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КЛИНИКО-АНАМНЕСТИЧЕСКИЕ ОСОБЕННОСТИ ФЕНОТИПА БРОНХИАЛЬНОЙ АСТМЫ ФИЗИЧЕСКОГО НАПРЯЖЕНИЯ У ДЕТЕЙ И ПОДРОСТКОВ

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АННОТАЦИЯ. На базе пульмонологического отделения ОДКБ г. Черновцы обследовано 60 детей школьного возраста, больных на бронхиальную астму. Изучены клинико-анамнестические характеристики фенотипа бронхиальной астмы физического напряжения у детей. Результаты позволят разработать дифференциальные диагностические подходы для дальнейшего выбора индивидуализированного лечения.

КЛЮЧЕВЫЕ СЛОВА. Бронхиальная астма, фенотип физического напряжения, дети.

CLINICOANAMNESTIC FEATURES OF EXERCISE-INDUCED ASTHMA RELATED PHENOTYPE IN CHILDREN AND TEENAGERS.

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ABSTRACT. We have examined 60 school children with asthma at the pulmonary department of Regional Pediatric Hospital in Chernivtsi. Study of clinical and medical history of asthma phenotype characteristics of physical activity in children. Results will develop differentiated diagnostic measures for selecting individuals Busi-treatment.

KEYWORDS. Bronchial asthma, exercise induced bronchial asthma, children.

Bronchial asthma is the most disputable and complicated problem in pediatric pulmonology. It is due to increasing incidence and prevalence, early onset of the pathology, its multifactor nature, late diagnosis, increased severe clinical manifestations of the disease, which contribute to worse quality of life, disability and other adverse effects in children [1, 4, 18, 21, 24, 34, 37]. According to WHO, among 15 million disabled patients in the world 1% are patients with asthma. The condition not only affects the mental, physical and social aspects of a sick child, but both morally and financially exhausts their family members [5, 12, 15].

The last decades have seen a significant increase in specialists' interest to the problem of exercise induced bronchial asthma (EIBA). This is due, on the one hand, to the creation of a convenient model for studying reverse bronchospasm in patients suffering from the disease, on the other hand, a constant puzzle for experts is its unfoundedly easy fit and fast reverse development. The problem topicality is due to the necessity to make the patient refractory to exercise. The presence of physical exclusion in patients with asthma - is one of the major psycho-emotional stressful factors that interferes with their normal way of life. This problem is particularly important for children, who are characterized by an active way of life.

We must distinguish between two terms that are often used in the literature:

• bronchospasm caused by exercise (Exercise-induced bronchospasm, EIB) - bronchial obstruction

and spasms that occur in response to exercise in humans with normal lung function at rest;

• Exercise-induced asthma, (EIA) – difficulty in a patient's breathing with asthma during and after exercise. The decline in FEV1 compared to that before exercise by more than 15% usually indicates the presence of EIA. According to several studies, the rate FEV0, 5 describes bronchoconstriction better than FEV1 and is better correlated with the degree of severity of clinical symptoms of asthma. According to the literature, the incidence of exercise induced asthma varies from 30% to 90% depending on the criteria for diseases and research methods [10, 15, 16, 20, 31]. Symptoms and exacerbation of exercise induced BA are provoked by many triggers, including viral infections, allergens, exercise, tobacco smoke and other pollutants. EIBA affects 90% of patients with asthma and 40% of patients with allergic rhinitis; among athletes and the general population prevalence ranges from 6% to 13%. EIBA often remains not diagnosed. Approximately 9% of EIBA patients have no clinical signs of asthma or allergy [28, 31].

A recent international document of asthma in children notes that age and specific triggers can be used to define the phenotypes of the disease [1, 9].

Using the most advanced immunological and instrumental study methods allows a definite conclusion that physical activity is one of the most important non-immune and drugless stimuli leading to the development of acute spasm of the airways in patients with asthma. Exercise induced bronchial asthma is one of the manifestations of the airway hypersensitivity. According to some researchers [11, 26], the term "exercise induced BA" suggests the development of bronchospasm after exercise in patients with atopic asthma. This view is reflected in the materials of Consensus "Bronchial asthma. Global Strategy "(2008-2012) [9, 10].

