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S. G. Opimakh
State organization "National institute of phthisiology and pulmonology named after F.G. Yanovsky National Academy of medical sciences of Ukraine" (NIPhP NAMS)

Evaluation of oxygen gas exchange in chronic obstructive pulmonary disease patients

Key words: *Chronic obstructive pulmonary disease, gas exchange abnormalities, hypoxemia*

Chronic obstructive pulmonary disease (COPD) is an important public health problem today in the medical, social and economic terms, it is one of the major causes of morbidity and mortality throughout the world, people are suffering from this disease for years and die prematurely from it or its complications [5]. One of the major complications of COPD is respiratory failure – failure to provide normal pulmonary arterial blood gas composition at rest or during moderate exercise [1].

Maintaining normal levels of arterial blood pH and an adequate supply of oxygen is a necessary condition for the functioning of cells, homeostasis and mitochondrial energy production. These conditions are provided by the complex interactions between the respiratory and cardiovascular systems, blood and cell metabolism, respiratory system is the first link of this chain complex [9]. Gas exchange abnormalities are the part of the pathophysiology of COPD. In the Global Initiative for Chronic Obstructive Lung Disease (GOLD) summarized that disturbances of gas exchange, which in sum leads to hypoxemia and hypercapnia, involved a number of mechanisms – a reduction of ventilation and ventilation drive, worsening respiratory muscle function due to high work of breathing in severe obstruction and hyperinflation, ventilation-perfusion disturbances etc. [11].

In assessing oxygen supply disorders in COPD patients several diagnostic tests are used. Analysis of arterial blood gases – the preferred method of evaluating gas exchange abnormalities, but taking arterial blood painful, difficult in patients with poor vascular access. Conditions for proper blood sampling – a steady state – without changes in oxygen therapy and ventilation parameters. For patients with chronic bronchial obstruction this time is 20-30 minutes. Blood – it is a living tissue, which after sampling and analysis continues to cellular metabolism, which changes the results - absorbed oxygen is produced CO_2 [7, 14]. However, exposure to air reduces the CO_2 content in the samples, which is why blood gas analysis should be carried out immediately [13].

Pulseoximetry – registration of the level of oxygen saturation of hemoglobin is appropriate only as an approximate method of determining hypoxia in patients with COPD as it has a number of limitations: examination obese patients, hypotension and deviations from normal hemoglobin in the blood can give incorrect results. The accuracy of the survey is reduced in disorders of microcirculation in a patient, and if the sensor is installed on the varnished nail. In any case, when the level of oxygen saturation <94% in patients COPD the analysis of the blood gases considered [10].

Unfortunately now in Ukraine, the blood gases analysis is not always available for COPD patients because of the high cost of equipment and supplies. Normal results of the blood gases analysis cann't conclusively indicate the absence of the gas exchange abnormalities, because blood gas composition as an important component of homeostasis and may be normal due to compensatory mechanisms even in severe COPD.

In addition to the blood gases analysis and pulseoximetry clinicians used method for determining the diffusion capacity of the lungs for the diagnosis of gas exchange between alveolar air and blood of the lung capillaries. DLCO reduced in patients with COPD, especially in the presence of widespread emphysema, but the disadvantage of the technique is the low specificity of the diagnostic test. Normal DLCO results exclude the presence of severe emphysema, but it does not apply to the its early stages [10]. In addition, DLCO itself determination does not solve the question of whether hypoxemia developing in COPD patients.

We are interested in an analysis of the gas composition of exhaled air in assessing oxygen exchange in COPD patients. Modern cardiorespiratory diagnostic systems are equipped with gases analysis modules.

This study was performed with the aim to improve the gas exchange abnormalities diagnosis in patients with COPD by applying techniques capnometry. For this purpose the following tasks were decided:

– to compare the oxygen content in the exhaled air in patients with different stages of COPD and healthy individuals;

– to examine the level of oxygen uptake in patients with different stages of COPD and healthy individuals;

– to examine the relationship between the content of oxygen in capillary blood and in the exhaled air.

