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**TREATMENT OF PATIENTS WITH CHRONIC HEART FAILURE AND ANEMIA OR IRON DEFICIENCY****ЛЕЧЕНИЕ ПАЦИЕНТОВ С ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТЬЮ И АНЕМИЕЙ ИЛИ ДЕФИЦИТОМ ЖЕЛЕЗА****Khaniukov O.O./ Ханюков А.А.***d.med.s., prof. / д.мед.н., проф.*

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**Abstract.** Anemia and iron deficiency is widespread among patients with chronic heart failure (CHF) and is associated in such patients with reduced ability to exercise, a deterioration in the quality of life and a worse prognosis, regardless of the presence of anemia, so correction of iron deficiency is an actual issue in the context of the treatment of patients with CHF.

*This work presents review of literature about treatment of anemia and iron deficiency in patients with chronic heart failure.*

*Clinical studies of intravenous iron therapy in patients with symptomatic CHF and decreased left ventricular ejection fraction demonstrate that correction of iron deficiency is associated with significant increase in exercise tolerance, decrease in symptoms and hospital admissions, improvement in the quality of life. The use of iron carboxymaltosate in patients with CHF decompensation prevents subsequent decompensations. As for oral therapy with iron preparations, which are often used as the first line of therapy for iron deficiency in patients with CHF. Treatment with such a dosage form does not have sufficient clinical data to confirm its effectiveness.*

**Key words:** anemia, iron deficiency, chronic heart failure, treatment.

**Relevance:** iron deficiency is widespread among patients with chronic heart failure (CHF) and is associated in such patients with reduced ability to exercise, poor quality of life and worse prognosis regardless of the presence of anemia. The correction of iron deficiency becomes topical issue in the context of the treatment of patients with CHF.

Similarly, management of anemia tends to focus primarily on identifying its etiology, pathogenesis and further treatment corresponding to the cause, but rather common problem of determining the cause makes difficult the further treatment [1].

Existing current recommendations of the world associations of cardiologists on treatment of iron deficiency in patients with CHF (table 1) are formed on the basis of two randomized trials [2,3] and meta-analysis of randomized clinical research [4].



**Table 1. – Summary guideline recommendations for iron therapy in heart failure [5]**

Assosiation	Recommendations	Class of recommendation	Level of evidence
American College of Cardiology/American Heart Association/Heart Failure Society of America 2017 [6]	In patients with NYHA class II and III HF and iron deficiency (ferritin < 100 ng/ml or 100-300 ng/ml if transferrin saturation < 20%) intravenous iron replacement might reasonable to improve functional status and quality of life	I Ib	B
European Society of Cardiology 2016 [7]	Intravenous ferric carboxymaltose should be considered in symptomatic patients with HF with reduced EF and iron deficiency (ferritin < 100 ng/ml or 100-299 ng/ml if transferrin saturation < 20%) to alleviate HF symptoms and improve exercise capacity and quality of life	IIa	A
Canadian Cardiology Society 2017 [8]	Recommend intravenous iron therapy to consider for patients with HF with reduced EF and iron deficiency, in view of improving exercise tolerance, quality of life and reducing hospitalizations	Strong recommendation	Moderate-quality evidence

*HF – heart failure, EF – ejection fraction, NYHA - New York Heart Association Functional Classification*

According to the recommendations of the world associations of cardiologists, intravenous iron therapy is indicated for patients with CHF with reduced ejection fraction (EF) left ventricle (less 40%) and iron deficiency (ferritin less 100 mcg/l OR ferritin = 100-299 µg/l if transferrin saturation less 20%) (Table 1).

The AFFIRM-AHF [9] study, in addition to the recommendations regarding stable CHF, confirms the feasibility of starting to eliminate iron deficiency immediately after an episode of CHF decompensation for reducing the risk of subsequent hospitalizations.

Contraindications for the use of iron carboxymaltose in patients with CHF are – hypersensitivity to the active substance or any of the additional, drug components; known hypersensitivity to other drugs, iron for parenteral use; the presence of anemia



not associated with iron deficiency; evidence of iron overload or iron malabsorption [10].

