EARLY DIAGNOSTICS OF PULMONARY HEMODYNAMIC DISORDERS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND EFFECTS OF COMPLEX THERAPY

Introduction. Chronic obstructive pulmonary disease as a cause of death, ranks 4th in the world in the age group over 45 and is the only disease in which mortality continues to increase. Due to the widespread prevalence of ChOPD, direct medical and indirect costs associated with morbidity and premature mortality represent a serious economic and social problem for society in general and health authorities in particular [1,2]. Obviously, only an in-depth study of all aspects of this disease will help find a way out of the current impasse and in developing countries [3,10]. The risk of ChOPD varies from 1.85 to 2.88 per 1,000 population. According to the conclusion of the World Health Organization, in the last 10 years, ChOPD among the causes of death is in 4th

Annotation. The study found that patients with vascular endothelial function and diastolic dysfunction of the right ventricle (RV) in patients with chronic obstructive pulmonary disease (ChOPD) in dynamics are recommended to combine therapy with calcium channel antagonists to improve pulmonary hemodynamics.

Key words: chronic obstructive pulmonary disease, right ventricular hypertrophy, vascular endothelial function, right ventricular (RV) diastolic dysfunction, amlodipine.
place, being the cause of 4.9% of deaths of all diseases. According to experts, by 2020, ChOPD will take the 3rd place in the structure of total mortality [7,8,16]. Along with smoking, industrial pollutants such as dust, gases, smoke, toxic aerosols, which significantly increase the frequency and severity of the disease, are becoming an important risk factor for the development of ChOPD [9]. The data given in the literature by domestic and foreign authors indicate that about 15–20% of all cases of ChOPD are associated with professional activity [5, 4]. Chronic obstructive pulmonary disease is essentially a disease with features of a destructive process, which results in damage to the entire respiratory system, including the bronchi up to the terminal bronchioles, parenchyma and interstitium [1]. An important feature of the pathological process in ChOPD is its low reversibility [2]. The main method of treatment for such patients has long been the use of bronchodilators, starting with belladonna. However, as new knowledge about the essence of pathology was gained, new approaches to therapy were developed [8]. First of all, it became clear that ChOPD patients are not the same. They differ in the course of the disease, in symptomatology, in prognosis, in response to one or another therapy, which is defined as phenotypes [4,7,8]. Chronic obstructive pulmonary disease is a severe chronic airway disease and is a serious public health problem [1]. Currently, cardiovascular effects are considered as systemic manifestations of ChOPD, among which endothelial dysfunction appears as the primary link in the lesion of the vessel wall [2]. Dysfunction of the endothelium, already revealed in the early stages of the disease, aggravates the growing respiratory failure, hypoxemia and tissue hypoxia [3]. This contributes to the occurrence of pronounced disorders of systemic and pulmonary hemodynamics. In recent years, new data have been obtained on the role of disturbances in the functional activity of the endothelium in the pathogenesis of bronchopulmonary diseases [4,11]. Objective registration of the state of the vascular endothelium is important not only for assessing the degree of its dysfunction, selection of pathogenetically substantiated drug and non-drug treatment, but also for determining the prognosis of the course of the disease [5]. Despite the
emergence of new classes of drugs for the treatment of ChOPD, there remains a significant number of patients with severe forms of this disease who need long-term administration of a number of drugs [6]. In recent years, the role of nitric oxide in lung diseases has been actively studied [6,7], which is one of the most important mediators of the functioning of various organs and systems [8,3], and in treatment tactics, much attention is paid to amino acids with a therapeutic effect [8]. ChOPD is a complex chronic inflammatory disease that involves many structural and inflammatory cells, followed by the release of inflammatory mediators that lead to the formation of the main pathophysiological mechanisms of the disease [1,6]. Currently, about 50 cytokines and chemokines are known that play an important role in the pathogenesis of ChOPD [7], but their role in the control of pathophysiological processes is not fully understood. The study of markers of inflammation in the lungs is usually carried out during material collection using the methods of bronchoalveolar lavage (BAL), bronchobiopsy [8], as well as serum and urine to assess systemic effects.

