New Day in Medicine
Новый День в Медицине
NDM

TIBBIYOTDA YANGI KUN

Ilmiy referativ, marifiy-ma'naviy jurnal

AVICENNA-MED.UZ

ISSN 2181-712X.
EiSSN 2181-2187

11 (61) 2023

ТИББИЁТДА ЯНГИ КУН
НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
NEW DAY IN MEDICINE

Илмий-рефератив, маънавий-маърифий журнал
Научно-реферативный,
духовно-просветительский журнал

УЧРЕДИТЕЛИ:

БУХАРСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ ИНСТИТУТ
ООО «ТИББИЁТДА ЯНГИ КУН»

Национальный медицинский исследовательский центр хирургии имени А.В. Вишневского является генеральным научно-практическим консультантом редакции

Журнал был включен в список журнальных изданий, рецензируемых Высшей Аттестационной Комиссией Республики Узбекистан (Протокол № 201/03 от 30.12.2013 г.)

11 (61)

2023

ноябрь

www.bsmi.uz
https://newdaymedicine.com E: ndmuz@mail.ru
Тел: +99890 8061882

Received: 20.10.2023, Accepted: 27.10.2023, Published: 10.11.2023.

UDC: 616.12-008.46

INFLUENCE OF ERYTHROPOIETIN ON THE CLINICAL COURSE OF CHRONIC HEART FAILURE

Akhmedova Gulmira Ikhtiyarovna https://orcid.org/0000-0003-1716-8128

Bukhara State Medical Institute named after Abu Ali ibn Sina, Uzbekistan, Bukhara, st. A. Navoi. 1 Tel: +998 (65) 223-00-50 e-mail: info@bsmi.uz

✓ ***Resume***

Anemia was detected in 14 (24.8%) patients, including 12 patients with iron deficiency. By the end of 12 weeks of treatment, there was a significant increase of 36% in the distance walked according to the results of the 6-minute walk test, an improvement in the functional class of CHF according to NYHA, an increase in LVEF by 32.5%, an increase in hemoglobin level by 12.5% (p <0.001), hematocrit by 5.8% (p<0.001), red blood cells by 8% (p<0.001). Correction of anemia in patients with CHF and IHD with iron supplements and erythropoietin against the background of standard therapy leads to a significant improvement in the clinical course of CHF and IHD.

Key words: chronic heart failure, coronary heart disease, anemia, erythropoietin.

ВЛИЯНИЕ ЭРИТРОПОЭТИНА НА КЛИНИЧЕСКОЕ ТЕЧЕНИЕ ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТИ

Ахмедова Гульмира Ихтияровна https://orcid.org/0000-0003-1716-8128

Бухарский государственный медицинский институт имени Абу Али ибн Сины, Узбекистан, г. Бухара, ул. А. Навои. 1 Тел: +998 (65) 223-00-50 e-mail: info@bsmi.uz

✓ ***Резюме***

Анемия выявлена у 14 (24,8%) больных, в том числе у 12 больных с дефицитом железа. К концу 12 недель лечения отмечено достоверное увеличение на 36% пройденной дистанции по результатам теста 6-минутной ходьбы, улучшение функционального класса ХСН по NYHA, увеличение ФВЛЖ на 32,5%, повышение уровня гемоглобина на 12,5% (p<0,001), гематокрита на 5,8% (p<0,001), эритроцитов на 8% (p<0,001). Коррекция анемии у больных ХСН и ИБС препаратами железа и эритропоэтином на фоне стандартной терапии приводит к значительному улучшению клинического течения ХСН и ИБС.

Ключевые слова: хроническая сердечная недостаточность, ишемическая болезнь сердца, анемия, эритропоэтин.

