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INFLUENCE OF SMOKING ON THE CONCENTRATION OF NITRIC OXIDE IN THE EXPIRED AIR OF PATIENTS WITH COPD

Abstract. In recent years, the attention of researchers has been drawn to the study of the state of the vascular endothelium in various diseases. The endothelium produces vasorelaxing and vasoconstrictor substances, as well as a number of enzymes that affect their activation. In the last decade, close attention has been paid to such a vasoactive substance as NO. It is known that NO is one of the most important mediators characterizing inflammation in the respiratory system. Inaddition, it has been proven that the accumulation of NO leadstore laxation of the bronchi. The development of endothelial dysfunctionin COPD is determined by the presence of hypoxia and an increasein the content of various biological lyactive substances, as well as exposure to tobacco smoke.Since the main etiological factor in COPD is smoking, it is important to study the influence of this factor on the level of NO in exhaled air condensate. The aim of the study was to study the effect of active tobacco smoking on the level of NO in exhaled air in patients suffering from COPD. 28 men were examinedwith verifieddiagnosis of COPD duringremission.During the examination, all patients were divided into 2 groups:depending on the presence of the smoking factor. All patients underwent spirometry and determination of NO levels in exhaled air. It was found that the factor of tobacco smoking in patients with COPD in remission affects the level of NO concentration in exhaled air, causing it to significantly decrease compared to the level in non-smoking patients. The degree of tobacco load (duration and intensity of smoking) does not affect the level of NO concentration in exhaled air in patients with COPD in remission. The degree of nicotine dependence affects the level of NO concentration in exhaled air in patients with COPD in the remission phase. The level of NO concentration in exhaled air in smoking and non-smoking patients with COPD in the remission phase does not depend on the severity of broncho-obstructive manifestations.

Keywords: chronic obstructive pulmonary disease, tobacco smoking, nitric oxide inexhalein the air.

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ВПЛИВ ТЮТЮНОПАЛІННЯ НА КОНЦЕНТРАЦІЮ ОКСИДУ АЗОТУ У ПОВІТРІ, ЩО ВИДИХАЄТБСЯ У ХВОРИХ НА ХОЗЛ

Анотація. Увага дослідників останніми роками залучено до вивчення стану судинного ендотелію при різних захворюваннях. Ендотелій виробляє вазорелаксуючі та вазоконстрикторі речовини, а також ряд ферментів, що впливають на їх активізацію. В останнє десятиліття пильну увагу приділяють такій вазоактивній речовині, як NO. Відомо, що NO є одним з найважливіших медіаторів, що характеризують запалення дихальної системи. Крім того, доведено, що накопичення NO призводить до розслаблення бронхів. Розвиток ендотеліальної дисфункції при ХОЗЛ визначається наявністю гіпоксії, підвищенням вмісту різних біологічно активних речовин, а також впливом тютюнового диму. Оскільки основним етіологічним фактором при ХОЗЛ є тютюнопаління, важливим є вивчення впливу цього фактора на рівень NO в конденсаті повітря, що видихається. Метою дослідження було вивчення впливу активного тютюнопаління на рівень NO у повітрі, що видихається у пацієнтів, які страждають на ХОЗЛ. Обстежено 28 чоловіків із верифікованим діагнозом ХОЗЛ у період ремісії. Під час обстеження усі пацієнти були поділені на 2 групи залежно від наявності тютюнопаління. Всім пацієнтам була проведена спірометрія і визначення рівня NO у повітрі, що видихається. Було виявлено, що фактор тютюнопаління у хворих на ХОЗЛ у період ремісії впливає на рівень концентрації NO у повітрі, що видихається, викликаючи його достовірне зниження порівняно з рівнем у пацієнтів, які не палять. Ступінь тютюнового навантаження (тривалість та інтенсивність тютюнокуріння) не впливає на рівень концентрації NO у повітрі, що видихається, у хворих на ХОЗЛ у фазу ремісії. Ступінь нікотинової залежності впливає на рівень концентрації NO у повітрі, що видихається, у хворих на ХОЗЛ у фазу ремісії. Рівень концентрації NO у повітрі, що видихається у хворих на ХОЗЛ, як курців, так і тих які не палять, у фазу ремісії, не залежить від ступеня бронхообструктивних проявів.

Ключові слова: хронічне обструктивне захворювання легень, тютюнопаління, оксид азоту в повітрі, що видихається.

