UDC 616.24-007.272-036.12-07.001.5

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Lung ventilation evaluation in patients with uncontrolled asthma

Key words: *bronchial asthma, lung ventilation, alveolar ventilation.*

Bronchial asthma (BA) - a chronic inflammatory disease of the airways in development of which cells and inflammatory mediators involved. Chronic inflammation combines with bronchial hyperreactivity, which is manifested by recurrent symptoms of wheezing, breathlessness, chest tightness, coughing, especially at night and early morning. These episodes are usually related to the widespread but variable bronchial obstruction, which reversed spontaneously or under the influence of therapy [3].

Despite episodic symptoms the inflammation in asthma persists constantly and occurs in all clinical forms of asthma in all age groups of patients. Inflammation alters the structure of the airways, defined as airway remodeling. These are processes of subepithelial fibrosis, hyperplasia and hypertrophy of smooth muscle, proliferation of blood vessels, increasing the number of goblet cells, increasing the size of submucosal glands. In patients with severe course of disease structural changes lead to bronchoconstriction, which is not completely reversed under the influence of available therapeutic agents [3].

Inherent to asthma bronchial obstruction can lead to disorders of gas exchange, especially through ventilation-perfusion imbalance. The feature of asthma is that even in patients without clinical symptoms and almost normal spirometry parameters may have been significant disturbances in gas exchange [13].

The most widespread means of assessing pulmonary ventilation in patients with asthma is spirometry, which makes it possible to determine the presence, severity of bronchial obstruction and its reversibility, variability (improvement or deterioration of respiratory function for some time), and the diagnosis of asthma. [3]. Bodyplethysmographia can detect increased airiness or hyperinflation of the lungs [6]. Neither spirometry or bodipletyzmohrafiya not possible to determine whether the effective alveolar ventilation in patients with asthma.

Analysis of arterial blood gases – the preferred method of evaluating lung ventilation effectiveness, but taking arterial blood painful, difficult in patients with poor vascular access. Conditions for proper blood sampling – a steady state – without changes in ventilation parameters. For patients with 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. However, exposure to air reduces the CO_2 content in the samples, which is why blood gas analysis should be carried out immediately [8]. Today in Ukraine Analysis of arterial blood gases is not always available for patients with asthma due to the high cost of equipment and supplies.

One of the ways for evaluating the effectiveness of pulmonary ventilation - the definition of alveolar ventilation. Alveolar ventilation and minute volume ventilation values are not identical. Alveolar ventilation – is the volume of air that not only reaches the alveoli, but also takes part in gas exchange. The actual minute ventilation in addition to alveolar ventilation includes ventilation airways not involved in gas exchange (anatomical "dead" space) and alveoli that are not properly perfused (alveolar "dead" space). The difference is minute and alveolar ventilation - a physiological "dead" space (VD, dead space), which is the sum of anatomical and alveolar "dead" space. The higher becomes volume physiological "dead" space in minute ventilation, the smaller the alveolar ventilation with the development of gas exchange disorders [14].

VD/VT ratio (the part of the "dead" space of the tidal volume) – is a sensitive indicator of gas exchange, reflecting compliance with ventilation to perfusion at rest as well as during exercise. In patients with respiratory problems VD/VT primarily due to increased non-uniformity of ventilation and perfusion in the lung, and in patients with heart failure and pulmonary vascular disease VD/VT, primarily due to impaired blood flow is increased in the lungs with preserved ventilation [14]. We believe that the definition of the indicator VD/VT can be a useful tool for assessment of alveolar ventilation in patients with asthma.

In asthma the imbalance of alveolar ventilation (Va) and circulation (Q), one of the key factors maintaining normal concentrations of arterial blood gases [6]. An objective assessment of Va/Q balance is the method of multiple inert gas elimination technique (MIGET), to which a mixture of six inert gases with different solubility administered intravenously to the patient. After 30 minutes (after equalization of gases concentrations in the body) an analysis of the content of inert gases in the exhaled air, in the arterial blood and blood from the pulmonary artery conducts. The results of the mathematical analysis of the data describing the distribution of ventilation and perfusion [10]. The main drawback of this method, we consider the high complexity of performance and its unavailability in Ukraine.