Materials and methods

This work was financed from the state budget of Ukraine.

The study was coordinated with the local Medical Ethics Committee of the NIPhP NAMS, participants were familiarized with the study protocol and signed an informed consent form to participate in the study..

The study involved 165 participants (104 men and 61 women) aged 24 to 84 years, mean age (57,0 ± 1,0) years, including 100 patients with COPD, 30 patients with asthma and 35 healthy subjects.

Inclusion criteria for COPD patients – women and men from 40 years inclusive, post-bronchodilator forced expiratory volume at timed interval of 1,0 second (FEV_1) < 80% of the predicted value and FEV_1 to forced vital capacity (FVC) ratio less than 70%, familiarization of the study protocol and sign informed consent to participate in the study, the ability to understand and perform maneuvers diagnostic procedures.

Inclusion criteria for asthma patients – women and men from 18 years inclusive, reversibility of bronchial obstruction – FEV_1 increasing > 12 % (or ≥ 200 ml) after administering short acting β_2-agoniasts, familiarization of the study protocol and sign informed consent to participate in the study, the ability to understand and perform maneuvers diagnostic procedures.

Inclusion criteria for healthy individuals – women and men from 18 years inclusive, absence the respiratory system pathology with a history and examination, spirometry results – the baseline FEV_1 > 80% of the predicted value and FEV_1/FVC ratio > 70%, familiarization of the study protocol and sign informed consent to participate in the study, the ability to understand and perform maneuvers diagnostic procedures.

Exclusion criteria – other, other than COPD and asthma, respiratory diseases (lung cancer, tuberculosis, sarcoidosis, cystic fibrosis, lung surgery history), severe uncontrolled progressive chronic diseases that can affect the results of investigation, mental disorders.

The diagnosis of COPD, astma and the selection of patients regarding the stages of COPD was performed on the base of Order of Ministry of Health of Ukraine № 128 from 19.03.2007 "On approval of clinical protocols of medical care in" Pulmonology"" [3]. Patients with COPD were divided into three groups depending on the stage of the disease. Healthy individuals in this study were considered participants with normal respiratory function, which at the time of the survey there was broncho pulmonary diseases. In total, the survey identified 5 groups of observations, which have the following names in further text:

I group – bronchial asthma patients (BA);
II group – stage II COPD patients (COPD_2);
III group – stage III COPD patients (COPD_3);
IV group – stage IV COPD patients (COPD_4);
V group – healthy individuals (control).

A group of BA patients amounted to 30 patients (11 men and 19 women) with a mean age (57,3 ± 2,3) years and the average FEV_1 (72,3 ± 1,8) %.

A group of stage II COPD patients amounted to 30 patients (23 men and 7 women) with a mean age (57,5 ± 2,1) years and the average FEV_1 (64,3 ± 1,5) %.

A group of stage III COPD patients consists of 45 patients (30 men and 15 women) with a mean age (59,0 ±1,8) years and the average FEV_1 (41,0 ± 0,8) %.

A group of stage IV COPD patients consists of 25 patients (21 men and 4 women) with a mean age (65,6 ± 1,8) years and the average FEV_1 (26,4 ± 0,6) %.

A group of healthy individuals amounted to 35 subjects (19 men and 16 women) with a mean age (48,0 ± 2,4) years and the average FEV_1 (99,1 ± 1,5) %.

Oxygen content in the exhaled air analysis was conducted for all participants on a set for the study of the cardiorespiratory system "Oxycon Pro", "Cardinal Health" (Germany), the following parameters were evaluated:

– oxygen uptake in ml per minute ($V'O_2$, ml/min),

– fractional concentration of oxygen in the air at the end of exhalation, % ($FETO_2$, end-tidal O_2 fraction, %),

– fractional concentration of oxygen in the air during of exhalation, % (FEO_2, expired O_2 fraction, %),

– volume ventilation liters per minute (V E, L/min).