ERITHROPOETINNING SURUNKAL YURAK ETKISHISHI KLINIK KURIGA TA'SIRI

Akhmedova Gulmira Ikhtiyarovna https://orcid.org/0000-0003-1716-8128

Abu Ali ibn Sino nomidagi Buxoro davlat tibbiyot instituti, O‘zbekiston, Buxoro, st. A. Navoiy. 1 Tel: +998 (65) 223-00-50 e-mail: info@bsmi.uz

✓ ***Rezyume***

14 nafar (24,8%) bemorda anemiya, shu jumladan, 12 nafarida temir tanqisligi aniqlangan. 12 haftalik davolanishning oxiriga kelib, 6 daqiqalik yurish testi natijalariga ko'ra yurish masofasining 36% ga sezilarli o'sishi, NYHA ma'lumotlariga ko'ra CHF funktsional klassining yaxshilanishi, LVEFning o'sishi kuzatildi. 32,5%, gemoglobin darajasi 12,5% (p<0,001), gematokrit 5,8% (p<0,001), qizil qon tanachalari 8% (p<0,001) ga o'sishi. CHF va IHD bilan og'rigan bemorlarda anemiyani temir preparatlari va eritropoetin bilan standart terapiya fonida tuzatish CHF va IHD klinik kursining sezilarli yaxshilanishiga olib keladi.

Kalit so'zlar: surunkali yurak etishmovchiligi, yurak tomirlari kasalligi, anemiya, eritropoetin.

Relevance

Epidemiological and clinical studies indicate the important role of anemia in cardiovascular disease (CVD) complications. In the last decade, the possibilities of treating anemia in patients with chronic heart failure (CHF) have been actively studied [1]. Anemia is an independent predictor of a high risk of adverse cardiovascular events over 6 years in individuals without CVD, especially at the age of 47-64 years [2,3]. Normally, the hemoglobin content in the blood of men is 130-160 g/l, in women - 120-140 g/l. In patients with CHF, anemia is more common than in the general population, and its prevalence, according to various authors, ranges from 15 to 55% [4,5]. A number of studies indicate that women predominate among patients with CHF and anemia [2].

Hemodynamic changes that develop during anemia lead to the gradual development of myocardial hypertrophy, increasing dilatation of the heart chambers, primarily the LV, and the formation of relative insufficiency of the valve apparatus [6]. In addition, the presence of anemia leads to persistent myocardial ischemia and, accordingly, worsens the prognosis of patients [4,7].

Treatment of patients with concomitant pathology always presents certain difficulties due to the fact that attempts to actively medicamentally influence one disease are associated with a real threat of iatrogenic exacerbation of concomitant pathology. A promising drug intervention in patients with CHF and anemia appears to be subcutaneous administration of recombinant human erythropoietin and intravenous infusions of iron [1,2,8].

Several recent studies conducted by European scientists have shown the positive effect of treatment with erythropoietin in combination with intravenous iron supplementation on the course of CHF (reducing the frequency of hospitalizations, improving the FC of CHF, increasing LVEF) [9,13].

The purpose of the work is to study the clinical effectiveness of corrective therapy for anemia in patients with CHF that has complicated the course of coronary artery disease (angina pectoris class II; atherosclerotic cardiosclerosis; atrial fibrillation).

Material and methods

We examined 58 patients (32 women, 26 men) with stage IIA/B CHF, complicating the course of coronary artery disease (angina pectoris class II; atherosclerotic cardiosclerosis; atrial fibrillation), with left ventricular ejection fraction (LVEF) <45% according to Simpson. All patients signed informed consent to participate in the study. The study protocol was approved at a meeting of the local ethics committee.

Criteria for not being included in the study: stage III CHF; oncological (including oncohematological) diseases; history of cerebrovascular accident; chronic kidney disease stage 5 (K/DOQI, 2006); anemia of pregnant women.

Exercise capacity (EA) was assessed using the 6-minute walk test (6WMT). Echocardiographic examination was performed using the Sonoline G50 device. Left ventricular myocardial mass (LVMM) was calculated using the formula of R. Devereux and N. Reichek [12].

The LVMM index was defined as the ratio of LVMM to body surface area. Before and after treatment, the dynamics of LVEF (%) and stroke volume (LVSV) were calculated. All patients underwent a clinical blood test before and after treatment: hemoglobin levels were assessed; hematocrit; erythrocyte indices - average hemoglobin content, average cell volume; serum iron concentration; serum urea and creatinine levels. Data on B12 levels, folate levels, and myelogram (if necessary) were obtained from patient-provided medical records.

