

**CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND ANEMIA**

Khusainova Munira Alisherovna
Assistant of Samarkand State Medical University

Raimbekova Aida Kairatovna
Student of Samarkand State Medical University

Israilova Shoxista Umirovna
Student of Samarkand State Medical University

Toshtemirov Mekhroj Oybekovich
Student of Samarkand State Medical University

Abstract

Anemia is one of the manifestations of systemic inflammation in chronic obstructive pulmonary disease (COPD) and is a factor aggravating the course of the disease.

Objective. To study gender peculiarities of anemia in COPD patients, to increase the effectiveness of treatment by using pharmacological preparations of erythropoietin and enteral iron.

Material and methods. Clinical data of examination of 74 patients with COPD II and III stages with anemia and the results of treatment of 49 patients who received pharmacological preparations of erythropoietin and enteric iron are presented and treatment results of 49 patients who received epoetin and sorbifer durules in addition to standard therapy.

Results. In COPD patients with anemia iron deficiency anemia was statistically significantly more frequent - in 63 (85,1%): in 39 (61,9%) women and 24 (38,1%) men. In 11 (14.9%) patients, normocytic anemia having parameters of anemia of chronic diseases. The frequency of iron deficiency anemia in patients of both sexes correlated with age and was predominantly moderately severe; the moderate degree of severity was statistically more often confirmed in women - 24 (61.5%) out of 39 patients, in men the predominance of the mild variant of iron deficiency - 14 (58.3%) out of 24 patients.

Conclusion. The prevalence of concomitant anemia in COPD was 26.5%; anemia was verified in 44 (33.7%) women, i.e. in every third patient, in men anemia was significantly less frequent - in 30 (20, 7%) patients. The presence of anemia significantly worsens the condition of patients, especially female patients, who are more concerned with dyspnea, impairment of well-being, fatigue, depression, and they need more frequent hospitalizations. Correction of anemia by erythropoietin and enteral iron preparations makes it possible to increase physical endurance of patients, reduce the intensity of cough, dyspnea and maintain positive dynamics of physical tolerance for a long time after completion of the course of antianemic therapy.

Keywords: chronic obstructive pulmonary disease; anemia; gender differences; erythropoietin.



Introduction

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality in the world, leads to significant and constantly growing economic and social damage, requires the introduction of modern treatment technology. Research on the gender aspects of COPD is still in its infancy, but these initial steps already give great hopes to scientists and practitioners.

The diagnosis of COPD is increasingly being made to middle-aged women who smoke moderately or do not smoke at all. Every year, the number of new cases of COPD in females increases approximately 3 times faster than in males. The study of the features of the course of COPD in women allows us to identify another phenotype of the course of COPD — the "female sex". One of the most important systemic manifestations COPD is the development of anemic syndrome.

Information on the prevalence of anemia in COPD is contradictory and ranges from 8 to 53%. It is necessary to develop principles and tactics treatment of COPD patients with anemic syndrome, which makes it possible to optimize comprehensive medical care for patients and improve the prognosis of the disease.

The aim of the study was to study the gender characteristics of anemia in COPD patients, to increase the effectiveness of treatment by using pharmacological preparations of erythropoietin and iron preparations.

MATERIALS AND METHODS

The work is based on the results of examination of 74 patients diagnosed with stage II and III COPD with anemia (44 women and 30 men, average age 67.1 ± 10.9 years) who met the criteria for inclusion in the main observation group, and the results of treatment of 49 patients who received epoetin beta (EPO) and sorbifer durules in addition to standard therapy. EPO was administered subcutaneously at the rate of 50 IU/kg 3 times a week to achieve normal hemoglobin levels, then a maintenance therapy was prescribed weekly for 3 months individual dose of EPO. Sorbifer durules was prescribed only when the iron deficiency nature of anemia was confirmed. The course of treatment with a full dose of iron was carried out for 3 months. The correction phase had a different duration depending on the individual iron deficiency. To prevent iron overload, ferritin, transferrin, and hemoglobin indicators were determined once a week in the correction phase and once every 4 weeks in the stabilization phase (3 months) and for 12 months of observation. To study the gender characteristics of patients COPD with anemia was compared with the results observations of 55 patients of the control group (29 men and 26 women) with a diagnosis of COPD of stage II and III without anemic syndrome. The groups were comparable in terms of basic anthropometric, clinical and anamnestic indicators, standard therapy received, and instrumental examination data. Criteria for excluding patients from the study: extremely severe COPD, bronchial asthma, malignant or hematological disease, autoimmune disease, cirrhosis of the liver, theophylline use, the presence of chronic renal failure, established sources of bleeding (complications of peptic ulcer disease, ulcerative colitis, etc.) and previously diagnosed anemia (megaloblastic, aplastic, hemolytic), EPO therapy,



administration of iron preparations or blood transfusion for 3 months before inclusion in the study.