It is also crucial to note that the efficacy and safety of intravenous therapy iron carboxymaltose has not been evaluated in patients with hemoglobin levels more than 15 g/dl. Therefore, the drug should not be used in this group of patients.

In addition, intravenous iron should be used with higher attention in patients with acute or chronic infections and should be discontinued in patients with established bacteremia [10].

Iron carboxymaltose contains 50 mg of iron per 1 ml. Level of iron deficiency is calculated by the Ganzoni formula [11]: body weight, kg x (target hemoglobin level, g / dl - the present hemoglobin level, g / dl) x 2.4 + 500

Maximum dose of iron carboxymaltose = 1000 mg iron (20 ml) per week.

Intravenous administration can be provided by injection or infusion. During the injection the drug is administered undiluted slowly (100 mg in minute or 1000 mg in 15 minutes). At administration by infusion, attention should be paid to the dilution of the drug, due to the level of dilution affects the stability of the drug. Iron breeding plan carboxymaltose for intravenous infusion is presented in table 2.

**Table 2. Dilution plan for ferric carboxymaltose for intravenous infusion [12]**

Iron dose	Volume of ferric carboxymaltose	Maximum amount of sodium chloride solution	Minimum administration time
500 mg	10 ml	100 ml	6 minutes
1000 mg	20 ml	250 ml	15 minutes

Diagnosis, treatment, as well as the timing of testing the effectiveness of treatment and subsequent observations are presented in the algorithm in Figure 1. It is crucial to remember that early reassessment of iron status (within 4 weeks after intravenous iron) should be avoided. The reason of it is that serum ferritin levels can significantly increase after intravenous iron administration and cannot be used as a marker iron status during this period.

Clinical studies have shown that intravenous iron carboxymaltose is well tolerated by patients with CHF [2, 3]. Most frequent side effects that occurred with a frequency between 0.1% and 10%. There are dizziness, headache, hypertension, hypophosphatemia, reaction at the injection site, nausea. Risk hypersensitivity between 0.1% and 1% [10].

The oral iron therapy is often used as the first line of therapy for iron deficiency in patients with CHF. The treatment of such a drug form does not have sufficient clinical data to support its efficiency The IRONOUT-HF clinical study, which compared the effect of oral iron therapy versus placebo in patients with CHF oral preparations, had shown to minimally replenish stocks iron and did not improve exercise tolerance or reduce symptoms of heart failure [13].