Patients with iron deficiency anemia were prescribed the drug epoetin alfa (Eprex; Silag AG, Switzerland). The drug was administered at a rate of 50 IU/kg body weight three times/week subcutaneously. If necessary, the dose was increased (no more than once every 4 weeks) by 25 IU/kg body weight 3 times/week until the optimal hemoglobin level was achieved. In addition, these patients were prescribed an iron supplement (Venofer®; Vifor International Inc., Switzerland), which was administered intravenously with 5 ml of Venofer® (100 mg iron) 3 times/week.

During the statistical analysis of the data, a statistical distribution series was constructed, the nature of the sample distribution was checked, and, based on the condition of normality of the distribution of empirical and theoretical frequencies, a confidence interval of the form M±SD was determined. Statistical data processing was carried out using the STATISTICA 6.0 program (StatSoft Inc).

Result and discussions

The age of patients included in the study ranged from 47 to 85 years (median 67 [62-73] years). The anamnestic duration of CHF was 5.07±0.11 years. Among the group of examined patients, 25 (43.1%) people had FC II CHF (NYHA), 33 (56.9%) had FC III.At the time of the study, all patients were receiving standard therapy for CHF, including ACE inhibitors, beta-blockers, antiplatelet agents, diuretics, and cardiac glycosides.Anemia was noted in 14 (24.8%) patients. Hemoglobin values ranged from 93 to 115 g/L in women and from 95 to 125 g/L in men. Thus, the majority of patients (n=12; 85.8%) had iron deficiency anemia.Assessing the incidence of anemia, we found the following: with FC II in patients with CHF, anemia occurred in 5 out of 25 (20%), and with FC III - in 9 out of 33 (27.3%) patients, but this difference was not statistically significant (p=0.113).Subsequently, patients with B12 and folate deficiency anemia (n=2) were excluded from the study due to different management of such patients.In general, for the group of patients with CHF, a direct proportional dependence of the severity of CHF on the level of hemoglobin (Hb) was revealed: FC II - Hb = 102.4±3.5 g/l; III FC - Hb = 97.5±3.4 g/l (p<0.05).

Before treatment, exercise tolerance (the number of meters walked in 6 minutes without shortness of breath) in the whole group of patients with anemia was reduced by more than 45% and averaged 265 (200-340) meters (norm >500 meters), in patients without anemia - 300 (220-352) meters (p = 0.348). Based on the literature data [2,13], against the background of standard therapy for patients with CHF and coronary artery disease, we treated anemia with erythropoiesis stimulants (erythropoietin and iron preparations), against the background of which there was a significant and comparable increase in the distance according to the 6WMT results by 35.8%, improvement in FC of CHF according to NYHA (p<0.001) (Table 1).

Table 1.

Dynamics of the studied clinical and instrumental parameters (n=12)

Parameters		At Baseline	After 12 weeks
of FC CHF, n (%)	II FC	4 (33,3)	7 (58,3)***
	III FC	8 (66,7)	5 (41,7)***
6WMT, m		265±24.2	360±32.7** *
ФВ LVEF, %		37.4±3.6	49.04±4.2 *
UO LVEF, ml		43.7±5.6	66.3±6.3**
*-p<0.05, **-p<0.01, ***-p<0.001 compared to baseline values. 6WMT=6-minute walk test, LVEF=left ventricular ejection fraction, LVSV=left ventricular stroke volume			

By the end of the 12th week of treatment, the level of hemoglobin increased significantly - by 12.5% (p <0.001), hematocrit - by 5.8% (p <0.001), erythrocytes - by 8% (p <0.001). However, the number of platelets, leukocytes, serum levels of cholesterol, creatinine, and glomerular filtration rate did not change significantly (Table 2). An increase in serum iron levels and hemoglobin concentration during treatment, respectively, was accompanied by an increase in exercise tolerance and an improvement in central hemodynamics: LVEF increased by 32.5% (from 37.4±3.6% to 49.04±4.2%; p<0.05), LVEF increased by 52.1% (from 43.7±5 .6 ml to 66.3±6.3 ml; p<0.01). Improving the pumping activity of the heart contributed to more effective relief of clinical signs of CHF and the transition of patients to a more favorable functional class.

