

The State Of Endothelium-Dependent Vasoregulation In The Dynamics Of Impact Of Various Therapy Regimes In Patients With Chronic Obstructive Lung Disease Complicated By Pulmonary Arterial Hypertension

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SUMMARY

The progression of pulmonary hypertension and the development of chronic pulmonary heart disease in COPD patients are closely related to the development of endothelial dysfunction and affective symptoms. We noted improvement in the parameters of diastolic function of the right ventricle, mean pulmonary arterial pressure, the level of stable metabolites of nitric oxide, endothelium-dependent vasoregulation and psychoemotional status in patients with COPD complicated by HPH, after complex treatment with ozone therapy and amlodipine against standard therapy.

Keywords: chronic obstructive pulmonary disease, pulmonary-endothelium function, respiratory function, therapy.

In recent decades there has been a steadily growing interest of researchers in the problem of pulmonary hypertension (PH). The development of PH and the formation of chronic pulmonary heart (CHPH) is the most serious complication of lung diseases. Among patients with pulmonary hypertension and CHPH, the greatest proportion is in patients with chronic obstructive pulmonary disease (COPD). According to statistical data, CHPH is diagnosed in time only in 25% of cases [1,7].

In recent years, Uzbekistan has seen an increase in the prevalence and mortality from lung diseases complicated by a chronic pulmonary heart. To optimize early diagnostics, adequate prevention and treatment of CHPH, it is necessary to clarify the factors that lead to its development and aggravate its course [2,8].

A number of authors note that in COPD there is vasoconstriction of the vessels of the small circle of blood circulation, leading to hypertrophy, dilatation, and deficiency of the right ventricle (RV) of the heart.

But the question of which pathogenetic mechanisms are at the root of these changes in COPD has not yet been resolved. According to most researchers, in patients with chronic lung diseases, the leading factor in the development of changes in hemodynamics and diastolic function of the right ventricle of the heart are disturbances in the ventilating capacity of the lungs, hypoxia and endothelial dysfunction [3,10]. With prolonged hypoxia and affective state in patients with COPD, the endothelial function contributing to vascular relaxation is significantly reduced, which can serve as a cause of narrowing of the lung vessels, the development of pulmonary hypertension and hypertrophy of the right ventricle (GRV) of the heart. In the study of peripheral blood flow disorders in patients with chronic obstructive pulmonary disease, great importance is attached to vasoregulatory function of the vascular endothelium. The role of endothelial function in the pathogenesis of PH was studied primarily in patients with primary PH. The work devoted to the study of changes in endothelial regulation of vascular tone in secondary PH in patients with COPD is extremely small [4,11]. It has now become apparent that neuropsychic factors have a negative effect on the state of internal organs through the autonomic nervous system [5]. Undoubtedly, prevention and therapy of COPD patients complicated by a pulmonary heart should be early, complex, rational, individual and multi-stage [6,12].

Significant advances in the treatment of CHPH in recent years are associated with calcium antagonists, which significantly improve survival and life expectancy in patients with chronic heart failure [13,14]. However, not all the effects of the drugs in this group have been sufficiently studied.

At the same time, it is important to search for alternative non-pharmacological methods of treating CHPH that can directly affect the pathogenetic

mechanisms of the development of COPD complications. One of such methods of therapy at the stage of exacerbation of CHPH, perhaps, is ozone therapy, applied against the background of basic treatment. The results of clinical studies on the use of ozonotherapy in patients with coronary heart disease, hypertensive disease, bronchial asthma with associated disorders of carbohydrate metabolism, chronic obstructive pulmonary disease, indicate its positive effects: metabolic, bioenergetic, anti-inflammatory, membrane-stabilizing, bronchodilator actions [15].

Purpose of the study. To study the state of diastolic function of the prostate, pulmonary hemodynamics and vasoregulatory function of the endothelium of peripheral vessels in patients with chronic pulmonary heart in the dynamics of complex treatment.

