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The Origin and Diagnosis of Iron Deficiency Anemia in a Modern Interpretation

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Annotation: Anemia is a group of diseases characterized by a decrease in the number of circulating red blood cells and/or hemoglobin per unit volume of blood for a given age and gender. Most often (80-95% of all anemias) in the real clinical practice of a therapist, chronic iron deficiency anemia (IDA) is encountered. Often, when discussing various aspects of the diagnosis and treatment of IDA, one can come across the position that everything about IDA has long been known and well known. However, in real clinical practice, for various reasons, pitfalls, reefs and shallows are forgotten, the underestimation of which can lead to certain difficulties in diagnosis and treatment. The presented review discusses the most important aspects of the diagnosis and treatment of IDA.

Keywords: sorbifer durules, clinical presentation, iron preparations, iron deficiency anemia, diagnostics, prevention, treatment.

Introduction: Anemia is a group of diseases characterized by a lower than normal number of red blood cells and/or hemoglobin (Hb) per unit volume of blood for a given age and gender.

According to WHO recommendations, the criterion for anemia for children is a decrease in Hb concentration to a level of less than 110 g / l, for women - less than 120 g / l (during pregnancy - less than 110 g / l), and for men - less than 130 g / l. Depending on the severity, anemia is classified as mild (Hb level in the blood is more than 90 g / l), moderate (Hb 70-89 g / l) and severe (Hb less than 70 g / l) [1].

In the real clinical practice of the therapist, chronic iron deficiency anemia (IDA) is often encountered (80-95% of all cases of anemia) - a painful condition resulting from impaired hemoglobin synthesis due to iron deficiency. In ICD-10, it falls under category D50 - iron

deficiency anemia.

According to WHO, more than 2 billion people worldwide have IDA, the majority of whom are women and children. In developed European countries and Russia, approximately 12% of women of childbearing age suffer from IDA, and almost half of these women have latent iron deficiency [1-5]. Children are less likely to be affected than adults [6].

The problem of IDA is most often encountered in practice by a therapist, general practitioner (family doctor), hematologist and obstetrician-gynecologist. According to the standards, the competence of these specialists includes the identification of IDA based on clinical signs and peripheral blood picture, the development of a program of diagnostic and treatment measures, and the justification of a program of preventive measures in patients with IDA, taking into account the presence of risk factors for its recurrence.

Often, when discussing various aspects of the diagnosis and treatment of IDA, one can encounter the position that "everything has been known for a long time and is well known" about this disease. However, the problem of IDA is still relevant, if in real clinical practice, for various reasons, traps, reefs and shores are often forgotten, their underestimation can lead to certain difficulties in diagnosis and treatment.

Below we present, in our opinion, the most important aspects of the diagnosis and treatment of IDA.

All anemias are secondary and usually represent a manifestation of the underlying disease. The presence of anemia always indicates some kind of disorder in the body. Therefore, even when IDA is given priority in the diagnosis, one should not forget about the need to search for its etiology.

chronic blood loss of various localizations: uterine (heavy menstruation, dysfunctional uterine bleeding), gastrointestinal tract (reflux esophagitis, erosive and ulcerative diseases of the stomach, tumors of the stomach and colon, Crohn's disease, ulcerative colitis, hemorrhoids, hemorrhoids), renal (glomerulonephritis, urolithiasis, with tumors), gingival, into closed cavities and tissues (isolated pulmonary hemosiderosis, ectopic endometriosis);

increased need for iron: pregnancy, lactation; intensive growth during puberty; premenopausal period; treatment of macrocytic (B12 deficiency) anemia with vitamin B12;

Insufficient intake of iron from food (for example, during fasting, vegetarianism and veganism), mainly due to the lack of meat products, does not compensate for its loss due to the destruction of red blood cells;

impaired iron absorption: enteritis of various origins; malabsorption syndrome; postoperative conditions (gastric resection with duodenal resection, small bowel resection), taking drugs that inhibit iron absorption; eating foods with high phytate or phenolic compounds;

Iron transport disorders (hypoproteinemia of various origins).

Research methods and materials: The diversity of factors underlying the development of IDA makes the problem of their differential diagnosis interdisciplinary, which requires doctors of various specialties to have competent skills and abilities to determine the cause of anemia [7, 8].

Three groups of the population are considered to be most vulnerable to anemia: preschool children (0-5 years); pregnant women; women of childbearing age (15-50 years) [9]. The incidence of these categories of the population in the Russian Federation is as follows (as a percentage of all cases of anemia): 26.5% - preschool children, 20.8% - pregnant women and 19.8% - women of childbearing age. In the World Health Organization's anemia prevalence rating, Russia is classified as a country with serious health problems (20-39.9% of the population suffers from anemia), which requires mandatory implementation of WHO recommendations to reduce the global risk of morbidity and mortality [10, 11].

