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THE EFFECT OF METABOLIC SYNDROME ON THE COURSE OF CORONARY HEART DISEASE

Boboerova Dildora Nabizhonovna
https://orcid.org/0009-0008-9388-7961
Bukhara State Medical Institute, Bukhara, Uzbekistan

Annotation. The aim of the study was to analyze the indicators of proinflammatory cytokines in patients with chronic obstructive pulmonary disease and concomitant coronary heart disease. Materials and methods of the study - 230 patients with exacerbation of chronic obstructive pulmonary disease were examined. The study included patients admitted to the pulmonology department with an exacerbation of COPD stage III with FEV1 < 50%. He underwent spirometry and ECG. Markers of inflammation in the blood (IL-6, C-RB, TNF-α) were studied upon admission to the hospital, after 10 days of treatment and 3 months after discharge of patients from the hospital.In the study group, patients receiving roflumilast had a decrease in TNF-α on average to normal figures.3 months after treatment in the control group, the level of TNF-α was normalized in 46.2% of patients, in the study group – in 84.5% of patients.

Keywords: chronic obstructive pulmonary disease, coronary heart disease, cytokine status, roflumilast.

Abstract. Today, chronic obstructive pulmonary disease (COPD) is considered as a serious medical and social problem that remains unresolved until the end. The incidence of patients and mortality from COPD continue to increase in the world. The reason for this, first of all, is the widespread use of smoking. It is shown that 4-6% of men and 1-3% of women over 40 years of age suffer from this disease [1-5].

It is known that COPD is based on a long–term inflammatory process that affects all structures of the lung tissue (bronchi, bronchioles, alveoli, pulmonary vessels) (A global strategy for the diagnosis, treatment and prevention of chronic obstructive pulmonary disease. Often, the "classic" local inflammatory process acquires a systemic character. At the same time, its essence completely changes [6-11].

In the last decade, coronary heart disease (CHD) has occupied one of the leading places in the structure of the treatment of patients with cardiovascular diseases (CVD) and mortality from them. In the USA and European countries, there are 30-40 thousand patients with coronary heart disease per 1 million population. Mortality from coronary heart disease in Russia among men is 56.6% of the total number of deaths in CVD, in women of the same age – 40.4% [12-17].

The course of the disease, treatment and prevention largely depend on concomitant diseases, against which CHD occurs. CHD and COPD are often concomitant diseases. 62% of COPD patients of older age groups have coronary heart disease [18-26].

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Among the common mechanisms of the pathogenesis of COPD and CHD, systemic inflammation should be noted. It is known that a high concentration of systemic markers of inflammation, such as TNF-α, C-RB, IL-18, IL-6, is associated with the aggravation of atherosclerosis and the formation of its complications. Therefore, in recent years they have been considered independent risk factors for the development of cardiovascular diseases in general, as well as acute coronary syndrome (ACS) in particular [27-33].

Serious attention in the study of the pathogenesis of coronary heart disease is paid to endothelial dysfunction (ED), as the earliest phase of vascular wall damage. Each endothelial function, which determines the thrombogenicity of the vessel wall, vasoreactivity, inflammatory changes and stability of the cholesterol plaque, is directly or indirectly related to the progression of coronary heart disease and the development of its complications. Several substances are considered as potential markers of ED, the production of which may indirectly reflect the function of the endothelium. We are talking about pro-inflammatory cytokines: interleukins (IL-8, IL-6, IL-1), tumor necrosis factor-α (TNF-α), Willebrand factor, selectins, C-reactive protein (CRP), etc.. In addition, TNF-α and IL-6 cytokines play an important role in the implementation of such processes as hypercoagulation of blood, the development of hyperlipidemia, impaired regulation of vascular tone, the formation of endothelial dysfunction, the development of acute coronary syndrome, the development of a negative inotropic effect and remodeling of the heart [34-39].

Significant risk factors for COPD and CVD are smoking, sedentary lifestyle, poor nutrition.

