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Iron Deficiency in Patients with Chronic Heart Failure

G. J. Zharylkasynova
Doctor of Medical Sciences, Bukhara State Medical Institute

G. I. Akhmedova, Ph.D
Student, Bukhara State Medical Institute

Abstract: In chronic heart failure (CHF), anemia is an independent risk factor for death. However, there are few data on the frequency of anemia and iron deficiency in patients with CHF.

Keywords: erythrocyte index, risk factor, chronic heart failure, anemia.

The aim of the study was to study the frequency of anemia and iron deficiency in patients with CHF who are being treated in a therapeutic hospital.

Material and methods. A total of 150 patients with CHF of the III–IVfunctional class (FC), mean age 72.5 ± 77.8 years, were examined. A general blood test was performed with the calculation of erythrocyte indices, the content of iron, ferritin, transferrin in the blood, as well as the saturation of transferrin with iron were determined.

Results. Mild anemia wasdetected in 26.5% of the examinedpatients, iron deficiency-in 72.1%. The incidence of anemia in FC IV CHF was significantly higher than in FC III CHF; iron deficiency was equally common in both groups. Hypoferremia was detected in 38.6% of patients: 34 patients with FC II-I, 26 patients with FC IV. The average ferritin level was less than 100 mcg /l and did not differ statistically in the groups (in FC III CHF – 46.64 ± 28.72mcg/L, in FC IV-45.63 ± 25.90 mcg/L). With an increase in FC IV CHF transferrin, the iron saturation of transferrin is statistically significantly lower.

Conclusions. In patients with FC III–IV CHF, anemia is noted in a quarter of cases, with FC IV CHF more often than with FC III CHF. Iron deficiency is much more common – in 3/4 of patients, regardless of FC.

According to various researchers, from 10 to 60% of patients with chronic heart failure (CHF) have anemia [2, 14]. Anemia most often develops in patients with severe CHF [2, 7]. The presence of anemia in patients with CHF is an independent risk factor for death [4, 7, 19].

However, the results of some studies indicate that a significant number of patients with CHF have iron deficiency, both in the presence and absence of anemia [9, 16, 18].

The development of iron deficiency and anemia in patients with CHF can be facilitated by microbleeding, iron retention in macrophages due to increased hepcidin synthesis, impaired absorption of iron in the gastrointestinal tract due to hemodynamic disorders [2, 6, 10].

However, there are few data on the frequency of anemia and iron deficiency in patients with CHF. The prevalence of iron deficiency in patients with CHF of different functional classes (FC) has not been studied either.

The aim of the study was to study the incidence of anemia and iron deficiency in patients with CHF treated in a therapeutic hospital.

MATERIAL AND METHODS

We examined 150 patients (44 men and 106 women) with FC III–IV CHF (mean age 72.57 ± 77.78 years) who were treated in the therapeutic department regional hospital of the Bukhara Regional Hospital for the increase in CHF symptoms. 120 patients had FC II–IV, 39 had a history of myocardial infarction, 134 had hypertension, and 8 had rheumatic heart disease.

FC III CHF according to the classification of the New York Heart Association (NYHA) was diagnosed in 105 patients, FC IV-45 patients.

A clinical examination, a 6-minute walking test, a general blood test using a MEK 6500 hematology analyzer (Nihon Kohden, Japan) with the determination of erythrocyte indices were performed, the level of NT-proBNP was studied by an enzyme-linked immunosorbent assay, and the level of iron, transferrin, and ferritin in blood serum was determined using a Sapphire-400 hematology analyzer (Hirose Electronic System, Japan) by end-point photometric method; the transferrin iron saturation coefficient (%) was calculated as the ratio of serum iron concentration (mmol/L) to transferrin concentration (mg/dl) multiplied by 398. Blood sampling for studies was performed in the morning on an empty stomach on the next day after admission.

Anemia was diagnosed in accordance with the recommendations of the World Health Organization – with a hemoglobin level of less than 130 g/l in men and less than 120 g/l in women [22]. The presence of iron deficiency was determined when ferritin the serum ferritin level was less than 100 mcg/l or the ferritin level in the range from 100 to 299 mcg/L and the transferrin saturation coefficient with iron was less than 20% in accordance with the recommendations of the European Society of Cardiology for the diagnosis and treatment of acute and chronic heart failure (2016) [3]. The NT pro BNP level in all patients included in the study was higher than 125 pg/ ml.

All patients underwent electrocardiography and ECHO cardioscopy using an expert-class GE Vivid-7 device (General Electric Medical Systems, USA).

Statistical analysis of the results was performed using the Statistic 10.0 program using Student's t-test, nonparametric methods. The differences were considered statistically significant at $p < 0.05$.

RESULTS AND DISCUSSION

41 patients with CHF (27.5%) had mild anemia, including 23 women and 18 men. Among patients with NYHA FC IV CHF, anemia was detected in 21 (45.7%), among patients with FC III CHF – in 20 (19.4%). The incidence of anemia in FC IV CHF is statistically significantly higher than in FC III CHF ($p < 0.05$).

The number of red blood cells in patients with anemia was 3.97 ± 0.60 × 1012/l, the hemoglobin content in the blood was 108.76 ± 10.58 g/l.

There were no statistically significant differences in the average number of red blood cells between groups of patients with CHF of different FC according to NYHA, however, the hemoglobin level in CHF of IV FC was statistically significantly lower than in CHF of III FC (Table 1). In patients with CHF of IV FC compared to patients with CHF of III FC, the average concentration of hemoglobin in the red blood cell It was statistically significantly lower, and the indicators of red blood cell variability by volume (RDW-CV and RDV-SD) were higher.

