



## Pathogenetic and Combined Treatment of Iron Deficiency Anemia with Drugs Increasing Erythropoiesis

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### ABSTRACT

An increase in the amount of iron in the body leads to stimulation of the synthesis of hepcidin, which reduces iron absorption in the intestine, transport and circulation. In turn, a decrease in iron absorption in the intestine leads to inhibition of hepcidin synthesis in the liver and, in feedback, to the restoration of iron uptake from food and intestines. So far, antibodies against hepcidin have not been obtained and it is not possible to measure its level in a clinical setting. Work in this direction is underway.

### Keywords:

hepcidin, iron amounts, transport protein, iron balance, liposomal iron, ferritin.

**Introduction.** According to the literature, IDA is observed in 30% of the world's population, and latent iron deficiency occurs 2 times more often [4]. In some regions of the Republic of Uzbekistan, latent iron deficiency reaches 50-60%.

The balance of iron in the body is maintained by the amount of incoming iron and its losses. The body ensures the balance of iron by regulating the process of its absorption in the intestines. In the case of the development of iron deficiency, the percentage of absorbed iron increases, with its excess, it decreases. In this process, hepcidin, a protein synthesized in the liver, is of key importance [1]. Hepcidin, an amino acid peptide, is a direct mediator in the pathogenesis of anemia in chronic diseases, directly reducing the absorption of iron in the small intestine, blocking its release from macrophages [5].

In addition to IDA, patients are diagnosed with anemia of chronic disease (ACD), which is characterized by sufficient iron reserves in the reticuloendothelial tissue of the body, but a

reduced level of serum iron and saturation of the main carrier and distributor of iron - transferrin (a transport protein that delivers iron to the bone marrow from tissue depots).). In patients with inflammatory bowel disease (IBD) (ulcerative colitis (UC), Crohn's disease), ACD and IDA are most often combined [3].

Today, the main link in the pathogenesis of ACD is considered to be hyperproduction of pro-inflammatory cytokines, such as TNF-alpha, interleukins 1, 6, 10, gamma-interferon. They lead to inhibition of erythropoietin synthesis and significantly reduce its effects aimed at enhancing the proliferation and maturation of erythroid precursors, as well as enhance free radical reactions and apoptosis processes [2]. The severity of anemia in IBD may increase due to the action of other factors (repeated episodes of blood loss, the influence of drugs, vitamin deficiency, etc.).

Thus, achieving success in the treatment of IDA is impossible without treating the underlying disease, eliminating, if possible, the etiological factor, reducing the activity of the pathological

process, and correcting the anemia itself. Treatment of anemia should be comprehensive and include nutritional optimization and the appointment of modern iron preparations, the effectiveness of which depends on the choice of the drug and the method of its administration.

**Purpose of the study.** The aim of the study is to study the pathogenesis and concomitant treatment of iron deficiency anemia with drugs that enhance erythropoiesis.

**Materials and research methods.** To accomplish our task, we selected a total of 60 patients with iron deficiency anemia and conducted pathogenetic and combined treatment with drugs that enhance erythropoiesis.

**Research results.** Characteristics of patients of the 1st (main) group who took a combination of liposomal iron and vitamin C: age of patients - from 25 to 80 years (mean age  $47.5 \pm 3.6$  years); women - 26, men - 14. Anemia of mild severity (Hb 90-109 g/l) was in 26 patients, the average level of Hb in these patients reached  $106 \pm 2.2$  g/l.

Anemia of moderate severity (Hb 70-89 g/l) was in 14 patients, the average level of Hb in this group reached  $83.1 \pm 1.4$  g/l. The average level of Hb in the group as a whole was  $97.9 \pm 2.2$  g/l. The level of serum iron initially in the group averaged  $4.9 \pm 1.2$   $\mu\text{mol/l}$ , the average level of ferritin before treatment was  $24.45 \pm 10.6$   $\mu\text{g/l}$ , transferrin was  $2.72 \pm 0.9$  g/l, reticulocytes -  $4.0 \pm 2.2$  (Table 2).

