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ВЕДУЩИЕ ВОЗБУДИТЕЛИ ВНЕГОСПИТАЛЬНОЙ ПНЕВМОНИИ И ИХ ИММУНОСУПРЕССИВНЫЕ СВОЙСТВА

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Резюме. Внегоспитальная пневмония развивается на фоне нарушенного микробиоценоза полости ротоглотки II-III степеней за счет элиминации из биотопа или формирования дефицита автохтонных облигатных анаэробных (Lactobacillus spp.), факультативных анаэробных и аэробных бактерий (S. salivarius, L. lactis); контаминации и увеличения количества в биотопе условно-патогенных (S. pneumoniae, H. influenzae, M. catarrhalis, S. aureus, K. pneumoniae) бактерий. Ведущими возбудителями внегоспитальной пневмонии на современном этапе являются S. pneumoniae (55,55 %), H. influenzae (22,22 %), M. catarrhalis (14,82 %), S. aureus, K. pneumoniae. Возбудители проявляют антилизоцимную, антикомплементарную и антиимуноглобулиновую (IgM, IgG, IgA) активность.

Ключевые слова: внегоспитальная пневмония, микрофлора, иммуносупрессивные особенности.

THE PROMINENT PATHOGENS OF COMMUNITY-ACQUIRED PNEUMONIA AND THEIR IMMUNE-DEPRESSIVE PROPERTIES

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Abstract. The community-acquired pneumonia develops on the background of II-III degrees violation of microbiocenosis of orhopharynx due to elimination or development of deficit of obligatory anaerobic and aerobic bacteria (Lactobacillus spp.), facultative anaerobic and aerobic bacteria (S. salivarius, L. lactis); due to contamination and increasing the amount of conditionally pathogenic (S. pneumoniae, H. influenzae, M. catarrhalis, S. aureus, K. pneumoniae) bacteria. The prominent pathogens of out-hospital pneumonia were S. pneumoniae (55,55 %), H. influenzae (22,22 %), M. catarrhalis (14,82 %), S. aureus, K. pneumoniae. The pathogens had anti-lysozyme, anti-complement and anti-immunoglobulin (IgM, IgG, IgA) activity.

Key words: community-acquired pneumonia, microflora, immune-depressive properties.

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INDICES OF EXHALED BREATH CONDENSATE IN CHILDREN WITH EOSINOPHILIC PHENOTYPE OF BRONCHIAL ASTHMA

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Summary. The indices of exhaled air condensate have been studied in 160 children with different phenotypes of bronchial asthma. It has been demonstrated that there occur changes in children with the noneosinophilic phenotype of bronchial asthma as compared with the patients with the eosinophilic phenotype of the disease that are indicative of a higher activity of inflammatory processes in the respiratory tracts. The proteolytic activity according to azocasein lysis more than 1,5 ml/h had the highest diagnostic value of detection of noneosinophilic phenotype: spesiphity 84,7 %, the predictable value of a positive result 79,1 %, the odds ratio 7,5, the posttesting probability of positive result 79,1 %.

Key words: children, bronchial asthma, exhaled breath condensate.

Introduction. Currently, bronchial asthma in children is considered as a disease characterized by chronic inflammation of the airways, in development of which many different cells and cellular elements play the role [6]. It is believed that under the antigenic stimulation the primary effectors' cells (epithelial cells of the respiratory tract, mast cells, and macrophages) associated with Ig E, release inflammatory mediators, causing a development of inflammatory reaction both immediate and late type.

The main mediators that initiate the acute phase of inflammation are interleukins, tumor necrosis factor-α, interferon-γ, which activate a cascade of immunological reactions and promote access to the peripheral circulation of histamine, leukotrienes and chemotaxics factors of eosinophils and neutrophils as well as other inflammatory mediators [1].

Recently the first results of study researches of these processes in biological fluids such as exhaled breath condensate or saliva that can be obtained by non-invasive methods, have been appeared [7, 8]. It has been studied that under bronchial asthma considerable changes in exhaled breath condensate appeared, including its physical and chemical properties, acid-base balance, accumulation both nitric oxide and hydrogen peroxide, as well as aldehydes, prostanoids and cytokines [5, 9, 10].

However, most studies of exhaled breath condensate have been carried out in adults, but in children are almost absent, which assign the topicality of this research, aimed at study of inflammatory processes and improvement of individualized treatment for children with different phenotypes of bronchial asthma.

The aim of the research. To study indices of exhaled breath condensate at eosinophilic and noneosinophilic phenotypes of bronchial asthma in school age children.

Patients and methods. To achieve the aim, of the study, the examination of 160 school age children with bronchial asthma (BA), which received inpatient treatment in the regional children's hospital in Chernivtsi, has been performed. The clinical comparison group were formed according to the number of eosinophils in the sputum of patients by the classification of P. Haldar and I. Pavord (2007): patients with presence of 3 % or more of eosinophils in sputum were attributed to the eosinophilic phenotype of BA, but children with the number of eosinophils in the sputum less than 3 % were ascribed to noneosinophilic asthma phenotype.