Materials and methods of research. A total of 53 patients with COPD were examined (age 49.7 ± 2.8 years, duration of the disease 10.7 ± 2.9 years) in whom the disease was complicated by the development of PH with a mean pulmonary arterial pressure (PAPsr) greater than 25 mm. Gt; Art. Also 40 patients with COPD were examined (age 56.9 ± 2.6 years, disease length 16.8 ± 3.7 years), in whom the disease was complicated by GVR (thickness of the anterior wall of the prostate heart > 5 mm, with anterior-posterior RV more 2.5 cm) and 20 healthy individuals (ZL).

Patients were randomized according to the treatment method and divided into 3 subgroups, respectively: subgroup A - 14 COPD patients with GPG (1a) and 17 patients with COPD with LH (2a) received standard therapy (CT) according to international recommendations GOLD (2006); Subgroup B - 12 patients with COPD with GPL (1b) and 17 patients with COPD with LH (2b) on the background of CT received amlodipine (A) at a dose of 5-10 mg per day and ozone therapy (RT); Subgroup B - 14 COPD patients with HRV (1c) and 19 patients with COPD with PH (2c), in whom standard therapy was combined with OT. Ozone therapy was performed as an intravenous injection of ozonized saline ($1000 \mu\text{g} / \text{l}$) daily, for a course of 10 infusions. The effectiveness of treatment regimens was evaluated in dynamics on the 10th day of therapy. Psycho-emotional status of patients was assessed on the basis of psychological testing using the Spielberger test to detect reactive anxiety (RA) and trait anxiety (TA).

Endothelium-dependent vasodilation (EDV) was evaluated using Doppler brachial artery (BA) c using ultrasonic Toshiba SSH 60A system (Japan) postoyannovolnovom mode. Measured maximum systolic blood flow velocity (MCC, m / s) and circulatory vascular resistance index (VRI, ed.) In response to compression assay (CA). Doppler echocardiography was performed with the help of the Shimadzu 500A ultrasound system (Japan) using the

Hatle L., Angelsen B method (1985), with an estimation of the diastolic function: the ratio of early and late diastolic filling (E / A), isovolume relaxation time (VIR, M / s), deceleration time of the maximal speed of early diastolic filling (DF, m / s), atrial filling fraction (AFF,%), mean pulmonary arterial pressure (PAP, mmHg) and stable metabolite level of oxide nitrogen (SMON) in plasma rovi. The ventilatory capacity of the lungs (CL) was determined by estimating the volume of forced expiration in 1 second (FEV1,%), vital capacity of lungs (FVC,%), and Tiffno index (FEV1 / FVC,%).

Results are processed using the Excel software package, using Student's t-test. Differences between the parameters studied were considered reliable at $p < 0.05$.

Results of the study and discussion. The dominance of disturbing affect in the structure of the personality is confirmed by the results of psychometric analysis using Spielberger's method, using the scale of reactive anxiety and personal anxiety. All patients with COPD have high anxiety as a stable personality trait. The Spielberger scale in patients with COPD with HRV and PH revealed a significant increase in personal anxiety at 38.6 and 32.5%, and especially reactive anxiety by 40.4% and 38.2%, respectively (compared with healthy individuals). The data obtained by us in a subgroup of patients with COPD complicated with HRV showed that the level of reactive anxiety and the level of personal anxiety is higher in comparison with patients with COPD complicated by PH.

The study found that in patients with COPD complicated by HPH, there is an imbalance in the levels of stable metabolites of nitric oxide (MNO) in the blood plasma and a decrease in the ability of the vessels of PA to active endothelium-dependent vasodilation. Thus, analysis of the results of samples with reactive hyperemia showed that in patients with HRV the maximum systolic blood flow velocity was significantly decreased and correlated with the severity of the disease. In patients with chronic obstructive pulmonary disease, the MSS in response to KP was reduced, compared with the indicators of healthy individuals by 32.9 and 19.2%, respectively, the DIC increased by 38.6 and 28.0%. In parallel with the worsening of AFL and endothelium-dependent vasodilation, there is a violation of the diastolic function of the heart.

