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COMORBID COURSE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND ISCHEMIC HEART DISEASE: PATHOGENETIC ASPECTS OF COMPLICATION PREVENTION

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Abstract

Chronic obstructive pulmonary disease (COPD) is characterized by a high prevalence of cardiovascular comorbidity, with ischemic heart disease (IHD) playing a leading role. The prevalence of IHD in patients with COPD reaches 30–45% and is associated with a twofold increase in the risk of developing pulmonary hypertension (PH). PH is detected in 40–70% of COPD patients; however, timely diagnosis is made in only 25% of cases, which determines an unfavorable prognosis and an increase in mortality by 1.8–2.3 times. The key pathogenetic mechanisms of PH formation in COPD include endothelial dysfunction, chronic hypoxia, systemic inflammation, and oxidative stress, leading to pulmonary vascular remodeling and right ventricular dysfunction. Psychoemotional and neurovegetative disorders play a significant role in disease progression. Modern approaches to prevention and treatment emphasize the importance of early detection of comorbid pathology and comprehensive pharmacological and non-pharmacological therapy aimed at correcting endothelial dysfunction and reducing the risk of complications.

Keywords: chronic obstructive pulmonary disease; ischemic heart disease; pulmonary hypertension; endothelial dysfunction; comorbidity; dyspnea; complication prevention.

Chronic obstructive pulmonary disease (COPD) is characterized by a high prevalence of cardiovascular comorbidity, among which ischemic heart disease (IHD) occupies a leading position. According to epidemiological studies, the prevalence of IHD among COPD patients is 30–45%, while the comorbid course is associated with a twofold increase in the risk of pulmonary hypertension and chronic cor pulmonale [3,6]. One of the early clinical manifestations is progressive dyspnea caused by a combination of bronchial obstruction, chronic hypoxia, and coronary insufficiency [1,7]. Prevention of complications includes early detection of comorbid pathology, correction of risk factors, smoking cessation, and optimization of basic bronchopulmonary and cardiological therapy, which allows reducing hospitalization rates by 20–25% and improving disease prognosis [8,11].

Progression of pulmonary hypertension (PH) in patients with chronic obstructive pulmonary disease is one of the most severe complications, significantly worsening prognosis and quality of life [1,2]. According to modern epidemiological studies, PH of varying severity is detected in 40–70% of COPD patients, with its incidence directly correlating with disease duration and severity of bronchial obstruction [3,6].

Among all forms of pulmonary hypertension, COPD is one of the leading causes of secondary PH, as confirmed by international registries and clinical observations [1,7]. Despite this, timely diagnosis of PH is achieved in only about 25% of cases, which is due to the subtlety of clinical manifestations at early stages and insufficient physician alertness [5,7]. Several studies have shown that the presence of PH in COPD patients increases mortality risk by 1.8–2.3 times compared to patients without vascular complications [8,9].

Endothelial dysfunction plays a key role in the pathogenesis of pulmonary hypertension in COPD, developing against the background of chronic hypoxia, systemic inflammation, and oxidative stress [4,6]. Impairment of endothelium-dependent vasodilation is accompanied by decreased nitric oxide production, increased vascular tone, and remodeling of pulmonary arteries [4]. These changes lead to increased pulmonary vascular resistance and progressive elevation of pulmonary artery pressure [2,9].

The development of pulmonary hypertension in COPD contributes to structural and functional changes of the right ventricle, including hypertrophy, dilation, and impaired diastolic function [3,10]. According to echocardiographic studies, signs of right ventricular diastolic dysfunction are detected in more than 60% of patients with COPD complicated by PH and are associated with an unfavorable prognosis [10].

Psychoemotional and neurovegetative disorders also play an important role in disease progression, exacerbating vascular dysregulation and negatively affecting the course of COPD and PH [6,9]. Modern treatment concepts emphasize the need for a comprehensive, multistage, and individualized approach to the management of patients with COPD complicated by cor pulmonale [6,7].