Prior to the test the patient explaining the essence of the procedure. A survey conducted in the sitting position, the patient is breathing ambient air for 5 minutes through a mouthpiece with a nose clip to the entire flow of air inhaled or exhaled, passed through the analyzer. Then within 3 minutes recorded data of the gas analysis. The device displays the average of the concentration or partial pressure of O_2 of every four successive respiratory cycles.

Given the complexity of performance and a high risk of complications of arterial puncture we conducted analysis of blood gases and acid-base status of capillary blood. It is known that the study of capillary blood is non-invasive, less painful and difficult and at the same time is the same exact as the study of arterial blood relative terms pH, partial pressure of carbon dioxide and oxygen saturation, as deemed adequate alternative of arterial blood analysis [8]. Regarding the partial pressure of oxygen is the lower its level in the arterial blood, than the more accurate analysis of capillary blood reflects its contents. In hyperoxia (eg, during oxygen therapy) there are significant differences between the results of the analysis of the partial pressure of oxygen in arterial and capillary blood, in these cases, interpretation of the capillary blood test requires caution [6].

Capillary blood gases analyses was performed by micromethod using the analyzer "ABL5", "Radiometer" by the method of the manufacturer [15]. Analyzed partial oxygen tension (PaO_2, mm Hg), for the evaluation of the data, the following reference values of the oxygen content of capillary blood were used [7]: PaO_2: 60 – 80 mm Hg.

We thank the staff of the clinical and functional department NIFP NAMS for help in blood gases analyzing.

Data collection and mathematical processing carried out by licensing software products included in the package Microsoft Office Professional 2007 license Russian Academic OPEN No Level № 43437596. Statistical analysis was performed using mathematical and statistical features MS Excel, as well as additional statistical functions developed by S.N. Lapach, A.V. Tschubenko, P.N. Babich [2]. The parameters studied in this work were evaluated by determining the mean (M), the mean error (m), reliability (t), the level of significance (p). Correlation analysis was carried out using the parametric Pearson correlation with subsequent authenticated results using Student's criterion.

Results and discussion

For all 165 study participants the gas composition of exhaled air was analyzed. Mean value FEO_2 was the less in healthy individuals and COPD_2 patients – (16,8 ± 0,1) and (16,8 ± 0,2) % accordingly, and the highest – in COPD_3 patients (17,6 ± 0,1) % and COPD_4 patients (17,7 ± 0,1) %. Similar pattern of results with $FETO_2$ (table. 1), when in healthy subjects and COPD stage II patients is lower and is (15,5 ± 0,1) and (15,4 ± 0,1) % accordingly, and in COPD_3 patients (16,2 ± 0,1) % and COPD_4 patients (16,1 ± 0,2) % is more high. For FEO_2 and $FETO_2$ the difference between the groups of patients COPD_2 – COPD_3; COPD_2 – COPD_4; COPD_3 – control; COPD_5 – control is statistically significant, $p < 0,01$.

Oxygen uptake ($V'O_2$) was the highest in COPD stage II patients (364 ± 14) ml/min. And the lowest in COPD stage III patients (291 ± 17) ml/min. and COPD stage IV patients (290 ± 18) ml/min., that objectively describes the disruption of the oxygen consumption in patients with severe and very severe course of COPD. Moreover, the decrease in oxygen uptake in patients with COPD with severe and very severe course is statistically significant with respect to COPD stage II patients ($p < 0,01$).

In the literature we found no studies on the oxygen content in the air during and at the end of exhalation to compare results. Our calculations show that between the O_2 exchange parameters and bronchial obstruction (the extent of which is the basis for the spirometry classification of COPD) observed a pattern. For example, in healthy individuals with normal bronchial patency during exhalation air contains relatively «little» O_2, and in COPD stage IV patients with impaired bronchial patency rather – «a lot» of O_2.