Signs of EIBA have been quite well detected by history taking and physical examination during functional load tests. After some physical activity (running, testing on bicycle or step test) for 6 minutes some patients had asthma bronchospasm, which develops acutely after 2, 5 or 10 minutes. There was airway obstruction, which is usually felt by the patient as breathlessness and is easily recorded by functional tests that reflect the speed change in exhaled air flow - peak expiratory flow rate (PEF), maximum volume velocity (MVV 25, 50, 75), forced expiratory volume in 1 second (FEV1) [6, 14, 19, 27]. However, during the first few minutes of load there is a phase of bronchiectasis which at the end of the load test turns into bronchospasm [21]. Most patients with severe asthma as early as in 3-4 minutes of the load had to interrupt the tests due to a rapid bronchospasm. Over the next 30-60 minutes bronchospasm ended. During this period the patient was refractory to physical activity, and only after its end a repeated exertion leads to a reverse, but much less pronounced bronchospasm [7, 14, 31]. Reduction of FEV0, 5 by 13% compared to that before exercise is a significant clinical sign of exercise induced asthma [3, 35]. Pathogenesis of reverse obstruction in exercise induced asthma, despite an intensive study, is still not fully elucidated [1, 4, 19].

Thus, the study of clinical-anamnestic characteristics of exercise induced asthma phenotypes in children is of great practical importance to the development of differential diagnostic measures for selecting individualized treatment.

Materials and methods. To achieve this goal we have examined 60 school children with asthma by a simple random sampling at the pulmonary department of Regional Pediatric Hospital in Chernivtsi.

We formed two clinical observation groups: the first clinical group (I) consisted of 30 children with exercise induced asthma phenotype, that is with signs of asthma after exercise and bronchospasm index more than 15%, references to their worse condition after exercise in history. The second clinical group (II) included 30 children with asthma that was not associated with physical activity. In I and II clinical groups the proportion of children who were in acute phase of the disease, amounted to 27 (90%) and 25 (83,3%, P> 0,05) pediatric patients respectively.

For the main clinical signs the comparison groups did not differ significantly (Table. 1).

Table 1

Comparative characteristics of the groups monitoring the main clinical signs

Clinical sign		Clinical groups		P
		I, n=30	II, n=30	
Average age, years (M±m)		12,03±0,61	11,08±0,62	>0,05
abiding place (%, P±m)	town	11(36,67±7,9%)	10(33,33±8,6%)	>0,05
	village	19(63,33±7,9%)	20(66,67±9,0%)	>0,05
sex, (%, P±m)	boys	19(63,33±8,8%)	19(63,33±8,8%)	>0,05
	girls	11(36,67±8,8%)	11(36,67±8,8%)	>0,05

The average age of children at the time of the survey over 13 years prevailed in the first clinical group (53% versus 40% (P > 0,05) children of the second clinical group), although with no clear statistical significance. Thus, the main clinical characteristics of the comparison groups were comparable.

We used the classification of asthma according to the Unified clinical protocols of primary and secondary (specialized) medical aid, approved by the Ministry of Health of Ukraine (№ 868 of 8.10.2013) [40], and the International Global Initiative as to the diagnosis and treatment of asthma (GINA-2011) [9].

The severity of bronchial obstruction syndrome (BOS) on admission of patients to the hospital during the period of atacks, the disease was evaluated by a point system.

Results.

As to the degree of severity of the disease 10 (33,4±8,6%) schoolchildren of the first clinical group had its moderately severe course while 19 patients (63,3 ± 8,8%) suffered from severe asthma. The representatives of the comparison group experienced mild course in three children (10,0 ± 5,5%, P> 0,05), moderately severe in 18 (60,0 ± 8,9%, P <0,05) and severe asthma was recorded in 9 patients (30,0 ± 8,4%, P <0,05). The onset of the disease assessment in groups of observation showed that among the examined children the so-called "asthma with late onset» was recorded [25, 39]. Thus, the onset of the disease after 3 years was observed in 56.7% of patients of the first clinical group compared to 60,0% (P> 0,05) of the comparison group.