In recent years, it has been shown that the use of vasoactive therapy, including pulmonary vasodilators, in patients with severe pulmonary hypertension associated with COPD may contribute to reduced mortality and improved functional status; however, data on the efficacy and safety of such therapy remain limited. In this regard, interest in non-pharmacological treatment methods aimed at correcting endothelial dysfunction and hypoxia has increased [11,12].

Recent studies indicate the promise of comprehensive non-pharmacological approaches capable of improving endothelium-dependent vasoregulation, reducing inflammation, and slowing the progression of pulmonary hypertension in patients with COPD [10,12].

Aim of the Study

To investigate the features of right ventricular diastolic function and endothelium-dependent vasoregulation of peripheral vessels in patients with chronic obstructive pulmonary disease comorbid with ischemic heart disease during comprehensive therapy.

Materials and Methods

A total of 53 patients with COPD complicated by pulmonary hypertension (mean age 49.7 ± 2.8 years, disease duration 10.7 ± 2.9 years), with mean pulmonary artery pressure exceeding 25 mmHg, were examined. Additionally, 40 patients with severe COPD (mean age 56.9 ± 2.6 years, disease duration 16.8 ± 3.7 years) and 20 practically healthy individuals forming the control group were examined.

Patients were randomized according to treatment methods and divided into three subgroups. Subgroup A received standard therapy in accordance with GOLD recommendations. Subgroup B received standard therapy combined with amplipulse therapy. Subgroup C received standard therapy combined with Zupa granules (ZG) and amplipulse therapy.

Endothelium-dependent vasodilation was assessed using brachial artery Doppler ultrasound with a compression test. Echocardiographic examination included assessment of right ventricular diastolic function (E/A ratio, IVRT, DT, atrial filling fraction) and mean pulmonary artery pressure. Plasma levels of stable nitric oxide metabolites were determined. Pulmonary function was evaluated using FEV_1, FVC, and Tiffeneau index. Psychoemotional status was assessed using the Spielberger anxiety scale.

Statistical analysis was performed using Student's t-test; differences were considered significant at $p < 0.05$.

Results and Discussion

All patients with COPD comorbid with IHD demonstrated high levels of anxiety, mainly due to reactive and trait anxiety. The most pronounced affective disorders were observed in patients with pulmonary hypertension. Reactive anxiety exceeded control group values by 38–40%, and trait anxiety by 32–39%.

Patients with COPD and PH showed a significant decrease in stable nitric oxide metabolites and marked impairment of endothelium-dependent vasodilation, accompanied by increased vascular resistance and deterioration of pulmonary hemodynamics. Endothelial dysfunction was combined with changes in right ventricular diastolic function, manifested by prolonged isovolumic relaxation time, reduced early diastolic filling, and increased contribution of atrial systole.

The use of amplipulse therapy and the combination of ZG with amplipulse therapy against the background of standard treatment resulted in significant improvement in endothelium-dependent vasoregulation, increased nitric oxide metabolite levels, decreased mean pulmonary artery pressure, and improvement in right ventricular diastolic function parameters. The most pronounced positive changes were observed in the combined therapy group. Simultaneously, a reduction in dyspnea severity and affective symptoms was noted.

Standard therapy without inclusion of vasoactive and non-pharmacological methods did not have a significant effect on pulmonary hemodynamics or right ventricular diastolic function.

Conclusions

1. The severity of pulmonary hypertension and the degree of right heart remodeling in patients with COPD comorbid with IHD are directly related to the severity of endothelial dysfunction and disease duration.
2. Reduced endothelium-dependent vasodilation of peripheral vessels correlates with impaired right ventricular diastolic function and increased pulmonary vascular resistance.
3. Inclusion of amplipulse therapy in the comprehensive treatment of COPD complicated by pulmonary hypertension contributes to improved endothelial function, reduced pulmonary artery pressure, decreased dyspnea, and reduced affective disorders, which is important for preventing disease progression.

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