As part of the reform of primary health care in the diagnosis and treatment of anemia in children,

a leading role is given to the district pediatrician and a general practitioner working with a mixed population (children and adults). When providing preventive advice to patients as part of a medical examination, the district doctor and general practitioner should remember the classic thesis that a child born to an anemic mother is also potentially anemic.

Iron deficiency in women is mainly caused by blood loss. In adolescent girls, women of childbearing and menopausal age, iron deficiency often develops in cases of heavy and prolonged menstruation, dysfunctional uterine bleeding, uterine fibroids, endometriosis, the presence of intrauterine contraceptive devices, and significant blood loss during gynecological and surgical operations.

A large epidemiological study conducted in America showed that women, even in the absence of clinical signs of anemia, consistently exhibit iron deficiency throughout the reproductive years [12].

Uterine fibroids and endometriosis are the most common gynecological diseases that are prone to rejuvenation; the percentage of anemia in pregnant women is also increasing, therefore the issue of timely diagnosis, adequate, modern treatment and prevention of IDA in women is becoming increasingly urgent [2, 3, 13-16].

However, the presence of a complicated gynecological history does not preclude the need to look for other causes of iron loss in women. In particular, gastrointestinal (GI) bleeding is the second most common cause of iron deficiency in women and the first in men [17-20].

Currently, iron deficiency is predisposed (in the presence of risk factors) and three stages are distinguished: prelatent, latent, and IDA [21, 22].

Prelatent deficiency is characterized by a decrease in tissue iron stores without a decrease in erythropoiesis expenditure. This stage has no clinical manifestations. The only laboratory criterion for this stage is a decrease in serum ferritin levels (<20 μg/L).

Latent iron deficiency is considered a functional disorder and accounts for 70% of all cases of iron deficiency. Latent deficiency is observed in the absence of clinical signs of anemia syndrome, with complete depletion of depot iron reserves. However, in this case, in the clinical picture, various signs of sideropenic syndrome or hyposiderosis can already be noted: dry skin, cracks on the surface of the skin of the hands and feet, in the corners of the mouth (angular stomatitis); glossitis, papillary atrophy, accompanied by pain and redness of the tongue; brittleness, thinness, splitting of the nails, deformation of the nails (koilonychia), which can also have a spoon shape; hair loss and premature graying; taste disturbance (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, car exhaust fumes, which completely disappear with the use of iron supplements; dysphagia (difficulty swallowing solid and dry food). Sideropenic syndrome occurs due to tissue deficiency of iron, which plays an important role as a coenzyme in many metabolic processes in various organs and tissues, especially epithelial tissues that require rapid renewal, including the skin and mucous membranes, suffer.

Results: In latent iron deficiency, hemoglobin levels remain normal, so this condition is often not recognized. However, a complete blood count may already show a decrease in the mean corpuscular hemoglobin content (MCH) and mean corpuscular hemoglobin concentration (MCHC) of hemoglobin in erythrocytes, a decrease in the mean corpuscular volume (MCV) of erythrocytes, a change in their size, shape and color (anisocytosis, poikilocytosis, anisocytosis). A biochemical blood test may show a decrease in the concentration of ferritin and iron in the blood serum and an increase in the total iron binding capacity (TIBC) of serum.

Thus, iron deficiency can be diagnosed in prelatent and latent stages, but for this it is necessary to carefully collect anamnesis and know the diagnostic signs in general and biochemical blood tests. This is especially relevant for women of reproductive age and pregnant women, since iron

deficiency in pregnant women can develop at any stage of pregnancy due to increased consumption and / or insufficient iron intake, when the iron balance is on the verge of deficiency, and various factors that reduce or increase iron consumption can lead to the development of IDA, which is often detected in pregnant women. In the absence of severe forms of the disease, when screening is carried out in a population with a low prevalence of IDA, it is necessary to focus not on the anamnesis and clinical manifestations (signs of anemia and sideropenia), but on changes in laboratory parameters: Hb, hematocrit, color index, MCV, MHC, MCHC.

Biochemical indicators with high specificity for iron deficiency (serum iron, total serum iron binding capacity, ferritin, iron-transferrin saturation coefficient) are recommended to be used only to confirm a diagnosis established on the basis of other tests (e.g., hematological) [6, 27, 28].

However, in clinical practice, iron deficiency is most often diagnosed at the IDA stage, when the clinical manifestations of anemia syndrome and a complete blood count show a decrease in Hb level, red blood cell count, and color index. Anemia syndrome is caused by tissue hypoxia, the manifestations of which are universal for all types of anemia. These include weakness and / or fatigue; pallor of the skin and mucous membranes (better determined in natural room lighting when Hb level drops to 100 g / l and below); headache and / or throbbing in the temples; dizziness, fainting. Other manifestations of anemia syndrome, which are not always associated with IDA in real clinical practice, include shortness of breath and palpitations during ordinary physical activity; decreased stress tolerance; increased angina pain in ischemic heart disease (IHD); the emergence of resistance to vasodilator therapy in coronary heart disease [8, 29].