Problem statement. In recent years, the attention of researchers has been drawn to studying the state of the vascular endothelium in various diseases. It has been established that the vascular endothelium plays an important role in the regulation of vascular wall tone and homeostasis, being a highly specializeda

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metabolically active monolayer of cells that lines all the vessels of the body [1, 2]. The endothelium produces vasorelaxing (nitric oxide (NO), prostacyclin, endothelial hyperpolarizing factor) and vasoconstrictor (endothelin-1, thromboxane A2) substances, as well as a number of enzymes that activate or inactivate them [2, 3]. In the last decade, close attention has been paid to such a vasoactive substance as NO [4, 10].The study of the role of the NO molecule in physiological and pathophysiological processes in the human body was awarded the 1998 Nobel Prize in Physiology or Medicine to the authors who made the greatest contribution to this research. It is known that NO is one of the most important mediators characterizing inflammation in the respiratory system [2]. In addition, it has been proven that the accumulation of NO leads to relaxation of the bronchi [9]. Normally, the concentration of NO in exhaled air averages 7 (from 3 to 11) ppb (part per billion - molecules per 1 billion water molecules) [5, 9].

The upper respiratory tract is predominantly involved in the formation of endogenous NO[6]. It is formed from the amino acid L-arginine. The reaction is catalyzed by the enzyme NO synthase, a hemoprotein whose properties are similar to cytochrome P-450, containing both oxidizing and reducing domains. Three isoforms of NO synthase have been identified: constitutive isoforms are found in endothelial cells (eNOS, or type 3) and neurons (nNOS, or type 1) and are activated by increasing intracellular calcium concentrations; inducible NO synthase (iNOS, or type 2) is produced by some cell types in the presence of endotoxins and inflammatory mediators such as cytokines [2, 7].

In COPD, there are enough factors that determine the development of endothelial dysfunction, namely: hypoxia, increased levels of various biologically active substances (cytokines, leukotrienes, etc.). Such factors include smoking [3, 8, 9]. Endothelial damage is observed in actively smoking people with normal lung function even before the onset of the main clinical symptoms of COPD [9]. The effects of tobacco smoke and inflammation of the bronchial wall are considered potential mechanisms of endothelial damage in patients with COPD. Modern studies show that in the early stages of COPD, which occurs without impairment of lung function, endothelial dysfunction may already be observed, which is accompanied by dysregulation of vascular tone and cell growth of the vascular wall [8].

Since the main etiological factor in COPD is tobacco smoking, in which the gas phase of tobacco smoke contains free radicals and reactive oxygen species formed from NO-/NO2 when interacting with reactive components of smoke, it is important to study the effect of tobacco smoking on the level of NO in exhaled air condensate.

However, there is no consensus on the effect of active smoking on the level of NO in the tissues of the respiratory tract and exhaled air condensate [6, 8].

According to some studies“a symptomatic” smoker shave lower levelsof NO in serum and exhaled breath condensate, while smokers with symptomsof COPD have several times higher levels of NO and its derivatives compared to healthy

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people [10]. Their numbere specially increases during periods of exacerbation of the disease [3, 5]. At the same time, some studies prove aninversere lationship between the concentration of exhaled nitricoxide and the intensity and duration of tobacco smoking inpatients with COPD [10].The presence of such data among domestic and foreign literary sources was the basis for determining the purpose of this study.

Purpose of the study. To study of the effect of active tobacco smoking on the level of NO in exhaled air in patients suffering from COPD.

Materials and methods of research. 28 men were examined (average age - 62.23 ± 3.56 years, average disease duration - 8.51 ± 2.87 years), **with verified diagnosis of COPD during**remission.The presence and severity of bronchial obstruction and the COPD group, as well as the phase of the pathological process, were established in accordancewith the criteria set out in the Order of the Ministry of HealthUkraine No. 555 dated June 27, 2013.**All patients received standard therapy depending on the stage of the disease and group.**

All subjects were divided into 2 groupsdepending on the presence of the smoking factor: group 1 consisted of 18 actively smoking patients (pack/year index - 39.53 ± 5.17); Group 2 included 10 patients who had never smoked.

To verify the diagnosis of COPD, indicators of pulmonary function (RF) were determined in all patients using a MasterLab spirograph (Jaeger, Germany): the levels of forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), and the FEV1/FVC ratio were analyzed; a test for the reversibility of bronchial obstruction with a short-acting β2-agonist was performed (salbutamol). Assessing the degree of obstructionwas carried out using a post-bronchodilation test (as recommended by GOLD, 2023).

The concentration of NO in exhaled air was determined using a Niox Mino device (aerocrine, Sweden). The studies were carried out from 8 to 10 am, on an empty stomach, beforetaking medications.

