



UDC 616. 24 – 007. 272 – 072 : 661. 5

INFLUENCE OF ANAMNESTIC PARAMETERS AND CLINICAL MANIFESTATIONS ON THE FORMATION OF ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH COPD**ВПЛИВ АНАМНЕСТИЧНИХ ПОКАЗНИКІВ ТА КЛІНІЧНИХ ПРОЯВІВ НА ФОРМУВАННЯ ЕНДОТЕЛІАЛЬНОЇ ДИСФУНКЦІЇ У ХВОРИХ НА ХОЗЛ**

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Annotation. Currently, COPD is considered as a systemic pathology. Cardiovascular disorders are distinguished among extrapulmonary manifestations, the earliest manifestations of which are endothelial dysfunction. However, in the literature there is ambiguity of data proving the influence of anamnestic, clinical parameters of COPD on the formation and progression of endothelial dysfunction.

The aim of the study was to study the relationship between the concentration of NO in the exhaled air in patients with COPD and some clinical and anamnestic parameters of their disease, depending on the stage and phase of the pathological process. 25 male patients with COPD stages I-IV in remission and exacerbation were examined; the control group included 11 practically healthy individuals.

A correlation was established between the concentration of NO in the exhaled air and the duration of the disease ($r = -0.67$, $p=0.02$) in patients with COPD stages III-IV during exacerbation, which may indicate the formation and progression of endothelial dysfunction with an increase in the duration of the disease. At the same time, in the remission phase in this contingent, the concentration of NO in the exhaled air did not depend on the studied parameter. Regardless of the stage and phase of the pathological process, age, the frequency of exacerbations per year, in patients with COPD indicators of external respiration function do not affect NO concentration in the exhaled air and, accordingly, are not significant parameters that determine the level of the studied marker among presented contingent.

Keywords: COPD, endothelial dysfunction, NO in exhaled air.

Introduction.

Currently, COPD is considered as a systemic pathology characterized by various extrapulmonary manifestations [2, 5], among which cardiovascular disorders deserve special attention, the earliest manifestation of which is endothelial dysfunction (ED) [3, 5].

It is known that the vascular endothelium is represented by a highly specialized metabolically active monolayer of cells capable of producing vasorelaxant (nitric oxide (NO), prostacyclin, endothelial hyperpolarization factor, etc.) and vasoconstrictor (endothelin-1, thromboxane A₂, etc.) substances, between which physiological conditions maintain equilibrium. It has been proven that NO is the most important factor in the pathogenesis of ED. Receptors located in the endothelium, transforming mechanical signals, induce NO synthase, which leads to NO accumulation and vasodilation due to a decrease in Ca²⁺ concentration in the cytoplasm [1, 2, 4]. In this regard, a large number of studies in COPD patients are currently devoted to the study of the state of the vascular endothelium and the



development of ED [1, 3]. At the same time, there is ambiguity in the literature proving the influence of anamnestic parameters and clinical manifestations of COPD on the formation and progression of ED, which determined the **purpose of our study** - to study the relationship between NO concentration in exhaled air in patients with COPD and some medical history data, and as well as clinical parameters of the disease, depending on the stage and phase of the pathological process.

Materials and methods of research

The study involved 25 men (mean age 61.13 ± 2.10 years, mean disease duration 11.97 ± 0.63 years) with COPD stages I-IV. All of them either never smoked or had abstained from smoking for more than five years. The diagnosis was established in accordance with the GOLD 2022 criteria and the order of the Ministry of Health No. 555 of 06/27/2013. All patients received standard therapy depending on the stage of the disease.

The exclusion criteria were: concomitant pathology of the cardiovascular system (according to the anamnesis, objective examination, measurements of blood pressure, ECG, echocardiography and blood lipid parameters).

Design of work - patients were divided into 2 groups depending on the stage of the disease: group 1 consisted of 13 patients with COPD stages I-II, group 2 consisted of 12 patients with COPD stages III-IV. All studies were conducted twice - in exacerbation and remission of COPD. The control group 3 included 11 practically healthy volunteers who never smoked, with normal indicators of respiratory function (PFR).

To verify the diagnosis of COPD, respiratory function parameters were determined using a MasterLab spirograph (Jäger, Germany): the levels of forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), FEV1/FVC1 ratio were analyzed; a test for the reversibility of bronchial obstruction was performed with a short-acting β_2 -agonist (salbutamol 400 μg). Also, in the course of this study, the concentration of NO in exhaled air was assessed using the Niox Mino apparatus (Aerocrine). Measurement of respiratory function and NO concentration in the exhaled air was carried out from 8 to 10 am, on an empty stomach, before taking medications.