Exacerbation of COPD is accompanied by an increase in pro-inflammatory cytokines (CRP, IL-1, IL-6, IL-8, etc.), acting as factors of destabilization of coronary heart disease. Therefore, it is advisable to evaluate the role of 8 anti-inflammatory drugs in exacerbation of COPD and the dynamics of concomitant coronary heart disease in this case.

Roflumilast is a representative of a new class of drugs – PDE-4 inhibitors. It has a fundamentally new mechanism of action aimed at the main links of the inflammatory process in COPD.

All of the above shows the urgency of the problem of the comorbid course of coronary heart disease and COPD, and also indicates the need to find ways to reduce the progression of coronary heart disease and COPD.

In our opinion, the use of the anti-inflammatory drug roflumilast in exacerbation of COPD could have a positive clinical effect and reduce the number of destabilizations of coronary heart disease [40-43].

In the literature, there are data on the beneficial effect of roflumilast on the course of COPD and a decrease in pro-inflammatory cytokines in the blood. However, the efficacy of roflumilast in patients with comorbid COPD and coronary heart disease has not been previously considered.

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Materials and methods. The study was conducted on the basis of the pulmonology department of the Bukhara Regional Multidisciplinary Medical Center for the period 2021-2022. The research protocol has been approved by the local ethics committee. All the examined patients got acquainted with the structure of the work, the purpose and objectives of the study. A prerequisite for inclusion in the study was the signing of a voluntary informed consent by the patient.

At the initial stage, 230 patients with exacerbation of chronic obstructive pulmonary disease were examined. The study included patients admitted to the pulmonology department with an exacerbation of COPD stage III with FEV1 < 50%. He underwent spirometry and ECG.

Patients with concomitant coronary heart disease were selected: stable angina pectoris, FC II, confirmed by ECG results. Their number was 110 patients.

At the second stage, the assessment of the clinical manifestations of COPD and coronary heart disease and their severity, the study of markers of inflammation in the blood was carried out. In patients with exacerbation of COPD, the phenotype was determined, as well as the number of exacerbations of COPD in the previous year. All selected patients had two or more exacerbations in the previous year. Of the COPD phenotypes, mixed prevailed.

Further, the studied patients were randomly divided into 2 groups, comparable in gender, age, and clinical manifestations of diseases. Further treatment was carried out. After 10 days, the level of markers of inflammation in the blood and blood pressure was monitored. Further treatment continued for another 3 months. Then a second examination was carried out to determine the level of markers of inflammation in the blood, clinical and instrumental indicators, clinical manifestations of diseases, quality of life. The age of patients is 50-75 years. The study included 29 (26.3%) women and 81 (73.7%) men with exacerbation of COPD and concomitant coronary heart disease.

When included in the study, all patients were prescribed basic anti-inflammatory therapy for COPD (M-cholinoblockers, β2-agonists, glucocorticosteroids, oxygen therapy, NSAIDs) and basic antianginal therapy (selective beta-blockers, statins, ACE inhibitors, disaggregants).

All patients were divided into 2 groups, comparable in gender, age, and clinical manifestations of diseases:

The control group consisted of 52 patients receiving standard therapy.

The study group consisted of 58 patients who received standard therapy and additionally received roflumilast at a dose of 500 mcg 1 time per day.

All patients underwent a standard examination, which included a general blood test, a general urine test, a biochemical blood test, a general sputum analysis, sputum culture with determination of sensitivity to antibiotics, chest X-ray, ECG, ECHO-KG. Spirography and ECG monitoring were performed at the first stage. Markers of inflammation in the blood (IL-6, C-RB, TNF-α) were studied upon admission to the

hospital, after 10 days of treatment and 3 months after discharge of patients from the hospital. During the entire observation period, the patients kept diaries of self-control. In them, they indicated the figures of blood pressure, heart rate and the number of angina attacks during the day. The quantitative assessment of dyspnea was performed on the MRC scale.

Results. At the beginning of treatment, there were no statistically significant differences between the study groups.