It should be noted that in patients with COPD complicated by CHPH, changes in the structure of filling of the pancreas in diastole were significantly expressed (table).

Table

Assessment of the level of CMNO, cardiorespiratory parameters and diastolic function of the right ventricle of the heart in patients with COPD complicated by a chronic pulmonary heart in the dynamics of various treatment regimens ($M \pm m$).

Indicators	Standart therapy		ST+A+OT		ST+OT	
	1a-group CHOPD with HRV (n=14)	2a- group CHOPD with PH (n=17)	1b- group CHOPD with HRV (n=12)	2b- group CHOPD with PH (n=17)	1c- group CHOPD with HRV (n=14)	2c- group CHOPD with PH (n=19)
CM _{No}	$\frac{6,36 \pm 0,26}{6,56 \pm 0,3}$	$\frac{5,39 \pm 0,2}{5,52 \pm 0,26}$	$\frac{4,69 \pm 0,2}{5,01 \pm 0,2}$	$\frac{4,39 \pm 0,1}{6,23 \pm 0,2^*}$	$\frac{4,51 \pm 0,2}{4,80 \pm 0,2}$	$\frac{5,38 \pm 0,2}{5,85 \pm 0,2^*}$
FEV ₁ , %	$\frac{27,5 \pm 1,2}{27,9 \pm 1,4}$	$\frac{38,8 \pm 0,9}{39,5 \pm 0,8}$	$\frac{42,8 \pm 0,9}{50,1 \pm 1,1}$	$\frac{46,1 \pm 1,6}{55,2 \pm 1,5^{**}}$	$\frac{39,4 \pm 1,3}{44,1 \pm 0,8^*}$	$\frac{44,6 \pm 0,5}{50,1 \pm 1,3^{**}}$
DT m/c	$\frac{210,30 \pm 0,94}{208,80 \pm 1,06}$	$\frac{192,3 \pm 1,6}{191,4 \pm 1,4}$	$\frac{214,60 \pm 1,42}{201,30 \pm 1,84^*}$	$\frac{201,1 \pm 1,4}{186,4 \pm 1,3^*}$	$\frac{214,20 \pm 1,21}{206,40 \pm 1,36^*}$	$\frac{196,1 \pm 1,5}{188,1 \pm 1,8^*}$
PADmid. mm. pt. ct	$\frac{34,9 \pm 0,6}{34,1 \pm 0,7}$	$\frac{28,2 \pm 0,5}{27,5 \pm 0,9}$	$\frac{33,1 \pm 0,5}{29,3 \pm 0,6^*}$	$\frac{28,1 \pm 0,7}{22,4 \pm 0,6^*}$	$\frac{28,9 \pm 0,5}{23,9 \pm 0,9^*}$	$\frac{36,7 \pm 0,2}{33,8 \pm 0,5^*}$

Note: in the numerator, the indices are before treatment, in the denominator after treatment (** p <0.005 and * p <0.05 the authenticity of the difference with the rates before treatment).

The decrease in filling indices found in early diastole is associated with a disturbance in the relaxation of hypertrophied myocardium of the heart's pancreas, as a result of which the decrease in intraventricular filling slows down and the FPN increases.

With the use of ozone therapy, as well as amlodipine and ozonotherapy against the CT background in COPD patients complicated by CLS, there was not only a decrease in LADA, DD, but also an increase in CMNO and endothelium-dependent vasodilation.