Table 2.

Dynamics of the studied laboratory parameters (n=12)

Indicator At	Baseline	After 12 weeks
Hemoglobin, g/l	97.5.5±5.6	109.7±5.6 * * *
Hematocrit, %	38,7±3,6	40,9±3,6***
Creatinine, mg/dl	1.28±0.02	1.24±0.03
Скорость Glomerular filtration rate, ml / min	51.4±5.2	53.1±4.2
Total cholesterol, mmol/	minl 5.6±1.2	5.7±1.3
*-p<0.05, **-p<0.01, ***-p<0.001 по compared to the initial values		

Discussion

The main mechanisms for the development of anemia in patients with CHF are as follows [2]:

• hemodilution - increase in circulating plasma volume (CPV); bone marrow dysfunction;

• iron deficiency - malabsorbtion, chronic blood loss (aspirin);

• chronic immunodeficiency - activation of tumor necrosis factor, causing a decrease in the synthesis and activity of erythropoietin;

• taking ACE inhibitors (decrease in the level and activity of erythropoietin in the bone marrow);

• renal failure - decreased production of erythropoietin, increased loss of erythropoietin in the urine. According to S.N. Tereshchenko et al. [2,5], anemia was detected in 27.4% of patients with CHF who were inpatients. According to our observations, the frequency of anemia was 24.8%, which corresponds to literature data [2,5].According to our data, the cause of anemia in 85.8% of patients was iron deficiency, 8.2% - vitamin B12 deficiency, and 6% - folic acid deficiency. In our opinion, the high incidence of iron deficiency anemia among the examined group of patients is associated with the elderly age of the patients.In our study, as in other works [2,14], there was a clear correlation between the level of hemoglobin and the FC of CHF. The higher the FC, the lower the hemoglobin level. Limitations of the study: patients with stage III CHF were excluded from our study; patients with B12 and folate deficiency anemia, because there is no point in using erythropoietin preparations for them; history of oncological (including hematological oncological) diseases; chronic kidney disease stage 5 (K/DOQI, 2006); anemia of pregnant women.

Erythropoietin may be a major factor in the correction of anemia, not only because of the infrequency of adverse reactions, but also because it causes the formation and release of young cells from the bone marrow into the blood.

Previous scientific studies have found that treatment of anemia with erythropoietin leads not only to an improvement in the condition of patients, but also to a decrease in LV hypertrophy, prevention of LV dilatation, an increase in LVEF, and a decrease in the need for diuretics by approximately 40% [1,2,13] . The effectiveness of intravenous iron administration in potentiating the action of erythropoietin is absolutely proven, which leads to increased tolerability (lower incidence of arterial hypertension) and helps to reduce the effective dose of the drug [1,2].

Recent studies conducted by European scientists have shown the positive effect of treatment with erythropoietin drugs in combination with intravenous iron administration on the course of CHF, which was confirmed by a decrease in the levels of TNF, brain natriuretic peptide and interleukin 6 [1]. At the same time, an increase in cardiac ejection fraction, a decrease in the need for high doses of diuretics, the need for repeated hospitalizations, and an improvement in renal function were observed [1,13].

Based on the literature data, against the background of standard therapy for CHF in patients with coronary artery disease and anemia, we stimulated erythropoiesis with erythropoietin and iron preparations. After 12 weeks of treatment, we received an increase in the distance according to the results of 6WMT by 36%, an improvement in the functional class of CHF, an increase in hemoglobin levels by 12.5%, hematocrit by 5.8%, LVEF increased by 32.5%, LV SV increased by 52, 1%. Clinical signs of heart failure were noticeably relieved. Our results are comparable with literature data [1,2,13].