We studied the possibility of capnometry in evaluating pulmonary ventilation in patients with asthma. Capnometry – is measurement and digital display of concentration or partial pressure of carbon dioxide in the air that inhales or exhales patient during the respiratory cycle [7]. By integrating capnometer and pneumotachometers in one device and the unique opportunity of capnometry to calculate CO2-free air portions during exhalation as the volume of the «dead» space and its part in the tidal volume makes it possible to evaluate the efficiency of alveolar ventilation.

This study was performed with the aim to investigate lung ventilation pecularities in patients with BA. For this purpose the following tasks were decided:

to investigate lung ventilation parameters in patients with BA and healthy subjects;

to compare lung ventilation parameters in patients with BA depending on disease control.

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 65 participants (30 men and 35 women) aged 24 to 74 years, mean age (52,3 ± 2,7) years, including 30 patients with asthma and 35 healthy subjects.

Inclusion criteria for asthma patients – women and men from 18 years inclusive, reversibility of bronchial obstruction – forced expiratory volume at timed interval of 1,0 second (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. Only asthma patients who have no signs of exacerbation of the disease at the time of the survey took part in the study.

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 FEV1/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 asthma 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 "" [2]. Healthy individuals in this study were considered participants with normal respiratory function, in whom there was no bronchoobstructive diseases at the time of the survey.

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 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) %.

To asthma patients Asthma Control Test (ACT) was performed. In clinical practice, it is recommended to use the classification of asthma by level of control of the disease, which involves the evaluation of the current clinical condition of the patient and the potential risks in the future. In general clinical practice, it is recommended to use a simple informative Asthma Control Test. Classification by level of control correlates well with the ACT. Interpretation of results: < 15 points - the lack of control of asthma, 16-18 points - partial control, > 20 points - good control [3].

Capnometry 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:

- the volume of «dead» space (part of the air that does not participate in gas exchange), ml (VD, ml);
- part of the «dead» space of the tidal volume,% (VD % VT)
- volume ventilation liters per minute (V´E, L/min),
- alveolar ventilation volume liters per minute (V´E, L/min).

Prior to the test the essence of the procedure explained to the patient. 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 data of the gas analysis recorded. The device displays the average of the concentration or partial pressure of O_2 of every four successive respiratory cycles.

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 [3]. The parameters studied in this work were evaluated by determining the mean (M), the mean error (m), reliability (t), the level of significance (p).

Results and discussion

For all 65 study participants capnometry was analyzed. To resolve the first task of our work we have found that the parameters of pulmonary ventilation in patients with asthma in general slightly different from those in healthy subjects. Thus, the average minute ventilation accounted (10,5 ± 0,3) l/min. In healthy subjects and (10,7 ± 0,4) l/min. in BA patients (Table 1). As for "dead" space ventilation, it was on average higher in patients with asthma – (173 ± 8) ml, compare to healthy subjects – (189 ± 8) ml, but without statistically significant difference. Higher, but without statistically significant difference, is the part of the "dead" space of the tidal volume in BA patients – (27,4 ± 1,3) %, while in healthy individuals it is (25,2 ± 0,9) %.

Table 1
Lung ventilation parameters in healthy subjects and in BA patients (M ± m)

Parameters	Healthy subjects n = 35	BA patients n = 30
V′E, L/min	10,5 ± 0,3	10,7 ± 0,4
VD, ml	173 ± 8	189 ± 8
VD%VT	25,2 ± 0,9	27,4 ± 1,3
VA, L/min	7,9 ± 0,4	7,8 ± 0,6

Note: without statistically significant difference between.

Next, based on our ACT we divided patients with asthma into 2 groups: with controlled (ACT > 20 points) and with uncontrolled (ACT < 20 points) course of disease. Clinical characteristics of patients are presented in Table 2. Patients with partial control (such person was 1 of ACT 16 points) were seen in the group with uncontrolled course.