Materials and methods. We examined 35 patients with ChOPD and 20 healthy individuals (LP). In patients, according to Doppler echocardiography, PH was determined (the level of mean pulmonary arterial pressure LAPav> 25 mm Hg) and the presence of RV without PH (thickness of the anterior wall of the RV according to echocardiography <5 mm, with anteroposterior size of the RV> 2.5 cm ). Patients were divided into 2 groups and a, b subgroups: 1a - gr. control group (CG) 8 patients with COPD with PH; 1b - column 7 patients with ChOPD with PDG received basic therapy (BT, GINA 2006), 2a - gr. 10 patients with ChOPD with PH; 2b - column 8 patients with ChOPD with PDG received BT and a combination of calcium antagonist dihydropyridine series amlodipine (A). For 10 days, patients received on the background of BT received a combination of a calcium antagonist of the dihydropyridine series amlodipine (An) 2.5-5 mg / day. Respiratory function (FVD) was assessed by spirography methods, with an assessment of lung vital capacity (FVC), forced expiratory volume in 1 sec (FEV1) and Tiffno's index (FEV1 / FVC); the study
of peripheral blood flow-endothelium-dependent vasodilation (EDVD) was carried out with an ultrasound device SonoScape SSI-8000 (China); blood oxygen saturation (SaO2) was assessed using the pulse oximetric method "OXY" (Germany); Doppler echocardiography was evaluated using a Vivid S60 ultrasound machine (Sweden) and SonoScape SSI-8000 (China) in accordance with the recommendations of the American Society. The results were processed using the Excel software package using the Student's t-test. Differences between the studied parameters were considered significant at p <0.05.

**Results and its discussion.** Before treatment, under conditions of increased myocardial oxygen demand, patients had a violation of the parameters of endothelium-dependent vasodilation: a decrease in the maximum blood flow velocity in the brachial artery after a reactive test (Vmax) - by 18.9% (group 1) versus 28.4% (2nd); an increase in the index of circulatory resistance (ICR) - by 18.2 and 29.1% (p <0.001 in relation to the control group). The data obtained correspond to the opinion of A.G. Chuchalin. [7] that the intensification of inflammatory phenomena leads not only to local changes, but also to significant systemic changes. Thus, disturbances in the peripheral mechanisms of regulation of vascular tone develop earlier and more significantly in patients with PH in ChOPD compared with ChOPD with PDG (p <0.05, in relation to indicators of LP). According to FVD, there was a decrease in the ventilation state of the bronchopulmonary system in all patients with PH and PDG. Thus, the FEV1 index in all patients was -46.1 ± 1.6%, (p <0.005), SaO2, respectively, 89.6 ± 1.4% (p <0.05), which is typical for an increase in bronchial obstruction. The results obtained revealed the relationship between the clinical course, an increase in LAP avg. and ventilation and perfusion disorders in patients with COPD. There was a tendency towards a more pronounced decrease in the fraction of atrial filling (FPF,%) of the pancreas in patients with ChOPD 2 - gr. LH and RV of the subgroups, respectively, by 1.05 and 1.08 times; and an increase in the time of deceleration of the maximum speed of early diastolic filling (VZ, m / s) by 1.07 and
1.15 times; a decrease in the ratio of early and late diastolic filling (E \ A), respectively, by 1.17 and 1.45 times (p <0.05), which indicates an increase in myocardial stiffness and impaired passive relaxation. After the therapy, there is an improvement in the studied parameters. Positive correlations were revealed between SaO2: isovolumic relaxation time (VIR, m / s) and VZ, respectively, 0.40 and 0.35 (p <0.05). After treatment in 2 gr. LH and RVD subgroups, in patients, the blood SaO2 values increased to 89.8 ± 0.7 and 92.3 ± 0.6%, respectively, by 1.10 and 1.16 times lower than the LP values (p <0.05). In the dynamics of the complex treatment with Am E \ A, the indicators increased by 7.9 and 4.0%, respectively, and the mean pulmonary artery pressure (LAPav) by 1.20 and 1.16 times (p <0.01). The use of BT alone does not have a significant effect on the parameters of pulmonary hemodynamics, providing only a decrease in LADav.

Correlation analysis showed that the increase in obstruction and hypoxemia are closely associated with the development of diastolic dysfunction of the pancreas. At the same time, the severity of the increase in LADav, has a significant dependence on the severity of ChOPD.

In our study, the use of amlodipine 2.5-5 mg / day against the background of BT in patients with COPD with PH led not only to a decrease in PAP avg, but was also accompanied by a positive shift in the ventilation-perfusion capacity of the lungs in group 2 of patients by 10.5% (p <0.01). LAD Wed after treatment in group 2 decreased by 15.7% (significance of the difference with the indicators before treatment p <0.05).

It should be noted that in patients with ChOPD and PH with an increase in PAP avg. changes in the structure of filling the pancreas in diastole. The mutual aggravation of disorders in the combination of cardiorespiratory pathology is based on the commonality of some links of pathogenesis - disorders of pulmonary and cardiac microcirculation, the development of hypoxemia and pulmonary hypertension.
It was found that in patients with ChOPD with PH receiving amlodipine against the background of BT, there is an improvement in the parameters of pulmonary hemodynamics and ventilation capacity and bronchial patency of the lungs.

**Conclusions.**

1. Violations of the peripheral mechanisms of regulation of vascular tone develop earlier and more significantly in severe clinical course of ChOPD with an increase in PAP cf. (p <0.05).

2. Complex treatment of patients with ChOPD with pulmonary hypertension, including amlodipine, reduces the tone of pulmonary vessels and simultaneously improves endothelium-dependent vasodilation of peripheral vessels.

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