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Bronchial lability Indices in children with phenotypically heterogeneous depending on debut time asthma

Keywords: *bronchial asthma, children, phenotypes, bronchial lability.*

In accordance with applicable national standards [4] and the recommendations of national experts [1, 6, 7] the main purpose of basic treatment of bronchial asthma (BA) is to achieve control. However, one aspect of inadequate control of asthma is its phenotypic heterogeneity, including depending of age debut (asthma early and late start), the nature of bronchial inflammation (eosinophilic and not eosinophilic), lower airway obstruction rate (torpid and labile obstruction), the answer to the basic therapy (steroid-sensitive and resistant BA) [2, 8, 11].

Differentiated approach to therapeutic tactics regarding BA with early and late start and associations of time debut with other characteristic phenomena will have predicted positive impact on treatment outcomes and achievement of control of the disease [10, 13]. Definition of phenotypic characteristics, along with the study of pathophysiological mechanisms for each phenotype, will be an important step and will give better chances of landing more effective individualized treatment programs [9, 12].

The aim of the study was to evaluate the different caliber bronchi lability exponents in children with BA with different disease phenotypes, depending on the time of the debut of the disease.

Materials and methods

With respect to the principles of bioethics there were examined 50 children with bronchial asthma on the basis of the pulmonary department of Regional Children's Hospital (Chernovtsy). By time debut of the disease there were formed two groups of clinical observations, particularly - in the first clinical group 25 children with early-onset phenotype have been included, the other 25 patients with a phenotype of late onset have been involved in a second clinical group. Both comparison groups did not differ significantly by the main clinical features. The data was so – the I clinical group consisted of 18 (72 %) boys, comparison group – 20 (80 %, $p\phi > 0,05$), upstaters in children with early onset phenotype – 17 (68 %) patients, in II clinical group – 14 (56 %, $p\phi > 0,05$), the average age of representatives of I clinical group was ($11,3 \pm 0,67$), in the comparison group – ($12,7 \pm 0,65$) years, $p > 0,05$.

Bronchial lability was determined according to the recommendations [3, 5, 15] by assessing their response to dosed physical exercises (DFE) and inhalation of short-acting β_2-agonist (salbutamol 200 mcg) followed by calculation of bronchial lability indicator as the sum of the components - bronchospasm indexes (IBS):

IBS = ((FEV_1 output - FEV_1 after DFE)/FEV_1 output) × 100 %

and bronchodilation (IBD):

IBD = ((FEV_1 after inhalation of salbutamol – FEV_1 output) / FEV_1output) × 100 %

where FEV_1 – forced expiratory volume in the first second, FEV_1output – Output parameter of FEV_1 after DFE/salbutamol inhalation.

Statistical analysis of the data was carried out from the perspective of biostatistics. For data that meet the normal distribution the arithmetic average of the sampling (M), the value of the standard deviation (s) and standard error (m), maximum and minimum values were determined. In assessing the probability of ratio difference the Student's coefficient (t) was calculated. The significant difference has been taken the difference at $p < 0,05$ [14].

Results and discussion

In the study of bronchial lability was observed the decrease in FEV1 after inhalation of salbutamol, which were recorded as negative values of IBD, in two children from the I clinical group and one child from the II clinical group. As the indicated bronchial response to inhalation of β_2-agonist cannot

Table 1

Indicators of bronchial lability in schoolchildren in clinical groups (M ± m)

Clinical groups		Number of children	IBS, %	IBD, %	IBL, %
I	Children with early asthma onset	23	16,2 ± 2,6	14,7 ± 2,5	30,8 ± 3,5
II	Children with late asthma onset	24	17,1 ± 2,5	10,8 ± 1,7	27,8 ± 3,1
P			< 0,05	< 0,05	< 0,05

Note: P - Student.'s probability criterion.

be considered as typical, so the results of these patients were excluded from further analysis of the lability of the bronchial tree.

Table 1 shows the values of bronchial lability in children from comparison groups in response to the DFE (IBS) and inhalation of salbutamol (IBD) and also the average values of integrative index of bronchial lability (IBL).