Conclusion

The prevalence of anemia diagnosed according to WHO criteria in patients with FC II-III CHF (NYHA), which complicated the course of coronary artery disease, was 24.8%. In the majority of patients with anemia (85.8%), the latter was of an iron deficiency nature. Our study confirmed the direct proportional dependence of the severity of CHF on the level of hemoglobin. Correction of anemia in patients with CHF with erythropoiesis stimulants (iron and erythropoietin preparations) against the background of standard therapy for CHF leads to a significant improvement in the FC of CHF.

LIST OF REFERENCES:

1. Silverberg D.S., Wexler D., Sheps D. et al. The effect of correction of mild anemia in severe, resistant congestiv heart failure using subcutaneous erytropoietin and intravenous iron. A randomized controlled study. // J Am Coll Cardiol 2001;37:1775-1780.

2. Tereshchenko S.N., Atroshchenko E.S., Uskach T.M. et al. Anemia as complication of chronic heart failure: prevalence, treatment, prognosis. // Ter Arkh 2008;80(9):90-5. Russian (Tereshchenko S. N., Atroschenko E. S., Uskach T. M. et al. Anemia as a complication of chronic heart failure: prevalence, prognosis, and treatment. Therapeutic Archive 2008;9:90-95).
3. Chernov V.M. ed. Anemia is a hidden epidemic. M.: MegaPro; 2004. Russian (Chernov V. M., editor. Anemia is a hidden epidemic , Moscow: MegaPro; 2004).
4. Arutjunov G.P. Anemia in patients with chronic heart failure. Serdechnaja Nedostatochnost' 2003;4(5):224-228. Arutyunov (Арутюнов G. P. Anemia y in patients with chronic heart failure. Heart Failure 2003;4(5):224-228).
5. Tereshchenko S.N., Dzhainani N.A., Uskach T.M., Kochetov A.G. Anemia and chronic heart failure. Kardiologija 2004;44(7):73-6. Tereshchenko S. N., Dzhainani N. A., Uskach T. M., Kochetov A. G. Anemia and chronic heart failure. Cardiology 2004;44(7):73-6).
6. Shilov A.M., Mel'nik M.V., Sarycheva A.A. Anemia in heart failure. Russkij medicinskij zhurnal 2003; 11(9): 545-548. Shilov (Шилов A.M., Melnik M. V., Sarycheva A. A. Anemia in heart failure. // Russian Medical Journal 2003;11(9):545-548).
7. Silverberg D.S., Iaina A., Wexler D. et al. The pathological consequences of anaemia. Clin Lab Haematology 2001;23(1):1-6.
8. Steinborn W., Doehner W., Anker S.D. Anemia in chronic heart failure – frequency and prognostic impact. // Clin Nephrology 2003;60(Suppl 1):103-107.
9. Singh A.K. et al. Correction of anemia with epoetin alfa in chronic kidney disease. // N Engl J Med 2006;355:2085-2098.
10. Sarnak MJ, Tighiouart H, Manjunath G, et al. Anemia as a risk factor for cardiovascular disease in the Atherosclerosis Risk in Communities (ARIC) study. // J Am Coll Cardiol 2002;40:27-33.
11. Guyatt G.H. Measurement of health-related quality of life in heart failure. // J Am Coll Cardiol 1993;22(4 Suppl A):185A-191A.
12. Devereux R., Reichek N. Echocardargraphic assesment of left ventricular mass in man. // Circulation 1977;55:613-618.
13. Silverberg D.S., Wexler D., Blum M. et al. The use subcutaneous erytropoietin and intravenous iron for the treatment of the anemia of severe, resistant congestiv heart failure improves cardiac and renal function, functional cardiac class, and makedly reduces hospitalization. // J Am Coll Cardiol 2000;35:1737-1744.
14. Wisniackl N., Aimson P., Lyle M. Is anemia a cause of heart failure in the elderly? // Heart 2001; 85 suppl I:4.

Entered 20.10.2023