Determination of the age of patients, duration of the disease and smoking, frequency of exacerbations per year, number of cigarettes smoked was carried out according toquestionnaire we developed. Nicotine dependence was assessed using the Fagerström questionnaire.

To statistically process the results obtained, the “Statistics 6.1” program was used to determine the arithmetic mean, the criterion for the significance of differences, and the level of significance of differences. A correlation analysis was also carried out between indicators of the level of NO in exhaled air and indicators of respiratory function, the degree of tobacco load (duration and intensity of smoking), as well as the degree of nicotine dependencebridges.

Results.The groups of patients were comparable in age, duration of the disease, number of exacerbations per year, and indicators of ventilation function (Table 1)

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Table 1

Characteristicsofpatients

Indicators	Groups	
	1 (n = 18)	2 (n = 10)
Age (M ± m, years)	59.05 ± 1.82	63.20 ± 1.11
Duration of the disease (M ± m, years)	5.90 ± 1.32	8.00 ± 1.58
Number of exacerbationsper year (M ± m)	3.00 ± 0.22	2.30 ± 0.37
FEV_1 (M ± m, % to due)	41.44 ± 1.93	44.84 ± 2.15
FVC (M ± m, % to due)	69.36 ± 2.11	74.60 ± 4.05

Note: p > 0.05 for each indicator in all groups of patients

Patients in groups 1 and 2 received comparable baseline therapy.The main indicators characterizing the smoking status and the degree of nicotine dependence in the group of smoking patients are presented in Table2.

Table 2

Indicators of smoking status in the group1

Indicators	Group 1
Duration of smoking (M ± m, years)	29.68 ± 3.47
Number of cigarettes smoked per day(M ± m, pcs)	21.30 ± 5.03
Smoker index (M ± m)	255.70 ± 50.01
Index pack of years (M ± m, p/year)	39.53 ± 5.17
Degree of nicotine dependence (M ±m, points)	5.98 ± 0.81

At the next stage, all patients underwent measurement of NO in exhaled air. Analyzing the data obtained, we found that in patients with COPD without exacerbation,the presence of the tobacco-smoking factor affects the level of exhaledNO. Thus, in patients of group 2, the level of NO in the exhaled air was significantly higher than in patients of group 1 (15.10 ± 1.82 ppb and 9.95 ± 1.30 ppb, respectively) (p <0.05).

In patients with COPD in the study groups who were in a stable condition, there was no correlation between the level of NO in exhaled air and parameters characterizing the ventilation function of the lungs.

In patients in the group1, no significant correlation was found between the level of NO in exhaled air and indicators characterizing smoking status (smoking duration, pack/year index), while a positive correlation was determined with the degree of nicotine dependencecorrelation relationship (r = 0.46, p < 0.05).

Discussion. Thus, in smoking patients with COPD during the period of remission, a decrease in the concentration of NO in exhaled air was determined by

approximately 1.5 times compared with patients who had never smoked. The results obtained may indicate the presence of one of the mechanisms for the development and progression of bronchoconstriction in patients with COPD due to long-term smoking. Besides,exposure to tobacco smokesignificantly reduces the concentration of exhaled breathNO in patients with COPD, which may indicate depletion of adaptive mechanisms of vascular regulation, endothelial dysfunction, development of endothelial damage and, as a consequence, progression of vascular and hemodynamic disorders in this group of individuals.

According to the data obtained, regardless of the presence of the tobacco-smoking factor, the degree of expression. These bronchoobstructive changes do not affect the level of NO in exhaled air in patients with COPD in remission. There was also no relationship foundbetween the level of NO in exhaled air and indicators characterizing the smoking status among the studied population. At the same time, a positive correlation was established with the degree of nicotine dependence and the level of exhaled NO, which indicates a tendency to increase the level of NO in exhaled air in smoking COPD patients with increased dependence on nicotine.

Conclusions.

1. Smoking factor patients with COPD in remission affects the concentration of NO in the exhaled air, causing it to significantly decrease compared to the level in nonsmoking patients.

2. The degree of tobacco load (duration and intensity of smoking) does not affect the concentration of NO in the exhaled the air in patients with COPD in remission.

3. The degree of nicotine dependence affects the concentration of NO in exhaled air in patients with COPD in remission.

4. The concentration of NO in exhaled air in smoking and non-smoking patients with COPD in the remission phase does not depend on the severity of bronchitis obstructive manifestations.

References:

1. Abrahmanova, L. M. Features of the expression of active forms of acidblood cells in patients with chronic bronchitis [Text] / L. M. Abrahmanova, U. R. Farkhutdinov, R. R. Farkhutdinov // Therapeutic archive. - 2001. - T. 73, No. 3. - P. 45–48.