Table 2
Clinical characteristics of BA patients depending on disease control (M ± m)

Indicators	Controlled BA patients, n = 10	Uncontrolled BA patients n = 20
Male (n, %)	3 (30 %)	8 (40 %)
Female (n, %)	7 (70 %)	12 (60 %)
Age, years	59,7 ± 2,7	56,1 ± 3,2
ACT, points	21,6 ± 0,4	11,8 ± 0,6*
Mean FEV_1, %	73,8 ± 4,2	71,5 ± 1,9

Note: * – statistically reliable difference of indicators between groups, p < 0,01.

In patients with controlled asthma ACT averages (21,6 ± 0,4) points, while uncontrolled - (11,8 ± 0,6) points, a statistically significant difference indices, p <0.01. By sex and age characteristics of the patients were comparable regardless of disease control. In patients with controlled asthma level of FEV_1 is greater, but without significant difference compared with patients with uncontrolled course.

Interesting features were smoking status of patients with asthma (table 3). It was found that among patients with controlled asthma 90 % were no smokers. The only smoker in the group have experience smoking 5 pack-years.

Table 3
Smoking status of BA patients depending on disease control (M ± m)

Indicators	Controlled BA patients, n = 10	Uncontrolled BA patients n = 20
No smokers (n, %)	9 (90 %)	12 (60 %)
Past smokers (n, %)	0 (0 %)	7 (35 %)
Current smokers (n, %)	1 (10 %)	1 (5 %)
Smoking history for people who smoke or have smoked, pack years	5,0	25,8 ± 8,8

Note: no correct mathematical bases for determining statistically significant difference between indexes of the observation groups.

Among patients with uncontrolled asthma 40 % have a history of smoking index between 1,5 and 40 (!) pack-years (mean - (25,8 ± 8,8) pack-years). The data correspond to a recognized position that smoking contributes to more severe, uncontrolled asthma course. Also, smoking decreases the effectiveness of anti-inflammatory therapy, which also contributes to the loss of control of the disease [4].

In addressing the second objective of our work found that the minute ventilation is not very different among the groups of patients with asthma (table 4).

Table 4
Lung ventilation indicators in BA patients depending on disease control (M ± m)

Indicators	Controlled BA patients, n = 10	Uncontrolled BA patients n = 20
V′E, L/min	11,0 ± 0,4	10,5 ± 0,6
VD, ml	176 ± 11	211 ± 8*
VD%VT	24,6 ± 0,5	30,5 ± 1,5*
VA, L/min	8,3 ± 0,2	7,3 ± 0,4*

Note: * – statistically reliable difference of indicators between groups, p < 0,05.

In patients with uncontrolled asthma "dead" space ventilation volume is (211 ± 8) ml, which is statistically significantly higher than the rate for patients with controlled

course – (176 ± 11) ml, p < 0,05. Thus, the part of the "dead" space of the tidal volume in uncontrolled asthma patients is – (30,5 ± 1,5) %, when in subjects with controlled asthma it is statistically reliable smaller – (24,6 ± 0,5) %, p < 0,05. Obviously, with an equal minute ventilation in patients with high VD% VT alveolar ventilation will lower, that is (7,3 ± 0,7) l/min. in patients with uncontrolled asthma, up 14% and was significantly lower than in controlled asthma – (7,3 ± 0,4), p < 0,05.

We explain our findings that violations of pulmonary ventilation in patients with uncontrolled asthma flow may be associated with damage to of small-caliber airways and the development of lung hyperinflation. Thus, according to bodyplethysmography provided by patients who took part in the study, the value of the residual lung volume at a controlled course is nearly normal and is (121,3 ± 10,5) % from predicted values, and if uncontrolled course is much greater – (132,6 ± 8,3). Standard normal values of lung volumes is a range of 80 to 120 % of the predicted values [9].

We raised the question whether there is a natural development of lung hyperinflation in patients with a mean FEV1 (71,5 ± 1,9) %? According to the literature this may be the case, because we found evidence that the formation of air «traps» observed not only at a moderate, but also for mild asthma [11]. In the study of the concentration of nitric oxide in the exhaled air, found that in the stable asthma detected inflammatory lesions not only the distal airways but in lung acinar areas [12].

There is evidence that inflammation in the distal airways are more intense in severe and uncontrolled asthma course. With the defeat of the distal airways pulmonary hyperinflation formation is associated in patients with asthma [5].