A trend towards more pronounced lability due to more significant dilatation in response to inhalation of β_2-agonist is observed in children with early-onset asthma phenotype. Thus, a positive bronchomotor testing with β_2-adrenoceptor agonist was observed in greater proportion of patients from the I clinical group (60,8 %), and only in a third part of the representatives of the comparison group (33,3 %, Pϕ > 0,05). In addition, low lability (IBL less than 17 %) is attributable to 30,4 % of children with asthma of early onset phenotype and only to every fifth patient with late onset asthma (20,8 %, Pϕ > 0,05). However, severe airway lability (IBL over 30 %) was observed in the same frequency in both clinical groups (39,1 % and 33,3 % in I and II groups respectively, Pϕ > 0,05).

The trend to more severe bronchospasmodic reaction to DFE has been recorded among the members of the clinical group II. Severe spastic reaction (IBS over 20 %) was attributable to more than one third (37,5 %) of children with asthma late onset, but among the patients of the I clinical group actual indices have been registered only in 17,4 % of patients (Pϕ > 0,05).

For a more detailed analysis of the sensitivity of the airways to DFE with a glance to a bronchodilator effect of β_2-adrenoceptor agonist the evaluation of parameters of lability of different caliber bronchi has been performed (Table 2).

It should be noted that parameters of lability of small and medium-sized bronchi were slightly more evident in children with early onset asthma phenotype. The most bronchospasmodic reaction in response to the DFE and dilated airways response to inhalation of short action β_2- adrenoceptor agonist were defined at the level of medium-sized bronchi in children in both clinical groups.

During the analysis of small-sized bronchi lability the attention has been attracted by presence of atypical bronhodilatational reaction to DFE in 17,4 % of children in the I clinical group and in 12,5 % representatives of the comparison group.

The significant spasm of small bronchi (IBS> 25 %) has been observed in one-third (33,3 %) part of patients with early-onset asthma phenotype, in the II clinical group specified value IBS was determined in every fifth child (20,8 %, Pϕ > 0,05). However, a slight spasm of small bronchi (IBS < 10 %) more frequently have been detected in children with late onset asthma (20,8 %) than in children with early debut of the disease (8,7 %, Pϕ> 0,05).

Table 2

Parameters of lability of different caliber bronchi in children from clinical groups (M ± m)

Bronchi caliber	Lability parameters	Children with early asthma onset, n = 23	Children with late asthma onset, n = 24	P
Small calibre	IBS	16,5 ± 4,6	12,4 ± 5,6	< 0,05
	IBD	27,4 ± 7,2	20,6 ± 5,6	< 0,05
	IBL	44,3 ± 7,7	33,9 ± 4,7	< 0,05
Medium caliber	IBS	29,6 ± 8,4	18,4 ± 3,7	< 0,05
	IBD	33,6 ± 6,0	32,2 ± 5,5	< 0,05
	IBL	53,2 ± 7,3	50,6 ± 5,5	< 0,05
Large caliber	IBS	15,2 ± 5,0	18,0 ± 3,7	< 0,05
	IBD	29,6 ± 8,4	30,2 ± 6,3	< 0,05
	IBL	45,8 ± 7,2	48,0 ± 5,6	< 0,05

Note: P – Student.'s probability criterion.

Dilatation index of small bronchi was more than 30 % in 44,5 % of children with early onset asthma, and only in 25 % of representatives of the comparison group (Pϕ > 0,05). Severe dilated response to inhalation of salbutamol (IBD > 50 %) was observed more frequently in patients of the I clinical group (17,4 %) than in the second clinical group (8,2 %, Pϕ > 0,05).

Along with the tendency toward more severe lability of small-sized bronchi in children of the I clinical group the value of IBL for this caliber did not exceed 20 % (in 21,7 % and 25,0 % of cases in the first and second groups, respectively) with equal frequency in representatives of both clinical groups. However, IBL > 60 % was recorded in 26,1 % of children in the I clinical group and only in 8,2 % of patients with late asthma onset phenotype (Pϕ > 0,05).