In the process of pulmonary ventilation resumed gas composition of the alveolar air. Alveolar ventilation directly affects the content of O_2 and CO_2 in the alveolar air and thus

Table 1

Oxygen exchange indicators in the examined groups, (M ± m)

Indicators	I group (BA) n = 30	II group (COPD_2) n = 30	III group (COPD_3) n = 45	IV group (COPD_4) n = 25	V group (control) n = 35
FEO_2, %	17,1 ± 0,1	16,8 ± 0,2	17,6 ± 0,1	17,7 ± 0,1	16,8 ± 0,1
	p < 0,05 between the groups I–III* p < 0,01 between the groups I–IV; II–III; II–IV; III–V; IV–V*				
$FETO_2$, %	15,7 ± 0,1	15,4 ± 0,1	16,2 ± 0,1	16,1 ± 0,2	15,5 ± 0,1
	p < 0,05 between the groups I–III* p < 0,01 between the groups II–III; II–IV; III–V; IV–V*				
V´E, L/min.	10,7 ± 0,4	11,1 ± 0,4	12,2 ± 0,5	12,6 ± 0,6	10,5 ± 0,3
	p < 0,05 between the groups I–III; II–IV* p < 0,01 between the groups I–IV; III–V; IV–V*				
V´O_2, ml/min.	329 ± 16	364 ± 14	291 ± 17	290 ± 18	338 ± 15
	p < 0,05 between the groups III–V; IV–V* p < 0,01 between the groups II–III; II–IV				

Note: * – statistically significant difference between the specified observations groups.

determines the nature of gas exchange between blood and air fills the alveoli. Gases contained in atmospheric, alveolar and exhaled air, have a certain fractional concentration (table 2) [4].

Table 2
Gases composition of atmospheric, alveolar and exhaled air, %

Gases composition of air	Atmospheric air	Alveolar air	Exhaled air
O_2	20,85	13,5	15,5
CO_2	0,03	5,3	3,7
N_2	78,62	74,9	74,6
H_2O	0,5	6,3	6,2
Total	100,0	100,0	100,0

Table 2 quote provisions is normal physiology, which coincides with our clinical examination, because when examining control group, the oxygen concentration at the end of exhalation is really 15,5 %. We figure out if a healthy person inhales air from the concentration O_2 20,85 %, and exhales the average concentration of O_2 during exhalation 16,8 %, then while she consumpts 4,05 % oxygen. Similarly, we assume that a patient COPD stage IV exhales air with an average concentration O_2 17,7 %, that metabolizes 3,15 % oxygen, that 23 % less compare to healthy person. For patients with stage III COPD this trend also sensible.

Automatically calculated during the gas composition analysis of the air oxygen uptake value ($V\acute{O}_2$)in COPD stages III and IV patients – (291 ± 17) and (290 ± 18) ml/min. accordingly for 16 % then in healthy subjects – (338 ± 15) ml/min.

Pearson correlation coefficient r for indices FEV_1 and FEO_2 is -0,35 ($p < 0,05$), and for a couple of comparisons FEV_1 and $FETO_2$ – -0,27 ($p < 0,05$) accordingly. According to the results of the correlation analysis results of spirometry and analysis of oxygen content in the exhaled air, we can conclude, that promotes bronchial obstruction violation oxygen uptake, but not the only factor in the possible formation of hypoxemia, because the coefficient of correlation of 0,35 and 0,27 indicates a weak correlation.

The explanation that not only one bronchoobstruction influences gas exchange disorders is lies in the characteristics of pulmonary blood flow and ventilation. In the paper J.M.B. Hughes, who is devoted to the principles of gas exchange in patients with COPD, said that almost always the cause of arterial hypoxemia is ventilation (V) to perfusion (Q) imbalance. To understand the nature V/Q imbalance J.M.B. Hughes proposes to consider the hypothetical situation of sudden and simultaneous blockage of the left main pulmonary artery embolus and right main bronchi tumor bleeding. All right lung blood flow equal to cardiac output without ventilation will no oxygenation, V/Q value will be zero, and the content O_2 and CO_2 in blood, arising from the right lung to be equal to the mixed venous blood, which flow to it. Other lung with ventilation, but without blood flow, will act as a «dead» space with ratios V/Q, which tends to infinity, and alveolar content O_2 and CO_2 will be equal to that in the inhaled air. V/Q, that equal 0, and that tend to ∞, means no effective gas exchange. Gas exchange becomes effective in the sense V/Q 0,86. In reality, in patients COPD there is a wide scope of V/Q values in different parts of the lungs on both sides of the optimum value. The greater the scope, the greater becomes gas exchange abnormalities. Regions with decreased V/Q lead to arterial hypoxemia (and hypercapnia), and with increased V/Q – contribute to useless ventilation or «dead» space [12].