The average concentration of iron in the blood in the groups was within the normal range (Table 1). 2), however, with a higher NYHA FC of CHF, a lower level of iron in the blood was observed, and these differences were statistically significant. Hypoferremia was found in 59 patients (39.6%): 33 patients with FC III CHF and 26 patients with FC IV CHF. In the group with low blood iron levels, 25 patients (13 women and 12 men) were diagnosed with anemia.

The average transferrin content in both groups did not go beyond the normal range and did not have statistically significant differences (Table 2). Average ferritin level in patients with NYHA class III and IV CHF

Table 1. The number of erythrocytes, hemoglobin content and erythrocyte indices in patients with CHF of functional classes III and IV according to the (New York Heart Association classification)

Indicators	of CHF III FC	CHF IV FC
Erythrocytes,	1012± 0.63	4.56 ± 0.42 ± 0.64*
Hemoglobin, g/l	132.83 ± 18.34	126.30 ± 17.57 *
Average hemoglobin content in the red blood cell, pg	29.26 ± 3.05	28.67 ± 3.11*
Average hemoglobin concentration in the red blood cell, g/l	350.71 ± 25.06	340.65 ± 23.90*
RDW- CV, %	13.59 ± 1.92	14.69 ± 2.46 *
RDW-SD, fl	62.02 ± 10.14	66.92 ± 9.08*

Note: FC – functional class, CHF-chronic heart failure, RDW-CV – relative width of red blood cell distribution by volume (coefficient of variation), RDW-SD – relative width of red blood cell distribution by volume (standard deviation). * Differences between the parameters of patients with FC III and IV CHF are statistically significant ($p < 0.05$).

Table 2. Blood iron, transferrin, ferritin content and transferrin iron saturation in patients with chronic heart failure of functional classes III and IV according to the classification New of the (New York Heart Association Association)

Indicators	of CHF III FC	CHF IV FC
Iron, mmol/l	15.68 ± 7.23	12.54 ± 6.83 *
Transferrin, g/l	1.95 ± 0.42	1.99 ± 0.51
Ferritin, mcg/l	82.61 ± 68.15	74.90 ±0.28
Transferrin saturation coefficient Transferrin saturation coefficientwith iron, %	32.29 ± 14.21	26.07 ± 16.04*

Note: FC – functional class, CHF-chronic heart failure. * Differences between the parameters of patients with FC III and IV CHF are statistically significant ($p < 0.05$).

The statistical value did not differ significantly and did not exceed 100 μg/l (Table 2). Of 103 patients with FC III CHF, 68 (66.0%) had ferritin levels less than 100 μg/l (average 46.64 ± 27.72 μg/L), of 46 patients with FC IV CHF - in 32 (69 .6%) (average 45.63 ± 25.90 μg/l). In total, 100 patients had ferritin levels less than 100 μg/L.

The coefficient of transferrin iron saturation on average in both groups was above 20%. At the same time, a lower coefficient of transferrin saturation with iron was observed with a higher FC of CHF, and these differences were statistically significant (Table 2). Transferrin iron saturation coefficient of less than 20% with ferritin levels ranging from 100 to 299 μg/L was found in 6 patients.

Thus, 106 patients with CHF (71.1% of the total number examined) were diagnosed with iron deficiency in terms of blood ferritin and tranferrin iron transferrin saturation. The frequency of iron deficiency in NYHA FC III and IV CHF is almost identical. The number of patients with

CHF and iron deficiency was significantly higher than the number of patients with CHF and anemia.

The data obtained are especially relevant in the light of the results of some studies: they show that it is iron deficiency, and not a decrease in hemoglobin levels, that is primarily associated with a deterioration in the quality of life, a decrease in physical activity, and mortality in such patients [11, 13, 15].

The negative effect of iron deficiency on the course of CHF may be due to the involvement of iron in many types of metabolism and physiological processes. In particular, iron is part of such hemo-containing proteins as hemoglobin, myoglobin, neuroglobin, various enzymes - cyclooxygenase, cytochromes of the respiratory chain, cytochrome P450, catalase, peroxidase, NADH dehydrogenase, succinate dehydrogenase, xanthioxidase [1, 5, 17, 20] . The tissue oxidative capacity of muscles and exercise tolerance deteriorate in proportion to the worsening of iron deficiency, even when the hemoglobin level is normal [21].

Animal experiments have shown that iron deficiency causes diastolic dysfunction, dilatation, hypertrophy, and myocardial fibrosis [6].

Iron hydroxymaltosate supplementation in patients with CHF, regardless of the presence or absence of anemia, increases exercise tolerance and quality of life, as well as reduces the number of hospitalizations and deaths [8, 12, 15]. Thus, the diagnosis of iron deficiency in patients with CHF is of great practical importance, since its correction can significantly increase the effectiveness of therapy in such patients.

Conclusions

1. Mild anemia is diagnosed in about a quarter of patients with NYHA FC III–IV CHF who are treated in a therapeutic hospital, most often in patients with FC IV CHF.
2. Iron deficiency is observed in more than 70% of patients with FC III–IV CHF.
3. The frequency of iron deficiency in different FC CHF is almost identical.
4. The number of patients with CHF and iron deficiency is more than 2.5 times higher than the number of patients with CHF and anemia.
5. For the diagnosis of iron deficiency with the aim of subsequent correction, it is advisable to determine the level of ferritin in the blood and the coefficient of iron transferrin saturation in all patients with CHF transferrin. Iron deficiency in heart failure Vol. 23, No. 1, 2018 Bulletin of the Ivanovo Medical Academy 15

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