Program "Statistics 7" was used for static handling of the results with the definition of the arithmetic mean, significance criterion of differences and correlation analysis.

Results and its discussion

The characteristics of all examined patients according to the parameters of age, stage and disease duration, as well as the number of exacerbations of COPD per year are presented in Table 1, according to which patients of all groups were compared in age, which indicates the representativeness and comparability of this sample.

Disease duration and number of exacerbations per year (Table 1) were significantly higher in 2nd group, which is explained by more severe course of COPD in this group of patients.

Indicators of respiratory function in the groups, depending on the phase of the disease and in comparison with the control group (healthy people) are presented in Table 2.



Table 1 - Characteristics of the examined patients

Indicators	Groups		
	1 (n = 13)	2 (n = 12)	3 (n = 11)
Stage of disease	I-II	III-IV	Practically healthy
Age (M ± m, years)	59,05 ± 1,82	63,20 ± 2,38	57,72 ± 2,87
Disease duration (M ± m, years)	8,11 ± 0,49	15,83 ± 0,76*	-
Number of COPD exacerbations per year (M ± m)	1,02 ± 0,18	2,11 ± 0,26*	-

Note. * $p < 0.05$ for indicators in groups 1 and 2.

Table 2 - Indicators of respiratory function in groups depending on disease phase

Indicators	Groups				
	1 (n = 13)		2 (n = 12)		3 (n = 11)
	remission	exacerbation	remission	exacerbation	control
FEV1 (M ± m, % to due)	78,32 ± 3,67	67,95 ± 3,01*	41,22 ± 2,38	37,25 ± 2,51	98,32 ± 4,21
FVC (M ± m, % to due)	98,02 ± 3,81	86,70 ± 3,50*	69,68 ± 2,49	68,72 ± 3,85	111,83 ± 3,98
FEV1/FVC	68,56 ± 2,1	61,65 ± 1,78*	44,68 ± 2,25	40,67 ± 2,72	89,52 ± 1,46

Note. * $p < 0.05$ for indicators in group 1.

According to obtained data, the levels of FEV1 ($p=0.037$), FVC ($p=0.039$), and FEV1/FVC ratio ($p=0.015$) significantly decreased during exacerbation only in group 1, which may indicate a significant impairment of respiratory function in these patients. According to Table 2 respiratory function indicators were significantly lower in patients of second observed group with COPD, which is explained by a higher class of severity of main disease course (COPD stages III-IV). It should also be noted that all respiratory function indicators were significantly higher (1.2–2.7 times) in practically healthy individuals, than in patients with COPD, regardless of the stage or period of the disease - remission or exacerbation ($p < 0.05$).

Correlation analysis of examination results in patients with COPD made it possible to identify a significant negative correlation ($r = -0.67$, $p = 0.02$) between concentration of NO in the exhaled air and the duration of the disease in the 2nd group (COPD stages III-IV) in the period of exacerbations (Figure 1). At the same time, in the presented contingent during the remission period, it was not possible to establish a relationship between the studied parameters ($r = 0.12$, $p = 0.71$).

Most likely, in patients with severe COPD in exacerbation with chronic disease, NO production decreases, which can serve as an early sign of the formation and progression of ED, as well as have a negative impact on disease prognosis. At the same time, in patients in remission with severe COPD, the level of NO did not



depend on the duration of the disease, which may indicate a stable course of dysfunction of the vascular endothelium outside the period of exacerbation.

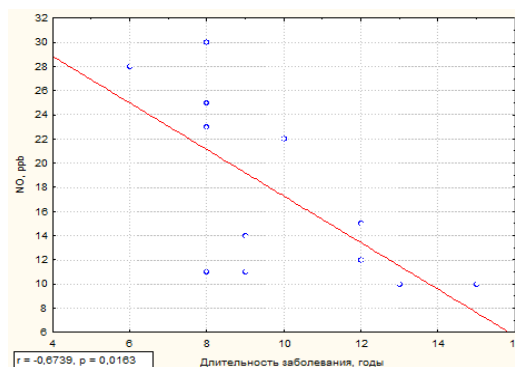


Figure 1. Interrelation between the level of exhaled NO and the duration of the disease in group 2 during exacerbation.