During treatment, in 8 patients who received a combination of liposomal iron and vitamin C, 1 capsule per day, due to recurrent blood loss (6 women had heavy menstruation, 1 man with UC had blood in the stool), 1 woman with peptic ulcer and gluten-sensitive celiac disease) after 1 month. treatment due to the lack of dynamics of Hb indicators, the dose of liposomal iron was increased to 2 capsules / day.

The value of the increase in Hb after 1 month. in general, the group was 19.3 g/l, after 2 months. - 24.3 g/l (with mild anemia, the increase is 15.3 g/l, with an average degree -

27.4 g/l). Normalization of the level of Hb in the blood after 2 months. taking the drug was noted in 24 patients (13 women and 11 men). An increase in the level of Hb against the background of taking liposomal iron was accompanied by an increase in serum iron, transferrin level, and the number of reticulocytes in the blood. In 23 patients after 2 weeks. there was a pronounced reticulocyte crisis.

Significant changes in the concentration of ferritin in the blood serum after 2 months. treatment did not occur.

It should be noted that normal serum ferritin levels vary widely (from 20 to 200  $\mu\text{g/l}$ ). Initially, 24 patients had a decrease in serum ferritin concentration  $< 20$   $\mu\text{g/l}$ , however, in some patients, its level reached high values, approaching the upper limit of normal. Perhaps this was due to the combination of IDA and ACD, in particular, in patients with IBD (2 with UC), in 2 patients with menorrhagia and salpingo-oophoritis. Being an "inflammatory protein", ferritin does not sufficiently specifically reflect iron stores in the human body, which results in the absence of a noticeable change in the average ferritin values in our study.

No side effects have been reported with the combination of liposomal iron with vitamin C. All patients noted good tolerability of the drug. In the main group, the relief of clinical signs of the disease (general weakness, dizziness during physical exertion) was ascertained by the 2nd visit (after 2 weeks). Such objective signs as pallor of the skin, tachycardia, hypotension were not observed at the 3rd visit (1 month after the start of treatment).

Anemia of mild severity was noted in 28 patients, the average level of Hb in these patients was  $99.09 \pm 2.8$  g/l. Anemia of moderate severity (Hb 70-89 g/l) was observed in 12 patients, the average level of Hb was  $78 \pm 3.2$  g/l. The average level of Hb in the whole group (40 people) was  $93.0 \pm 3.1$  g/l. The level of serum iron initially in the group reached an average of  $5.14 \pm 1.3$  mmol/l. The level of ferritin before treatment was  $37.9 \pm 10.2$   $\mu\text{g/l}$ , transferrin -  $2.59 \pm 1.3$  g/l, reticulocytes -  $5.0 \pm 1.7$  0/00.

**Conclusion.** Liposomal Iron with Vitamin C is an effective product for the treatment of IDA. The appointment of 1 capsule / day (30 mg of liposomal iron) provides for 2 months. a steady increase in Hb indicators with an increase in its level of  $\geq 20$  g / l in 60% of cases, at a dose of 2 capsules / day (60 mg of liposomal iron) - in 100% of cases. Normalization of the blood Hb level (against the background of a 2-month intake) was noted in 24 patients (60%), the magnitude of the increase in Hb after 2 months. treatment amounted to 24.3 g/l. Liposomal iron in combination with vitamin C is a safe and effective drug, well tolerated by patients and did not cause side effects in any case.

The preparation of 2-valent iron with vitamin C, chosen as a reference drug, prescribed 2 tablets per day (equivalent to 200 mg of 2-valent iron) for 2 months. provided an increase in hemoglobin with an increase in its level of  $\geq 20$  g / l in 82.5% of cases, at a dose of 1 table / day - in 80% of cases. Normalization of the level of Hb in the blood was observed in 31 patients (77.5%), the value of the increase in Hb after 2 months. treatment amounted to 34.0 g/l. The frequency of side effects was 17.5% (in the form of nausea, diarrhea and discomfort and pain in the epigastrium).

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