To the I group 84 children with eosinophilic phenotype of BA were referred, and II comparison group was formed by 76 patients with noneosinophilic asthma phenotype. The average age of children of the I group was 11,8±0,4 years (73,8 % of boys and 44,0 % of rural population), in the II comparison group the average age of patients was 11,1±0,4 years (57,9 % of boys and 43,4 % of rural population), that is clinical group were comparable by the main clinical characteristics.

Exhaled breath condensate (EBC) was collected for 15-20 min. using self-designed condenser (patent № 45346 UA A61V 5/08, filed: 10.11.2009).

The complex study of exhaled breath condensate included: determination of level of nitrogen monoxide metabolites [2], determination of total protein by the method of Lowry OH, content of both basic and neutral aldehyde- and ketone- derivatives of 2,4-dinitrophenylhydrazines (AKDNPH) [3]; proteolytic activity by lysis of azoalbumin, azocasein and azocollagen [4], catalytic activity [4].

Obtained results were analyzed using the software package «STATISTICA 7.0» StatSoft Inc. by means of parametric methods of calculation as well as methods of biostatistics and clinical epidemiology with the evaluation of indices' diagnostic value.

Results. Table 1 shows the results of analysis of indices of oxidative modification of proteins in exhaled breath condensate of children in the comparison group.

These results suggest that the content of total protein, AKDNPH both neutral and basic character was slightly higher in patients with noneosinophilic asthma, reflecting the greater activity of the airways' inflammatory process under that phenotype of disease. Thus, the fraction of children with noneosinophiic type of bronchial inflammation that had in EBC the level of basic AKDNPH more than 50 millimole/g of protein was 53,6 % compared to 33,3 % in the I comparison group. Despite on absence of significant difference at comparison groups according to the content of basic AKDNPH in exhaled breath condensate of children, the level of this indicator less than 50.0 50 millimole/g of protein allowed to verify the presence of eosinophilic phenotype of BA by a sensitivity of 70,8%, odds ratio 1,8 and positive post test probability 55,2 %.

In children with eosinophilic BA there has been noticed following proteolytic activities by lysis of: azoalbumin (1,45±0,07 ml/h), azocasein (1,25±0,06 ml/h) and azocollagen – 0,2±0,02 ml/h. In the comparison group, these indices of proteolysis were accordingly: 1,45±0,05 ml/h ($p>0,05$); 1,5±0,05 ml/h ($p<0,05$) and 0,19±0,02 ($p>0,05$). The research results give reason to believe that the proteolytic activity by lysis of azocasein was significantly higher in patients with noneosinophilic asthma, probably due to the greater degree of inflammation of the bronchi. Thus, such index of EBC as the proteolytic activity by azocasein lysis in the meaning of more than 1,5 ml/h was registered in 47,4 % of patients with noneosinophilic asthma phenotype in comparison to 15,4 % of children with eosinophilic type of the bronchial inflammation. Diagnostic value of that test's result in confirmation of the noneosinophilic phenotype of BA ran up to: specificity 70,8 %, the predictable value of a positive result 79,1 %, odds ratio 7,5, the post testing probability of positive result 79,1 %.

Taking into account that intense damage of proteins occurs during asthma exacerbation, studying in EBC of fibrinolytic activity markers in children with

Table 1

The content of both total protein and derivatives of proteins' oxidative modification in exhaled breath condensate

Bronchial asthma phenotypes	Total protein, g/L	AKDNPH, basic type, E 430 millimole/g of protein	AKDNPH neutral type, E 370 millimole/g of protein
Eosinophilic	3,92±0,29	49,2±6,02	5,56±0,53
Noneosinophilic	4,15±0,45	63,4±8,05	6,66±0,85
p	p>0,05	p>0,05	p>0,05

Table 2

Fibrinolytic activity of exhaled breath condensate in examined children

Bronchial asthma phenotypes	Indices of fibrinolytic activity, mcg azofibrin /ml per 1 hour		
	Total fibrinolytic activity	Non-enzymatic fibrinolytic activity	Enzymatic fibrinolytic activity
Eosinophilic	0,94±0,06	0,43±0,02	0,51±0,05
Noneosinophilic	0,83±0,03	0,38±0,02	0,47±0,02
p	>0,05	>0,05	>0,05

different types of airways' inflammation considered as worthwhile. Table 2 shows the indices of fibrinolytic activity in exhaled breath condensate of children at the comparison.groups.

