clinical Recommendations [23, 24] parenteral (intravenous and intramuscular) iron preparations in the treatment of IDA are indicated:

- in severe form of IDA (at present it is quite rare, in less than 3% of cases);
- intolerance to oral iron preparations;
- resistance to treatment with oral iron preparations;
- the presence of gastric ulcer or duodenal ulcer or gastrointestinal surgery, even in history;
- anemia associated with chronic inflammatory bowel diseases - IBD (ulcerative colitis, Crohn's disease);
- chronic kidney disease for the treatment and prevention of anemia in the pre-dialysis and dialysis periods;
- the presence of contraindications to the transfusion of red blood cells, including for religious beliefs (for example, representatives of the sect of Jehovah's Witnesses);
- the need to quickly saturate the body with iron (emergency surgery).

Other indications include: violation of intestinal absorption (bowel resection, malabsorption syndrome), extensive ulcerative surfaces on the gastrointestinal mucosa; treatment with erythropoietins, when the need for iron increases sharply, but for a short time (2-3 hours after administration of erythropoietin) due to its active consumption by erythrocytes.

Thus, in surgical practice (if it is necessary to quickly replenish iron in the body) and in gastroenterology (peptic ulcer and duodenal ulcer, a history of surgical interventions on the gastrointestinal tract, Crohn's disease, ulcerative colitis, malabsorption syndrome), parenteral iron preparations are considered as drugs of choice.

It should be noted that intravenous iron preparations can help overcome the blockade of iron metabolism (“hepcidin block”) and reduce the level of hepcidin in

patients with cancer and chronic diseases [25, 26]. The efficacy and safety of modern intravenous iron preparations are noted in the practical recommendations of an international group of experts on the diagnosis and treatment of anemia and ID in surgical patients in the perioperative period [27, 28], international [29–32] and domestic [33–36] guidelines for patient management. with Crohn's disease. Thus, the European consensus [29] states that intravenous iron supplementation should be the first line of therapy in patients with IBD, with a previous intolerance to oral iron supplements, with Hb levels  $<100 \text{ g / l}$  and in patients requiring therapy. erythropoietins. After successful normalization of complete blood counts, resumption of therapy with intravenous iron preparations is indicated when serum ferritin ( $<100 \mu\text{g / L}$ ) or Hb level ( $<120$  or  $130 \text{ g / L}$ , depending on gender) decreases [29].

Modern intravenous iron preparations are an important component in the framework of current trends in surgical practice - bloodless surgery and patient blood management. Bloodless surgery (blood-saving technologies, blood-saving) is a direction in surgery and transfusiology aimed at developing technologies that contribute to the most complete preservation of the patient's own blood and the minimum use of donor blood components when performing extensive surgical interventions [37, 38].

PCR is an evidence-based, interdisciplinary approach to optimizing the treatment of patients who may require a blood transfusion. The MCP covers all aspects of patient examination and treatment related to the decision-making process for blood transfusion, including the use of appropriate indications, as well as minimization of blood loss, including medication. MCP can reduce the need for transfusion of allogeneic blood components and reduce health care costs, while ensuring that blood components are available to the patients who need them [38–40]. In many respects, the MCP corresponds to the ideology of blood preservation [37], but somewhat goes beyond the scope of transfusiology and is aimed at improving the



clinical outcome by eliminating unnecessary blood transfusions. The ITUC is based on three “pillars”:

- 1) optimization of blood volume and erythrocyte mass;
- 2) minimization of blood loss (including medication tozno);
- 3) optimization of the patient's tolerance of anemia [38–40].

Thus, MCP optimizes the use of donated blood and reduces the risk associated with transfusion.

Blood transfusions for IDA are carried out to patients only for health reasons (with a drop in Hb <40-50 g / l), and the indication is not so much the level of Hb, but the general condition of the patient and his hemodynamics.

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