At the beginning of treatment, the average level of CRP was increased in patients of both groups. In the control group, CRP was increased by 38% on average and amounted to 6.9 mg/l. In the study group, CRP was increased by 42% on average and amounted to 7.1 mg/ml ($p<0.05$).

After 10 days, a second blood test was performed. The average level of CRP in patients of the control group decreased by 10% and amounted to 6.4 mg/l. In the study group, the level of CRP decreased by 14% and amounted to 6.2 mg/l ($p<0.05$).

3 months after the discharge of patients from the hospital, the level of CRP in the control group decreased on average by 18% from the initial figures and averaged 6.0 mg/l. In the study group, the level of CRP decreased by an average of 38% and amounted to 5.2 mg/ l ($p< 0.05$).

From the above, it can be seen that in the study group, patients taking roflumilast had a more pronounced decrease in CRP than in patients of the control group. Moreover, in the control group, a decrease in the level of CRP to normal figures was observed in 23% of patients. In the study group, the level of CRP normalized in 26% of patients.

At the beginning of treatment, there were no statistically significant differences between the study groups.

At the beginning of treatment, the average level of IL-6 was increased in patients in both groups. In the control group, the level of IL-6 was increased by 34% and amounted to 9.4 pg/ml. The level of IL-6 in the study group was increased by 30% on average and amounted to 9.1 pg/ml ($p<0.05$).

After 10 days, a repeated study of the blood test found that IL-6 in patients of the control group decreased by 9% on average and amounted to 8.8 pg/ml. In the patients of the study group, the level of IL-6 decreased by an average of 10%, which amounted to 8.4 pg/ml ($p<0.05$).

3 months after the discharge of patients from the hospital, the following changes occurred: the average level of IL-6 in the control group decreased by 17% from the initial values and amounted to 8.2 pg/ml, and in the study group there was a decrease in the level of IL-6 by an average of 21% from the initial figures, which amounted to 7.6 pg/ml ($p<0.05$).

From the above, it can be concluded that patients in the study group had a more pronounced decrease in IL-6 while taking roflumilast than patients in the control group.

At the same time, in the control group, a decrease in the level of IL-6 to normal figures was observed in 13.5% of patients. In the study group, the level of IL-6 was normalized in 24% of patients.

At the beginning of treatment, there were no statistically significant differences between the study groups.

At the beginning of treatment, an increased level of TNF-α was detected in both groups. The level of TNF-α in patients of the control group was increased by an average of 8% and amounted to 8.8 pg/ml. In the study group, the average TNF-α level was increased by 10% and amounted to 8.9 pg/ml ($p<0.05$).

After 10 days, the average TNF-α level in the control group patients decreased by 2% from the initial values and amounted to 8.6 pg/ml. Patients in the study group had a decrease in TNF-α levels by 5%, which amounted to 8.5 pg/ml ($p<0.05$).

3 months after the discharge of patients from the hospital, the average level of TNF-α in the control group decreased by 9% and amounted to 8.2 pg/ml. The level of TNF-α in the study group decreased by an average of 16% from the initial values and amounted to 7.6 pg /ml ($p<0.05$).

From the above, it can be seen that in the study group, patients receiving roflumilast had a decrease in TNF-α on average to normal figures. 3 months after treatment in the control group, the level of TNF-α was normalized in 46.2% of patients, in the study group – in 84.5% of patients.

Conclusion. COPD is often combined with coronary heart disease, due to systemic inflammation, confirmed by the dynamics of proinflammatory cytokines during COPD exacerbation (CRP level in the control group increased by an average of 38%, in the study group – by 42% ($p<0.05$); IL-6 index in the control group increased by an average of 34%, in the study group – by 30% ($p<0.05$); TNF-α level was increased in patients of the control group by an average of 8%, in patients of the study group – by 10% ($p<0.05$). The addition of roflumilast to anti-inflammatory therapy of COPD reduces the level of inflammatory markers in the blood, stabilizes the clinical manifestations of COPD, reduces the duration of myocardial ischemia, reduces the number of angina attacks and cases of hospitalization for coronary heart disease.

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