Evaluation of allergic history in examined schoolchildren showed that 19 children (63,3 ± 8,8%) from the first clinical comparison group and 14 students (46, 6 ± 9,1%, P> 0,05) of the second clinical group had signs of concomitant diseases such as allergic rhinitis and atopic dermatitis.

The average bed day values in patients of I and II groups of observation did not differ significantly and were 13,7 and 12,9 b/d, (P> 0,05) respectively.

Analyzing the social status of children, it should be noted that employment of parents did not influence the values in the comparison groups, but there were more frequent references to unemployed father in the first the clinical 15,8 ± 8,3% versus 8,7 ± 5.8% (P> 0.05), although with no clear statistical significance.

When studying the effect of the feeding type in the first year of life, on the asthma phenotype formation, there were no significant differences observed, but in assessing the degree of fatness by body mass index (BMI) of patients in the comparison groups it was noted that BMI over 22 kg / m2 was 25,9 ± 8,4% of patients with exercise induced BA, and in patients of the clinical group II - 6,8 ± 4,8% (Rφ <0.05).

Analyzing the average weight index at birth as one of the risk factors for asthma (in case of its excess over the average one) [4, 7, 37], we noticed that the number of children born weighing more than 3500 g, prevailed in the first group 60,7 ± 9,2% cases against clinical group II 46,7 ± 9,1%, (P> 0.05), although without statistical significance.

Given that infectious disease of early childhood in some cases possess both trigger and protective effect on the development of asthma [24, 32, 39], we analyzed their impact on the exercise induced asthma phenotype. The obtained data give reason to believe that infectious diseases the children suffered from in their early childhood did not promote further formation of this phenotype of BA. Thus, the proportion of children with exercise induced BA, who had not had children's infections was 50 ± 9,1% of cases in the first clinical group versus 3,4 ± 3,3% (P <0.05)in the second clinical group.

Burdened family history, especially on the father's side was observed in the first clinical group in 27,58 ± 8,3% of cases versus 3,45 ± 3,4% (P <0.05) in the second clinical group of supervision. As to the individual allergic history with almost equal frequency in patients of both clinical comparison groups we noted signs of allergic reactions to food, household and combined food and household allergens, but it was more pronounced in patients from the first clinical group 78,6 ± 9,6% versus 66,7 ± 13,6% in schoolchildren from the second clinical group.

In some papers [7, 26] they marked statistically significant relationship between physical activity and atopy. Our study also revealed burdened family history for atopic diseases. Allergy index in the first group was 0,118 ± 0,036 s.u. vs. 0,044 ± 0,022 s.u. (Rφ <0.05) in the second comparison group.

There were no significant differences in clinical groups of comparison concerning the parents' smoking. According to the literature mother's smoking [12, 38] is one of the factors that provoke asthma. Thus, the proportion of children whose mother smoked prevailed in the first clinical group, namely 31,25 ± 11,6% of cases versus 12,5 ± 8,3% (P> 0,05) of the second clinical group, although without statistical significance.

Patients with exercise induced asthma phenotype were characterized to a greater extent by trigger provocation of exacerbation caused by combined factors including ARD, physical and meteorological factors whose share amounted to 16,7 ± 8,79% (Rφ <0,05) against none of the of the second group children.

Exercise induced asthma phenotype was characterized by daytime symptoms which were observed more than once a week in 32,0 ± 9,3% cases against 11,1 ± 7,4% (Rφ <0,05) in the second observation group of children. The presence of nocturnal symptoms in the group of children with exercise induced asthma more often than once in 2 weeks was 36,0 ± 9,6%, against 11,1 ± 7,4% (P <0,05) in patients of the second observation group.

The frequency of exacerbations before examination in the hospital was almost the same in both groups of comparison. Thus, in the first clinical group exacerbations were recorded 3-4 times a year in 44,0 ± 9,9% of cases versus 27,8 ± 10,6% (P> 0,05) cases in the comparison group.

The clinical studies have shown that the severity of bronchial obstruction (in points) in the period of asthma attacks within 7 days of treatment in hospital in the comparison group of children was not significantly different (Table 2).