The total fibrinolytic activity of EBC in patients of II group more than 0,94 mcg of azofibrin/ml/h was determined in 30,8 % of cases, but in children of comparison group – in 21,0 % of cases. Non-enzymatic fibrinolytic activity of exhaled breath condensate that exceed 0.48 mcg of azofibrin/ml/h was observed in 30,8 % of patients with eosinophilic asthma phenotype, but in the comparison group – only in 15,8 % of cases (pφ>0,05).

In view of free radicals that are produced due to excessive oxidative stress in the airways, may participate in the development of bronchial obstruction during asthma exacerbation, assessment of antioxidant status in the examined children seemed to be appropriate. Therefore, catalase activity as a major intracellular antioxidant enzyme, was defined in exhaled breath condensate.

Thus, catalase activity in EBC was at the mean 54,9±10,42 micromole/min × mg of protein in patients with eosinophilic inflammation of the airways, but 38.3 ± 7,52 micromole/min × mg of protein (p>0,05) under noneosinophilic type of bronchial inflammation. Diagnostic value of detecting eosinophilic asthma phenotype by the activity of catalase more than 60.0 micromole/min × mg of protein in exhaled breath condensate came to: specificity of 82,6 %, odds ratio 1,7, post test probability of 59,8 %.

It has been noted that the content of nitrogen monoxide metabolites in EBC of children in the clinical groups hardly differed and was at the mean 46,4±4,33 micromole/L in patients with eosinophilic phenotype of BA and 46,7±3,32 micromole/L (p> 0,05) under noneosinophilic asthma phenotype. Although there has been no significant difference on the content of nitrogen monoxide in exhaled breath condensate of children at comparison group, the level of this index more than 55,0 micromole/L confirmed eosinophilic asthma phenotypes with a specificity of 78,6 % and odds ratio=1,1.

Analysis of the data has been showed that almost all of the mentioned indices had sufficient specificity but low sensitivity regarding detection of eosinophilic phenotype of BA. At the same time, their likelihood ratio remains quite far from the requirements that apply to the current diagnostic tests. Moreover, findings suggest that usage of such a well-known index of airways' inflammation as nitric oxide metabolites in EBC, is inexpedient for risk assessment of occurrence of eosinophilic asthma phenotype in school age patients.

Conclusions

1. Marked changes that indicate less active inflammation of airways have been recorded in exhaled breath condensate of children with eosinophilic asthma phenotype in comparison with patients with noneosinophilic phenotype of the disease.

2. Indices of exhaled breath condensate can be used for confirmation of eosinophilic bronchial asthma phenotype only as additional markers.

Future trends of research is to study spirometrical indices under the eosinophilic asthma phenotype in school age children.

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ПОКАЗАТЕЛИ КОНДЕНСАТА ВЫДЫХАЕМОГО ВОЗДУХА У ДЕТЕЙ С ЭОЗИНОФИЛЬНЫМ ФЕНОТИПОМ БРОНХИАЛЬНОЙ АСТМЫ

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Резюме. Изучали показатели конденсата выдыхаемого воздуха у 160 детей, больных бронхиальной астмой, при разных фенотипах заболевания. Показано, что у детей с неэозинофильным фенотипом бронхиальной астмы по сравнению с пациентами с эозинофильным фенотипом заболевания в конденсате выдыхаемого воздуха отмечаются изменения, которые подтверждают большую активность воспаления бронхов. Наибольшую диагностическую ценность выявления неэозинофильного фенотипа с определенных показателей имела протеолитическая активность по лизису азоказеина больше 1,5 мл/час: специфичность 84,7 %, предсказуемая ценность положительного результата 79,1 %, соотношение шансов 7,5, посттестовая вероятность положительного результата 79,1 %.

Ключевые слова: дети, бронхиальная астма, конденсат выдыхаемого воздуха.

ПОКАЗНИКИ КОНДЕНСАТУ ВИДИХУВАНОГО ПОВІТРЯ У ДІТЕЙ ЗА ЕОЗИНОФІЛЬНОГО ФЕНОТИПУ БРОНХІАЛЬНОЇ АСТМИ

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Резюме. Вивчали показники конденсату видихуваного повітря у 160 хворих на бронхіальну астму за різних фенотипів захворювання. Показано, що в дітей із неэозинофільним фенотипом бронхіальної астми порівняно із пацієнтами з еозинофільним фенотипом захворювання у конденсаті видихуваного повітря відмічаються зміни, які свідчать про більшу активність запальних процесів бронхів. Найвищу діагностичну цінність виявлення неэозинофільного фенотипу астми з вивчених показників відмічено за протеолітичною активністю за лізисом азоказеїну в конденсаті видихуваного повітря більше 1,5 мл/год: специфічність 84,7%, передбачувана цінність позитивного результату 79,1 %, співвідношення шансів 7,5, посттестова вірогідність 79,1 %.

Ключові слова: діти, бронхіальна астма, конденсат видихуваного повітря.

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