Criteria for inclusion in the main group of the study: the presence of reliable clinical and instrumental signs of COPD of stage II and III, according to the criteria of GOLD 2011; the presence of hematological criteria of anemia (WHO, 2001): hemoglobin level less than 130 g / l in men and less than 120 g / l in women; the presence of absolute iron deficiency; at the same time, the level of ferritin reduction is less than 10 mcg / l in women and less than 20 mcg / l in men, an increase in transferrin levels of more than 3.8 g / l; voluntary written consent of the patient to participate in the study.

Subjective assessment of cough and shortness of breath was carried out using a visual analog scale (VAS) and the Borg scale. To study the dynamics of exercise tolerance and objectification of the functional status of patients, a test with a 6-minute walking (TSMX) before and after treatment. At the same time, possible gender differences in the effectiveness of the therapy were clarified.

Statistical processing of the results was carried out in Microsoft Excel and Statistica 6.0 programs. The average value, standard deviation, reliability of differences and Student's criterion were calculated. The critical significance level (p) was assumed to be 0.05.

RESULTS

Among 277 patients with COPD of stage II and III (130 women and 147 men), according to the hemogram and in full compliance with the criteria for inclusion in the main study group, anemia was detected in 74 patients. The diagnosis of anemia was verified in all patients for the first time. Thus, the prevalence of anemia in COPD, according to our data, was 26.5%. At the same time, among women diagnosed with COPD of stage II and III, anemia was confirmed in 44 (33.7%) patients, i.e. in every third patient, anemia in men was significantly less common — in 30 (20.7%) patients ($p < 0.05$). In the main group, women aged 40 to 60 years were statistically more than men of the same age: 21 (47.7%) women and 7 (23.3%) men; while in the older age group (71 to 80 years), men with anemia were significantly more than women: 14 (46.7%) men and 12 (27.3%) women ($p < 0.001$). The average age of women with COPD with anemia was less than that of patients in the control group: 59.1 ± 7.8 and 65.7 ± 6.7 years. The average age of men in the comparison groups did not significantly differ (71.3 ± 8.5 and 73.3 ± 7.7 years, $p \geq 0.05$). Gender dimorphism revealed and when assessing the severity of the underlying disease against the background of anemia. The main group has a severe course Stage III COPD was more common in women than in men (59.3% vs. 40.7%, $p < 0.05$), in the control group of severe male patients there were statistically more than female patients (71.4% vs. 28.6%, $p < 0.05$).

When analyzing the anamnesis data, women of the main group on average considered themselves sick during 14.5 ± 2.1 years, whereas in the group of men this indicator was significantly higher — 24.7 ± 2.6 years ($p < 0.01$), in patients of the main group the duration of the disease from the moment of the first symptoms (cough in the morning, sputum separation) to the onset of symptoms of difficulty breathing, the average age in women was 6.5 ± 2.9 years, in men — 22.4 ± 8.9 years ($p < 0.05$). The average age of smoking initiation



in women and men in both groups did not significantly differ and was 25.6 ± 5.6 and 23.5 ± 4.7 years, respectively. Among non-smoking women, 22.7% noted the presence of such a factor as long-term (more than 15 years) passive smoking. No former smokers were registered among women, 17.4% of men were former smokers.

In our study, the analysis of the prevalence of concomitant diseases in patients was carried out COPD with anemia. In the whole group, 65 (92%) patients had concomitant diseases (on average, 3.9 ± 2.1 chronic diseases per 1 patient). Sexual dimorphism was reliably confirmed: the number of comorbid conditions in women was greater than in men ($p < 0.01$). Men are more likely to suffer from coronary heart disease, atherosclerosis, arrhythmias, women are more likely to suffer from concomitant hypertension, depression, bronchial asthma, diseases thyroid gland.

A comparative analysis of the anamnesis data revealed that $20.5 \pm 3.5\%$ of women in the main group had frequent exacerbations of COPD (3 times or more per year), this parameter was recorded only in $10.4 \pm 1.3\%$ of men. The gender specificity of complaints was characterized by the fact that in women with COPD with anemia, subjective feelings of fatigue, irritability, depression occurred significantly more often (70.2% versus 55.3% in men), at an earlier time and were characteristic of the age group from 40 to 60 years.

In general, in patients with COPD and anemia, the severity of shortness of breath was higher than in patients with COPD without anemia (6.9 ± 0.7 and 4.8 ± 0.9 , $p < 0.05$). At the same time, gender dimorphism of the severity of dyspnea was also revealed: in women with COPD, on average, the dyspnea index was significantly higher than in men, and amounted to 6.8 ± 0.7 points (in men, 4.9 ± 0.5 points, $p < 0.05$). Women had significantly lower body mass index than men of the main group (21.43 ± 2.8 kg/m² versus 24.68 ± 1.7 kg/m², $p < 0.05$). Bronchial conduction disorders of the obstructive type were detected at the level of both central and peripheral airways. Women had lower values all indicators of the function of external respiration — FVD.