In patients with a mild course of the disease, regardless of pathological process phase, a significant correlation between the level of NO and the duration of the disease was not registered (in remission - $r = -0.15$, $p = 0.63$, in exacerbation - $r = 0.47$, $p = 0.10$), which may confirm a less significant relationship between the level of the studied ED marker and the duration of the disease in the presented group of patients.

Also, there was no significant correlation between the level of NO in the exhaled air and the age of patients in group 1 (in remission - $r = 0.23$, $p = 0.47$, in exacerbation - $r = 0.14$, $p = 0.28$) and in group 2 (in remission - $r = -0.11$, $p = 0.37$, in exacerbation - $r = 0.20$, $p = 0.25$).

Thus, the age of patients, regardless of the stage and phase of the pathological process in the studied groups, was not a significant predictor affecting the level of NO in the exhaled air. Most likely, to study the effect of the age of patients on the state of the vascular endothelium, it is necessary to study the level of NO in the exhaled air in combination with other markers of ED.

In addition, an unreliable correlation was recorded between the level of NO in the exhaled air and the frequency of exacerbations in the year of COPD as in group 1 (in remission - $r = -0.06$, $p = 0.84$, in exacerbation - $r = -0.17$, $p = 0.57$), and in group 2 (in remission - $r = -0.16$, $p = 0.61$, in exacerbation - $r = 0.23$, $p = 0.47$). And also, no relationship was found between the main indicators characterizing the respiratory function and the level of NO in the exhaled air. Thus, the correlation with FEV1 in group 1 was $r = -0.18$, $p = 0.57$ in remission and $r = -0.21$, $p = 0.48$ in exacerbation; in group 2, $r = 0.28$, $p = 0.53$ in remission and $r = 0.19$, $p = 0.35$ in exacerbation.

Thus, regardless of the stage and phase of COPD, the number of disease exacerbations per year and the respiratory function parameters are not associated with changes in the level of NO in the exhaled air in the studied cohort of patients, being, most likely, less significant markers indicating the progression of ED.

Conclusions:

1) In non-smoking patients with COPD stages III-IV during exacerbation with



an increase of disease duration, the concentration of NO in the exhaled air decreases, which most likely may indicate the formation and progression of endothelial dysfunction.

2) In non-smoking patients with COPD stages III-IV in remission, the concentration of NO in the exhaled air does not depend on disease duration, which may be associated with a stable state of the vascular endothelium.

3) In non-smoking patients with COPD, regardless of the stage and phase of pathological process, age, frequency of exacerbations per year, indicators of external respiration function do not affect the concentration of NO in the exhaled air and, accordingly, are not significant parameters affecting the level of the studied marker.

Prospects for further research.

In further studies of the influence of COPD anamnestic and clinical parameters on development and formation of ED, it is advisable to take into account the level of NO in the exhaled air in combination with laboratory (endothelin-1, alveolar macrophages, etc.) and instrumental (occlusive test, test with nitroglycerin) indicators of vascular endothelial dysfunction.

References

1. The effect of smoking on the concentration of nitric oxide in the exhaled air in patients with chronic obstructive pulmonary disease / T. A. Pertseva, E. Yu. Gashinova, N. A. Efimova // Ukrainian Journal of Pulmonology. - 2010. - No. 3. - S. 66-68.

2. Clinical significance of changes in nitric oxide metabolism in pulmonology / T. V. Zvyagina, T. V. Anikeeva, T. M. Belokon // Ukrainian Journal of Pulmonology. - 2012. - No. 1. - P. 66-68.

3. Indicators of endothelial function and the functional state of the respiratory system with varying degrees of severity of ventilation disorders in patients with COPD / V. V. Efimov, V. I. Blazhko, L. S. Voeikova et al. // Ukrainian Therapeutic Journal. - 2011. - No. 3. - P. 44-47.

4. The role of nitric oxide in the pathophysiology and treatment of chronic obstructive pulmonary disease / O. Yu. Kytikova, T. A. Gvozdenko, M. V. Antonyuk et al. // Bulletin of physiology and pathology of respiration. - 2019. - No. 71 - P. 105-111. - Access mode: <https://riorpub.com/ru/nauka/article/27894/view>

5. Global Initiative for Chronic Obstructive Lung Diseases (GOLD). Global strategy for diagnosis, management, and prevention of chronic obstructive pulmonary disease. <https://goldcopd.org/2022-gold-reports-2/>

Статья отправлена: 01.07.2022 г.
Єфімова Н.О.