The maximum systolic velocity after the compression test increased by 6.7 and 7.6% (p <0.05). A decrease in the index of circulatory resistance of blood vessels was determined - by 6.9 and 7.2% (p <0.05). There were positive changes in the parameters of the diastolic function of the right ventricle. In therapy with amlodipine and ozonotherapy in patients with COPD complicated by GPG and LH, there was a significant decrease in indices: the time of isovolytic relaxation, respectively, by 9.7 and 10.5%, the time of slowing the maximum speed of early diastolic filling by 6.6 and 7.3%, atrial filling fractions - by 11.8 and 13.9%, LADsr - by 13.1 and 15.7%. Against the background of the therapy, the ratio of E / A increased by 11.5 and 12.4% (p <0.05), respectively, and the increase of CMNO by 9.7 and 10.6%. The affective symptomatology decreased: RT by 5.1%, RT by 7.1%.

Ozone therapy against CT in COPD patients resulted in an increase in the maximum systolic velocity after the compression test by 5.9 and 5.2% and a decrease in the index of the circulatory resistance of the vessels, by 6.2 and 6.7%,

respectively (p <0.05). The decrease in the indices of isovolytic relaxation was found, respectively, at 4.6 and 5.1%, the time of slowing the maximum speed of early diastolic filling by 3.8 and 4.1%, the atrial filling fraction by 8.3 and 9.9 %, LADsr - by 8.7 and 9.5% (p <0.05). The ratio of early and late diastolic filling increased by 7.7 and 8.3% (p <0.05), respectively, and an increase of 6.1% and 8.1% in CMNO. The affective symptomatology decreased: RT by 4.8, LT - by 5.4%.

The obtained data made it possible to state a more pronounced improvement in the parameters of CMNO, EZVD, ACL, diastolic function of the cardiac pancreas and affective symptoms in the dynamics of regimens of complex therapy with amlodipine and ozone therapy in patients with COPD with LH, compared with patients with COPD complicated by GPZH.

The results of the study noted that regimens of standard therapy had no effect on changes in the indices of diastolic function of the prostate heart and the level of mean pulmonary arterial pressure.

As a result of the study, the vasodilating effect of ozonotherapy and amlodipine was confirmed, which was manifested by a decrease in pulmonary arterial pressure and an improvement in the indices of the diastolic function of the heart's pancreas.

Studies have shown that before the start of treatment, the increase in affective symptoms, decrease in AFL, CMNO, and changes in vascular ability to active vasodilation are parallel to disturbances in the structure of filling of the prostate in the diastole. These changes are significantly expressed in patients with COPD with GVR compared with the indices of patients with COPD with LH. Mutual complication and progression of violations of peripheral and central hemodynamics is based on the commonality of some links of pathogenesis: the development of disturbances of AFL and CMNO level,

pulmonary-cardiac microcirculation and pulmonary hypertension (Vermeire P, Pride N.B et al., 2001; Fisnman A.P., 2004). The progression of LH and the development of chronic pulmonary heart disease in COPD patients are closely related to the development of endothelial dysfunction, which should be taken into account when developing a treatment plan for this category of patients (Mukharlyamov NM, 1995; Groechenig E., 1999). We noted improvement in the parameters of diastolic function of the right ventricle, mean pulmonary arterial pressure, CMNO level, EECD and affective symptoms in patients with COPD complicated by CLS, occurring after complex treatment with ozonotherapy and amlodipine on the background of CT.

Conclusions:

1. The degree of pulmonary hemodynamics, the hemodynamic load on the right heart, the increase in the size of the prostate and the thickness of the prostate in patients with CLS directly depend on the severity of systemic endothelial dysfunction and the duration of the disease.

2. The decrease in the ability of peripheral vessels to active vasodilation positively correlates with the state of diastolic function of the heart's pancreas and the tone of the pulmonary vessels necessary for normal gas exchange of lung tissue.

3. Ozone therapy and amlodipine on the CT background significantly corrects the level of CMNO, improving endothelium-dependent vasodilation and diastolic function of the right ventricle of the heart, reducing the level of mean pulmonary arterial pressure and affective symptoms of COPD patients complicated by varying degrees of CLS.

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