With the formation of hypoxemia and hypercapnia in the body starts compensatory mechanism - increasing the minute ventilation [12]. With respect to the results of our work volume of minute ventilation at rest was highest in COPD stage IV patients– (12,6 ± 0,6) l/min. (table 1), statistically significantly higher relative to COPD stage II patients (11,1 ± 0,4) l/min., BA (10,7 ± 0,4) l/min. and in healthy individuals (10,5 ± 0,3) l/min. minute ventilation in COPD stage III patients (12,2 ± 0,5) l/min. was statistically significantly higher relative to healthy individuals and BA patients.

Capillary blood gases analyses was performed to 20 COPD patients (15 men and 5 women), including with COPD II stage – 3 patients, with COPD III stage – 10 patients, with COPD IV stage – 7 patients. The results of the investigation are presented in tabl. 3.

In two patients with hypoxemia (observation number 1 and 19) values FEO_2 and $FETO_2$ above the average in the observation group. In general, bond oxygen in capillary blood from FEO_2 and $FETO_2$ that: correlation coefficient between PaO_2 and $FETO_2$ is -0,41, and between PaO_2 and FEO_2 – -0,49. Thus, high FEO_2 and $FETO_2$ levels may indicate risks of hypoxemia.

Conclusions:

1. In COPD stages III and IV patients oxygen content in the exhaled air is statistically significant higher compared with stage II COPD patients and healthy subjects;

2. In COPD stages III and IV patients the oxygen consumption from the air during pulmonary ventilation for 16 - 23% less compared with healthy subjects;

3. The high values FEO_2 and $FETO_2$ correlate with decreased PaO_2 (the coefficient of correlation is -0,49 and -0,41 accordingly).

The practical implementation of the results of this work can improve the delivery of care to COPD patients in terms of identifying more undiagnosed cases. If in the process of cardio-respiratory stress test the doctor constants the high content of oxygen in the exhaled air, it is the basis to determine whether the patient has typical for COPD complaints. This shortness of breath (which gradually progresses or worsens during exercise or constant), prolonged cough, sputum production and long history of influence disease risk factors in individuals older than 40 years [11]. We recommend to guide such patients to spirometry and lung specialist advice in order to confirm the diagnosis of COPD and assign appropriate treatment.

Table 3

The oxygen content in the exhaled air and capillary blood of patients

№ observation	FEO_2, %	$FETO_2$, %	PaO_2, mm Hg
1	17,7	16,1	52
2	17,6	16,0	67
3	17,5	15,8	62
4	17,2	15,8	69
5	18,5	17,0	65
6	18,3	16,7	61
7	17,1	15,3	68
8	16,2	14,5	69
9	16,9	15,5	66
10	17,9	16,2	64
11	16,3	14,8	73
12	17,3	15,7	63
13	18,1	16,3	64
14	17,5	15,9	63
15	18,1	16,7	72
16	17,4	15,4	61
17	17,3	15,6	71
18	16,7	15,1	72
19	18,2	16,7	59
20	17,9	16,7	65
Mean	17,5 ± 0,1	15,9 ± 0,2	65,3 ± 1,2

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ОЦЕНКА НАРУШЕНИЙ ОБМЕНА КИСЛОРОДА У БОЛЬНЫХ ХРОНИЧЕСКИМ ОБСТРУКТИВНЫМ ЗАБОЛЕВАНИЕМ ЛЕГКИХ

С. Г. Опимах

Резюме. *При хроническом обструктивном заболевании легких (ХОЗЛ) происходят многочисленные патофизиологические нарушения, в том числе нарушения газообмена. Нами изучается возможность неинвазивного определения показателей обмена кислорода с помощью анализа газового состава выдыхаемого воздуха и исследуется соответствие этих результатов содержанию кислорода в крови у больных ХОЗЛ.*

Данная работа выполняется с целью усовершенствовать диагностику нарушений газообмена у больных ХОЗЛ.