According to the survey data, hypochromic microcytic iron deficiency anemia (IDA) was statistically significantly more common in COPD patients — in 63 (85.1%) patients, mainly in women — in 39 (61.9%, $p < 0.05$). In 11 (14.9%) patients with a slight predominance in males (6 men and 5 women), normochromic normocytic anemia was verified, having the parameters of anemia of chronic diseases (AHZ). The frequency of IDA in patients of both sexes correlated with age, anemia was predominantly moderate — in 34 (54%) patients; at the same time, the average severity was statistically more often confirmed in women — in 24 (61.5%) of 39 patients, in men the mild variant of iron deficiency prevailed — in 14 (58.3%) of 24 patients ($p < 0,01$). The degree of activity of the systemic inflammatory process in patients of the main group with IDA is higher than in patients without concomitant anemia; at the same time, a higher degree of activity is more often recorded in women than in men. An inverse correlation was found between the level of C-reactive protein and the indicators of hemoglobin and hematocrit ($r = -0.37$, $p < 0.05$). Hemogram indicators in IDA have gender dimorphism, which consists in the fact that with mild anemia in men, hemoglobin indicators (120.4 ± 5.1 g/l) and hematocrit ($35.5 \pm 1.4\%$) were significantly higher



than in women (100.7 ± 10.2 g/l, $29.3 \pm 2.3\%$, $p < 0.05$). With anemia of moderate severity, these indicators did not have significant differences.

The frequency of AHZ in COPD patients of both sexes correlated with age, was statistically more common in patients older than 60 years — in 9 (81.8%) patients and was predominantly mild in 7 (63.7%) patients ($p < 0.05$).

The severity of anemia in the whole group was minimal — in 38 (51%) of 74 COPD patients with anemia, statistically unreliable prevalence of moderate anemia. It can be concluded that patients with COPD have both mild and moderate anemia equally. A direct correlation between the indicators of FEV1 was revealed, hemoglobin, hematocrit in anemia of both mild and moderate severity without gender differences: FEV1 (Hb: $r = 0.37—0.75$; FEV1: $r = 0.45—0.77$ — mild anemia; Hb: $r = 0.35—0.78$; FEV1 : $r = 0.45—0.79$ — anemia of moderate severity, $p < 0.01$). Against the background of treatment with EPO and sorbifer durules, hemoglobin increased significantly — by 18% ($p < 0.05$), hematocrit — by 6.8% ($p < 0.05$), erythrocytes — by 18% ($p < 0.05$), iron — by 56% ($p < 0.05$), ferritin — by 10.8% ($p < 0.05$), the level of transferrin decreased — by 21% ($p < 0.05$), LCC — by 22% ($p < 0.05$; Table 5). There was no gender dimorphism in the initial characteristic of cough in the main observation group, but after 3 months of therapy, cough indicators on the VAS scale decreased from 8 (8; 9) to 5 (5; 6) points and after 12 months of observation remained at a lower level compared to the initial values — from 8 (8; 9) to 6 (7; 8), in the control group, cough indicators did not significantly differ from the initial values — 8 (8; 9) points.

CONCLUSION

The prevalence of concomitant anemia in chronic obstructive pulmonary disease, according to our data, was 26.5%. The diagnosis of anemia was verified in 44 (33.7%) women, i.e. in every third patient, and in 30 (20.7%) men. At the same time, anemia in women aged 40 to 60 years is more common than in men of this age. The presence of anemia significantly worsens the condition of patients, especially women, who are more concerned about shortness of breath, impaired well-being, fatigue, depression, and they need more frequent hospitalizations. Iron deficiency anemia in patients with chronic obstructive pulmonary disease was statistically more common and mainly in women. With a slight predominance of males, normochromic normocytic anemia was verified, which has the parameters of anemia of chronic diseases. The results of the study show that in patients with chronic obstructive pulmonary disease with anemia, optimal and stable control of the anemia syndrome is possible, improvement of the condition due to reducing shortness of breath, cough intensity, increasing exercise tolerance, reducing the frequency of exacerbations for a long time after completing the course of antianemic therapy. Such control was achieved through the use of a complex of basic therapy for chronic obstructive pulmonary disease and a 12-week course of subcutaneous administration of low doses of erythropoietin against the background of enteral oral administration of iron preparation. The results obtained allow us to recommend the use of antianemic therapy for standard practice in chronic obstructive pulmonary disease with concomitant anemia.

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