2. Biochemical markers of inflammation and obstruction [Text] / N. V. Kulakova, V. A. Nevzorova, P. L. Lukyanova, B. I. Geltser // Clinical medicine. - 2000. - T. 78, No. 3. - P. 36–39.

3. Brindicci C. Nitricoxidesynt has eisoenzyme expression and activity in peripherall ungtissue of patients with chronic obstructive pulmonary disease / Brindicci C, Kharitonov SA, Ito M, etal // American Journal of Respiratory and Critical Care Medicine. 2015;181(1):21–30.

4. Exhaled Nitric Oxide as a Biomarker in COPD and Related Comorbidities / M. Malerba, A. Radaeli, A. Olivini, G. Damiani, B. Ragnoli, P. Montuschi // BioMed Research International – 2014 – P.7.

5. Exhaled Nitric Oxide as a Biomarker in COPD and Related Comorbidities / MalerbaM, RadaeliA, OliviniA, DamianiG.//*Journal of Breath Research.*2017; 5(4) 044201.

6. Kharitonov SA Exhaled markers of pulmonary disease [Text] / SA Kharitonov, PJ Barnes // American Journal of Respiratory and Critical Care Medicine. - 2005. - Vol. 163. - P. 1693–1722.

7. Nitric oxide in health and disease of the respiratory system / Ricciardolo FLM, Sterk PJ, Gaston B, Folkerts G. // Physiological Reviews. 2014; 84(3):731–765.

8. Relationship between exhaled nitricoxide and treatment responsein COPD patients with exacerbations / Antus B, Barta I, Horvath I, Csiszer E // Respirology. 2016; 15(3):472–477.

9. Review of exhaled oxide in chronic obstructive pulmonary disease / Gelb AF, Barnes PJ, George SC, Ricciardolo FL, Di Maria G, Zamel N. // Journal of Breath Research. 2014; 6(4)047101.

10. Soter S. Predictings putumeosinophiliain exacerbations of COPD using exhaled nitricoxide / Soter S, Barta I, Antus B. // Inflammation. 2013;36(5):1178–1185.

Література:

1. Abrahmanova, L. M. Features of the expression of active forms of acidblood cells in patients with chronic bronchitis [Text] / L. M. Abrahmanova, U. R. Farkhutdinov, R. R. Farkhutdinov // Therapeutic archive. - 2001. - T. 73, No. 3. - P. 45–48.

2. Biochemical markers of inflammation and obstruction [Text] / N. V. Kulakova, V. A. Nevzorova, P. L. Lukyanova, B. I. Geltser // Clinical medicine. - 2000. - T. 78, No. 3. - P. 36–39.

3. Brindicci C. Nitricoxidesynt has eisoenzyme expression and activity in peripherall ungtissue of patients with chronic obstructive pulmonary disease / Brindicci C, Kharitonov SA, Ito M, etal // American Journal of Respiratory and Critical Care Medicine. 2015;181(1):21–30.

4. Exhaled Nitric Oxide as a Biomarker in COPD and Related Comorbidities / M. Malerba, A. Radaeli, A. Olivini, G. Damiani, B. Ragnoli, P. Montuschi // BioMed Research International – 2014 – P.7.

5. Exhaled Nitric Oxide as a Biomarker in COPD and Related Comorbidities / MalerbaM, RadaeliA, OliviniA, DamianiG.//*Journal of Breath Research.*2017; 5(4) 044201.

6. Kharitonov SA Exhaled markers of pulmonary disease [Text] / SA Kharitonov, PJ Barnes // American Journal of Respiratory and Critical Care Medicine. - 2005. - Vol. 163. - P. 1693–1722.

7. Nitric oxide in health and disease of the respiratory system / Ricciardolo FLM, Sterk PJ, Gaston B, Folkerts G. // Physiological Reviews. 2014; 84(3):731–765.

8. Relationship between exhaled nitricoxide and treatment responsein COPD patients with exacerbations / Antus B, Barta I, Horvath I, Csiszer E // Respirology. 2016; 15(3):472–477.

9. Review of exhaled oxide in chronic obstructive pulmonary disease / Gelb AF, Barnes PJ, George SC, Ricciardolo FL, Di Maria G, Zamel N. // Journal of Breath Research. 2014; 6(4)047101.

10. Soter S. Predictings putumeosinophiliain exacerbations of COPD using exhaled nitricoxide / Soter S, Barta I, Antus B. // Inflammation. 2013;36(5):1178–1185.