The main laboratory criteria for IDA include a low color index; erythrocyte hypochromia, microcytosis; decreased serum iron levels; increased serum total iron binding capacity, and decreased serum ferritin levels.

Since 2018, a clinical blood test (at least in the volume that determines the concentration of Hb in erythrocytes, the number of leukocytes and the erythrocyte sedimentation rate) has been excluded from the list of mandatory tests during a general medical examination of the population under 39 years of age, and after reaching this age every 36.5 years: then at the same interval. Although, if there are indications, this study is still allowed. In the current situation, a complete collection of anamnesis and assessment of existing clinical symptoms are of great importance in terms of diagnosing IDA as part of a medical examination to determine the indications for a clinical blood test.

Clinical manifestations of iron deficiency appear after a long latent period, which corresponds to the depletion of the body's reserves of this element. The severity of symptoms can vary and depends on the cause, the rate of blood loss, the sex and age of the patient. The severity of the condition is associated with a decrease in the ability of blood and tissues to bind oxygen iron deficiency.

The main clinical manifestations of IDA include anemia, circulatory-hypoxic and sideropenicic syndromes (including visceral signs of sideropenia). In addition, secondary immunodeficiency syndrome may develop, which manifests itself as a tendency to frequent recurrence and chronicity of infectious and inflammatory diseases.

A decrease in the activity of some iron-containing enzymes in leukocytes impairs their phagocytic and bactericidal functions and inhibits protective immune responses. This is also facilitated by a violation of the formation of cytokines by leukocytes during iron deficiency, in particular interleukin-1, which plays an important role in cellular and humoral immunity and nonspecific defense mechanisms. Other immune disorders in IDA include a decrease in the number of lysozyme, beta-lysins, complement, some immunoglobulins, and T- and B-lymphocytes [1, 30, 31].

Visceral manifestations of circulatory hypoxic syndrome and sideropenia include:

damage to the gastrointestinal tract: glossitis, dysphagia, decreased acid-producing function of the stomach, sub- and atrophic gastritis, bloating, constipation, diarrhea;

changes in the cardiovascular system: shortness of breath, tachycardia, anginal pain, muffled heart sounds and the presence of a systolic murmur at the top, a decrease in the T wave on the ECG is possible;

CNS damage: decreased memory and ability to concentrate;

damage to the muscular frame and sphincters: muscle weakness under normal load, mixed urinary incontinence in the absence of changes in urine tests.

However, the above symptoms are not always associated with IDA. And then IDA can be detected completely by chance during the examination of patients who seek medical help for diseases that are aggravated by the development of anemia - unstable angina, heart or respiratory failure, vascular encephalopathy, intermittent claudication [28, 32-36].

It should be remembered that another group of clinical manifestations of anemia can be symptoms of diseases that led to the development of IDA: bleeding, gynecological pathology, gastrointestinal diseases, chronic hepatitis and liver cirrhosis, alcoholism, etc. [8].

Discussion: Often, during an appointment or medical examination, when a therapist draws the patient's attention to a decrease in hemoglobin and a decrease in red blood cells, he hears in response: “Yes, I have had this for a long time ... I'm already used to it ...” Long-term uncompensated iron deficiency leads to a profound weakening of endogenous hemoglobin and tissue manifestations of visceral syndrome: disorders of the cardiovascular system; decreased muscle tone, gradual development of muscle atrophy; disorders of the digestive system; menstrual disorders in women; the threat of abortion and premature birth in pregnant women; disorders of the nervous system: sharp mood swings, anxiety, increased excitability; other visceral and psychological pathological conditions.

In patients with coronary heart disease, anemia is one of the main conditions that can provoke or worsen ischemia [29, 36]. Clinical guidelines for chronic heart failure list anemia as a possible cause of this condition [37].

Conclusion: The most important aspect of the work of a general practitioner/therapist at the primary care stage is the prevention of IDA, which should be carried out in the presence of latent signs of iron (Fe) deficiency or risk factors for the development of such anemia. In this category of patients, Hb and serum Fe tests should be performed at least once a year.

The possibility of Fe deficiency with the subsequent development of IDA exists in the following categories of patients [27]:

a. donors who donate blood regularly (especially women);
b. pregnant women (especially with frequent recurrent pregnancies against the background of IDA);
c. women with prolonged (more than 5 days) and heavy bleeding;
d. premature babies or babies born from multiple pregnancies;

girls during puberty, rapid growth, increased physical activity (growing muscle mass absorbs a lot of Fe), limited meat products in the diet;

patients with persistent and difficult-to-relieve blood loss (with gastric, intestinal, nasal, uterine and hemorrhoidal bleeding);

Patients who use nonsteroidal anti-inflammatory drugs (NSAIDs) for a long time; Primary preventive measures for the prevention of anemia are aimed at maintaining a balance between Fe intake and loss [1, 11]. According to WHO, the main approaches to maintaining and replenishing

Fe in the body include the following [1]

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