### Conclusions:

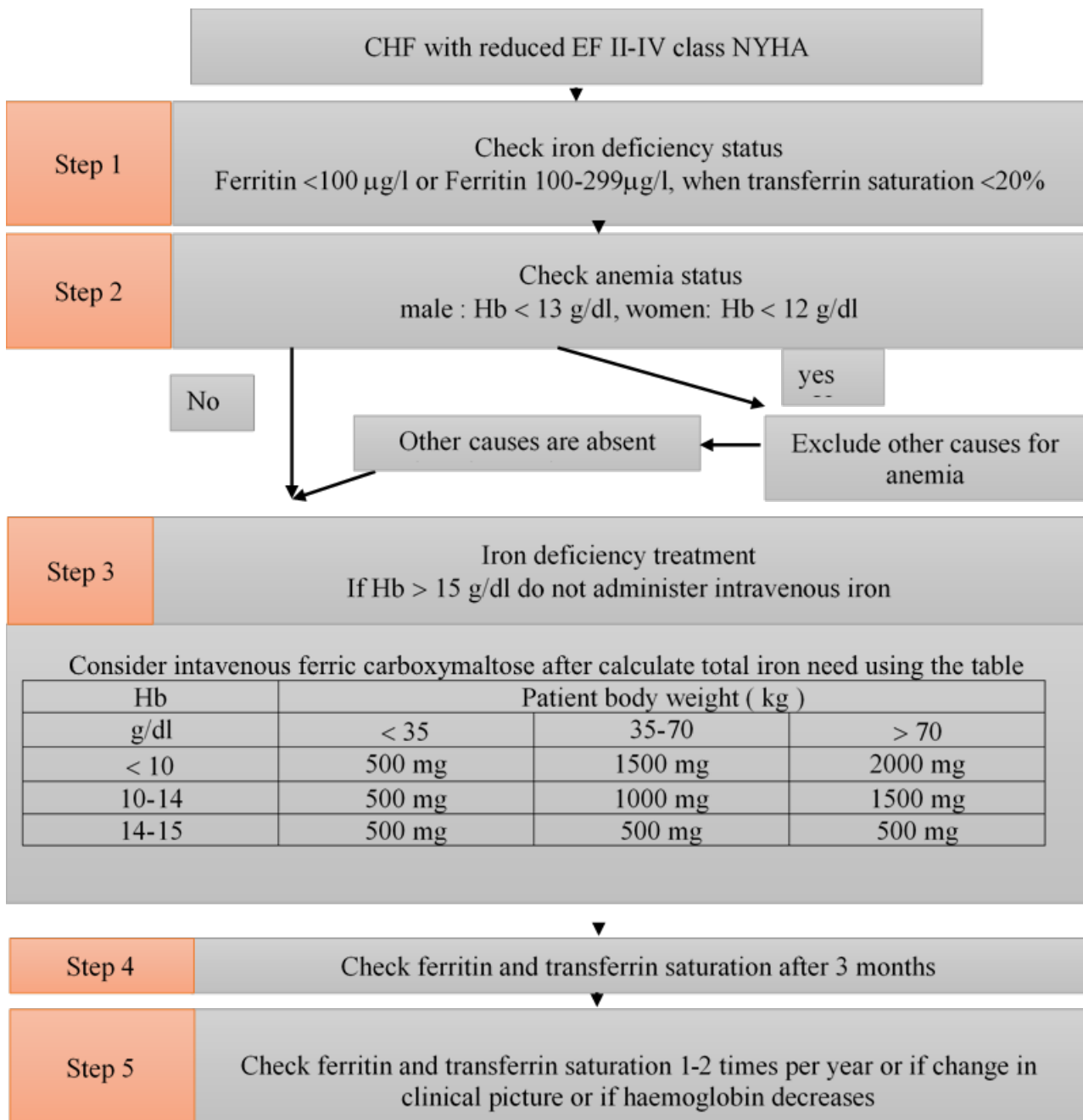
1. Clinical studies of intravenous iron therapy in patients with stable symptomatic CHF with reduced left ventricular ejection fraction demonstrate that



correction of iron deficiency is associated with significant improved exercise tolerance, reduced symptoms, improving the quality of life and reducing the frequency of hospitalizations.

2. The feasibility of treating iron deficiency in patients has been confirmed immediately after an episode of decompensation.

3. Oral iron therapy, which often is used as first line of therapy for iron deficiency in patients with CHF does not have sufficient clinical data to support its effectiveness.



**Fig. 1. Algorithm for screening/diagnosis and treatment/follow-up of iron deficiency in patients with chronic heart failure [12]**

**CHF – chronic heart failure, EF – ejection fraction, NYHA - New York Heart Association Functional Classification, Hb – haemoglobin level.**



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**Резюме.** Анемия и дефицит железа широко распространен среди пациентов с хронической сердечной недостаточностью (ХСН) и ассоциирован у таких пациентов со сниженной способностью к физическим нагрузкам, ухудшением качества жизни и худшим прогнозом, независимо от наличия анемии, итак коррекция дефицита железа – актуальный вопрос в контексте лечения пациентов с ХСН.

В данной работе представлен обзор литературы, посвященной лечению анемии и дефицита железа у пациентов с хронической сердечной недостаточностью.

Клинические исследования внутривенной терапии железом пациентов с симптомной ХСН и сниженной фракцией выброса левого желудочка демонстрируют, что коррекция дефицита железа ассоциировано со значительным увеличением толерантности к физической нагрузке, уменьшением симптомов, улучшением качества жизни и снижением частоты госпитализаций. Использование железа карбоксимальтозата у пациентов с декомпенсацией ХСН позволяет предупредить последующие декомпенсации. Насчет пероральной терапии препаратами железа, которые часто используется как первая линия терапии дефицита железа у пациентов с ХСН – лечение такой лекарственной формой не имеет достаточных клинических данных, которые подтверждали ее эффективность.

**Ключевые слова:** анемия, дефицит железа, хроническая сердечная недостаточность, лечение.



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