It is necessary to say that IBS has acquired negative values due to improvement of medium-sized bronchi patency after the physical exercises in 13,1 % and 12,5 % of children in first and second groups, respectively (Pϕ > 0,05).

Along with the tendency toward more severe lability indices of medium bronchi in children with early asthma onset phenotype the severe bronchospasmodic reaction (IBS > 25 %) was observed in 33,3 % of patients in the I clinical group and in 25 % - in the second clinical group (Pϕ > 0,05).

The majority of patients in the I clinical group had values of IBD recorded at the level of the medium-sized bronchi that exceeded 30 % (56,5 %). In the second clinical group specified values of IBD were observed in 41,6 % (Pϕ > 0,05). Severe airway response to salbutamol (IBD more than 65 %) as their expansion was observed in a small part of patients in both clinical groups (13,0 % and 8,2 % of children in I and II clinical group respectively, Pϕ > 0,05). A small dilated reaction of medium-sized bronchi (IBD less than 15 %) for inhalation of bronchodilators was observed in one third part of patients with late asthma onset phenotype (33,3 %), in patients with early debut of the disease indicated values of IBD have been recorded only in every fifth patient (21,7 %, Pϕ > 0,05).

The tendency towards the higher values of IBL for medium caliber in the first clinical group is demonstrated by a higher proportion of patients with early-onset asthma who had the values of this index at the level more than 50 % (56,5 %) as against the comparison group (45,8 %, Pϕ > 0, 05).

At the level of large caliber bronchi the lability indices were slightly higher in children with late asthma onset phenotype. In every sixth patient (13,1 %) with early-onset asthma the improvement of bronchial patency after DFE was marked and therefore the indices of IBS were negative. In the comparison group the number of children with negative values of IBS at the level of large-sized bronchi was slightly less (8 %, Pϕ > 0,05). However, the values of IBS > 30 % indicating to a pronounced bronchospasm after DFE were registered with equal frequency in representatives of both clinical groups (21,7 % and 20,8 % of patients in I and II group respectively).

Conclusions

1. Children with early asthma onset phenotype are characterized by a tendency to more severe bronchial lability due the bronchodilated response to short action β_2-adrenoceptor agonist.

2. More pronounced bronchospasmodic reaction in response to the DFE is typical in children with late asthma onset.

3. Lability indices of small and medium-sized bronchi are somewhat more pronounced in children with early asthma onset phenotype.

Prospects for future research are consisted in the study of children who suffer from asthma with various debut times, of features of paraclinical markers that reflect the main characteristics of the disease - inflammation and bronchial hyperresponsiveness.

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ПОКАЗАТЕЛИ ЛАБИЛЬНОСТИ БРОНХОВ У ДЕТЕЙ, БОЛЬНЫХ ФЕНОТИПИЧНО НЕОДНОРОДНОЙ В ЗАВИСИМОСТИ ОТ ВРЕМЕНИ ДЕБЮТА БРОНХИАЛЬНОЙ АСТМОЙ

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Резюме. *В статье представлены особенности лабильности бронхов у детей, больных бронхиальной астмой, с фенотипами в зависимости от времени дебюта. Показано, что детям, больным бронхиальной астмой с фенотипом раннего начала, присуща тенденция к более значительной лабильности бронхов за счет бронходилятационной реакции на β_2-адреномиметик короткого действия; в то же время, детям с бронхиальной астмой позднего начала – более значительная бронхоспастическая реакция в ответ на дозированную физическую нагрузку.*

Ключевые слова: *бронхиальная астма, дети, фенотипы, лабильность бронхов.*

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BRONCHIAL LABILITY INDICES IN CHILDREN WITH PHENOTYPICALLY HETEROGENEOUS DEPENDING ON DEBUT TIME ASTHMA

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Summary. *This paper presents the features of bronchial lability in children with bronchial asthma phenotypes, according to debut time. It is shown that children with asthma of early onset phenotype were characterized by a tendency to expressive bronchial lability due to dilation response to short acting β_2-agonists. However, children with late-onset asthma were characterized by expressive bronchospasm reaction after dosed physical exercises.*

Key words: *bronchial asthma, children, phenotypes, bronchial lability.*

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