Результаты. *В исследовании приняли участие 165 человек, которым был проведен анализ газового состава выдыхаемого воздуха. Среднее значение FEO_2 было самым низким у здоровых лиц и больных ХОЗЛ II стадии – (16,8 ± 0,1) и (16,8 ± 0,2) % соответственно, а самым высоким – у больных ХОЗЛ III - (17,6 ± 0,1) % и IV стадий – (17,7 ± 0,1) %. Аналогичный характер имеют результаты $FETO_2$. Поглощение кислорода ($V\dot{O}_2$) оказалось самым высоким у больных ХОЗЛ II стадии (364 ± 14) мл/мин и низким – у больных ХОЗЛ III (291 ± 17) мл/мин и ХОЗЛ IV стадии (290 ± 18) мл/мин. Коэффициент корреляции между показателями PaO_2 и $FETO_2$ равен – 0,41, а между PaO_2 и FEO_2 – 0,49.*

Выводы. *У больных ХОЗЛ III и IV стадий содержание кислорода в выдыхаемом воздухе статистически значимо более высокое по сравнению с больными ХОБЛ II стадии и здоровыми лицами, а поглощение кислорода из атмосферного воздуха в процессе легочной вентиляции на 16–23 % меньше; повышенное содержание кислорода в выдыхаемом воздухе ассоциируется с гипоксемией.*

Ключевые слова: *хроническое обструктивное заболевание легких, нарушения газообмена, гипоксемия*

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С. Г. Опимах
ГУ «Национальный институт фтизиатрии и пульмонологии им. Ф.Г. Яновского НАМН Украины»,
03680, Украина, Киев, ул. Амосова, 10
тел./факс: 380(44)275-62-42
e-mail: diagnost@ifp.kiev.ua

EVALUATION OF OXYGEN GAS EXCHANGE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

S. G. Opimakh

Summary. *In chronic obstructive pulmonary disease (COPD) numerous pathophysiological disorders including disorders of gas exchange take place. We study the possibility of non-invasive determination of oxygen gas exchange by gas analysis of exhaled air and investigate the compliance between these results and the oxygen content in the blood in COPD patients.*

The purpose of the study: *This study aimed to improve the diagnosis of gas exchange abnormalities in COPD patients.*

Results: *For the 165 study participants gas analysis of exhaled air was conducted. Mean FEO_2 was lowest in healthy subjects and in COPD stage II patients – (16,8 ± 0,1) and (16,8 ± 0,2) % respectively, while the highest – in COPD III patients (17,6 ± 0.1) % and COPD IV (17,7 ± 0,1) %. Similar pattern of results has $FETO_2$. Oxygen uptake ($V\acute{}O_2$) appeared highest in COPD stage II patients (364 ± 14) ml/min and lowest in COPD III patients (291 ± 17) ml/min and COPD IV (290 ± 18) ml/min. The correlation coefficient between the indicators PaO_2 and $FETO_2$ is -0.41, and between PaO_2 and FEO_2 – -0,49.*

Conclusions: *In COPD stages III and IV patients oxygen content in the exhaled air is statistically significant higher compared with stage II COPD patients and healthy subjects, the oxygen consumption from the air during pulmonary ventilation for 16–23% less; the high oxygen content in the exhaled air associated with hypoxemia.*

Key words: *Chronic obstructive pulmonary disease, gas exchange abnormalities, hypoxemia*

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S. G. Opimakh
SO «National Institute of Phthisiology and Pulmonology named after F.G. Yanovsky NAMS of Ukraine»
03680, Ukraine, Kyiv, M. Amosova str., 10
tel./fax: 380(44)275-62-42
e-mail: diagnost@ifp.kiev.ua