Table 2

Dynamic inference of bronchial obstruction severity in children from the comparison group during the period of asthma attacks

Clinical group, number of patients	Bronchial obstruction severity (in points), M±m						
	day 1	day 2	day 3	day 4	day 5	day 6	day 7
I n= 30	11,08±1,08	10,25±1,09	8,29±0,97	6,25±0,83	5,20±0,66	4,08±0,57	2,90±0,42
II n= 30	11,08±0,85	10,52±0,89	8,08±0,69	6,10±0,52	4,88±0,4	3,70±0,38	3,20±0,75
P	>0,05	>0,05	>0,05	>0,05	>0,05	>0,05	>0,05

However, the severity of attacks in the patients of the first clinical group on the first day of hospitalization which was higher than 16 points was recorded in 25% of children, while in the second group 8% of patients (Pφ <0,05) had these values.

Starting from the second day of hospitalization patients with exercise induced asthma phenotype tended to BOS prevalence of more than 16 points – in 25%, and in the comparison group in 12% (P> 0,05). On the third and fourth days of hospitalization the severity of BOS, that was more than 16 points in clinical groups decreased under the influence of desobstructive therapy, but was still higher in the first group 8,3% vs. 4,2% in patients of the second observation group (P > 0,05).

Signs of intoxication were observed in 16,7 ± 6,8% of patients from the first clinical group and 6,7 ± 4,6% of children (P> 0,05) in the second clinical supervision group. Such clinical signs as the nature of cough and tympanitic chest in comparison groups were not significantly different. It is noted that T> 37C was observed in patients from the first clinical group in 33,3 ± 8,6% cases against 13,3 ± 6,2% (Pφ <0,05) in children from the second clinical supervision group. 43,3 ± 9,4% of the first group felt pressure in the chest against 16,6 ± 6,79% (P <0,05) cases in the second clinical group.

Such clinical signs as shortness of breath, wheezing, events of rhinitis were similar in both groups of observation. Hyperemia of pharynx and tiemannite were characteristic for the schoolchildren from the first clinical group 40,0 ± 8,9% and 73,3 ± 9,4% to 23,3 ± 7,7% versus 60,0 ± 8,9% (P> 0,05) respectively in the second observation group.

Thus, the analysis of the data showed that among children with exercise induced asthma phenotype at the onset of the disease so-called "late start" (over 6 years) asthma prevailed; as to the disease severity - every third child suffered from severe asthma (RR = 2,0 (95% CI 1,1-3,6), OR = 4,03 (95% CI 1,4-11,8). This category of patients was characterized by the fact that the sick child's father did not work, the weight of patients at birth exceeded 3500g (RR = 1,3 (95% CI 0,8-2,2), OR = 1,8 (95% CI 0,6-5,0), BMI was over 22 kg / m2 (RR = 1,7 (95% CI 0,4-7,7), OR = 4,4 (95% CI 0,8-23,4), the family history was burdened with atopic diseases on the father's side (RR = 2,1 (95% CI 0,3-15,7), OR = 11,6 (95% CI 1,3-106,7); allergy severity index (RR = 1,8 (95% CI 0,5-6,8) OR = 3,7 (95% CI 0,5-29,7) a triggering role in asthma exacerbations with combined factors prevailed (ARD, physical and meteorological factors) during the period of attacks on the first day of hospitalization every fourth child was observed with more pronounced BOS over 16 points (RR = 1,7 (95% CI 0,4-7,6), OR = 3,8 (95% CI 0,7-21,3). In patients with БАФН daytime symptoms of the disease with frequency greater than once a week was noted (RR = 1,5 (95% CI 0,4-6,5), OR = 3,8 (95% CI 0,7-20,5), nocturnal symptoms with a frequency of more than every other week (RR = 1,6 (95% CI 0,4-6,7), OR = 4.5 (95% CI 0,8-24,2) and severe limit of physical activity (RR = 1,6 (95% CI 0,2-12,3), OR = 5,4 (95% CI 0,6-49,2). The group of children with exercise induced asthma phenotype who were in the hospital was characterized by such signs as intoxication, a feeling of chest pressure (RR = 1,8 (95% CI 0,7-4,4), OR = 3,8 (95% CI 1,1-12,7).

Conclusions. Thus, taking into account individual clinical and epidemiological risk for clinically-anamnestic parameters in the development of exercise induced asthma in children can not only increase the effectiveness of individual adequate treatment, but also improve monitoring of the disease course.

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