Thus, the patients with uncontrolled asthma is characterized by: a history of smoking, lung hyperinflation formation with an increase the part of the «dead» space in the tidal volume and decrease of alveolar ventilation efficiency.

Conclusions

1. Lung ventilation parameters in patients with asthma without exacerbation in general slightly different from those in healthy subjects;

2. The effectiveness of alveolar ventilation is reduced by 14% in uncontrolled asthma due to high waste «dead» space ventilation.

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ОЦЕНКА ЛЕГОЧНОЙ ВЕНТИЛЯЦИИ У БОЛЬНЫХ БРОНХИАЛЬНОЙ АСТМОЙ С НЕКОНТРОЛИРУЕМЫМ ТЕЧЕНИЕМ

С. Г. Опимах

Резюме. *Характерная для бронхиальной астмы (БА) обструкция бронхов может привести к расстройствам газообмена. Особенностью БА является то, что даже у больных без клинических симптомов и с практически нормальными результатами спирометрии могут иметь место значительные нарушения газообмена, в том числе за счет снижения альвеолярной вентиляции. Данная работа выполняется с целью изучить особенности легочной вентиляции у больных БА.*

Материалы и методы исследования. *В исследовании приняли участие 35 здоровых лиц и 30 больных БА (30 мужчин и 35 женщин), которым проводили капнометрию. Больным БА проведено Астма-Контроль Тест (АКТ).*

Результаты. *Среди больных с неконтролированным течением 40 % лиц имеют анамнез курения с индексом (25,8 ± 8,8) пачко-лет. У больных с контролированным течением астмы объем вентиляции*

«мертвого» пространства составляет (211 ± 8) мл, а доля «мертвого» пространства в дыхательном объеме – (30,5 ± 1,5) %, что статистически значимо превышает этот показатель для больных с контролированным течением – (176 ± 11) мл и (24,6 ± 0,5) % соответственно (p < 0,05). Альвеолярная вентиляция у больных с неконтролированным течением заболевания более низкая – (7,3 ± 0,4) л/мин, чем при контролированной БА – (8,3 ± 0,2) л/мин (p < 0,05).

Выводы. *Параметры легочной вентиляции у больных БА вне обострения в целом незначительно отличаются от таковых у здоровых лиц, а при неконтролируемом течении БА эффективность альвеолярной вентиляции снижается на 14 % за счет высокой бесполезной вентиляции «мертвого» пространства.*

Ключевые слова: *бронхиальная астма, легочная вентиляция, альвеолярная вентиляция.*

Научно-практический журнал «Астма и аллергия», 2014, № 1

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LUNG VENTILATION EVALUATION IN PATIENTS WITH UNCONTROLLED ASTHMA

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Abstract

Background. *Bronchial obstruction as characteristic feature of bronchial asthma (BA) can lead to gas exchange disorders. The distinction of asthma is that even in patients without clinical symptoms and almost normal spirometry parameters may have been significant gas exchange disorders including that due alveolar ventilation reducing.*

The purpose of the study. *This study aimed to investigate lung ventilation pecularities in patients with BA.*

Results. *Among patients with uncontrolled course of 40 % have a smoking history with index (25,8 ± 8,8) pack-years. In patients with uncontrolled asthma «dead» space ventilation volume is (211 ± 8) ml, and part of the «dead» space of the tidal volume – (30,5 ± 1,5) %, which is statistically significantly greater than that rate for patients with controlled asthma – (176 ± 11) ml and (24,6 ± 0,5) %, respectively, p < 0.05. Alveolar ventilation in patients with uncontrolled disease course is lower, namely (7,3 ± 0,4) l/min. than when controlled asthma – (8,3 ± 0,2), p < 0.05.*

Conclusions. *Lung ventilation parameters in patients with asthma without exacerbation in general slightly different from those in healthy subjects, but the effectiveness of alveolar ventilation is reduced by 14 % in uncontrolled asthma due to high waste «dead» space ventilation.*

Key words: *bronchial asthma, lung ventilation, alveolar ventilation*

Theoretical and practical J. «Asthma and Allergy», 2014, 1

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