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ASSESSMENT OF RISK FACTORS FOR BRONCHIAL ASTHMA ASSOCIATED WITH CONNECTIVE TISSUE DISPLASIA IN CHILDREN LIVING IN SAKHA REPUBLIC (YAKUTIA)

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The article presents the results of the examination of 33 children with bronchial asthma in the pulmonology department of the children's consultation clinic of the Pediatric Center of the Republic of Sakha (Yakutia). 2 groups were formed due to the detected external signs of connective tissue disorder. Comparative analysis of BA clinical characteristics was described. The BA course associated with moderate and severe CTD was characterized by moderate forms and tendency to lower disease control, worse prognosis. Most children with BA in both groups had body weight deficient. All children with BA associated with CTD had musculoskeletal pathology as well as other comorbid diseases. Significant risk factors have been identified, such as the effects of parental smoking, the presence of pets, and low rates of breastfeeding.

Keywords: bronchial asthma in children, connective tissue disorder, children, allergies.

Introduction. Bronchial asthma (BA) is one of the important problems of pediatrics and clinical medicine, in general. [6, 19–21]. International and domestic program documents on BA emphasize the clinical heterogeneity of the disease, manifesting both in differences between individual patients, and also in the pathological process dynamics in each patient [21]. Connective tissue disorder (CTD) deserves special attention out of many causes for the development of individual features of BA course - this is a heterogeneous group of diseases of connective tissue of a polygenic-multifactorial nature, combined into phenotypes based on the commonality of external and/or visceral features [17].

CTD is a widespread pathology from 13 to 85.4% according to various researchers [7, 13, 14, 16]. The works on CTD effect on the structure and function of the bronchopulmonary system noted disorders of the elastic framework of the lungs: a change in the architectonics of pulmonary tissue in the form of interalveolar septum destruction and underdevelopment of elastic and muscle fibers in small bronchi and bronchioles, leading to reduced elasticity of pulmonary tissue with the formation of emphysematous bulls; polycystic disease on the background of bronchial obstruction and the formation of spontaneous pneumothorax. Congenital defect of the cartilage and connective tissue framework of the trachea and bronchi leads to impaired mobility (dyskinesia), the emergence of bronchiectases, pneumosclerosis. Tracheobronchial dyskinesia promotes bronchospasm [6, 18, 19]. The involvement of several organs and systems in the pathological process in children with CTD at the same time can explain more severe, non-classical manifestation of clinical symptoms in respiratory diseases, including BA [2, 4, 9, 13].

Attention to the BA problem associated with connective tissue disorder is explained by the early development of severe forms of the disease, complications, difficulties in selecting management programs for both adult patients [8, 11, 14] and children [5, 12, 13, 15].

The research aim is to study BA risk factors in children with CTD living in the Republic of Sakha (Yakutia).

Research materials and methods. The study included 33 patients with BA of Yakut nationality aged from 4 to 16 years old, examined in the pulmonology department of the children's clinic of the Pediatric Center of the Republic of Sakha (Yakutia). The research criteria included: proven diagnosis of bronchial asthma; informed consent of patients' parents to participate in the research, Yakut nationality. Criteria for exclusion from the research were: patients under 4 years of age; lack of informed consent to participate in the study, children with established hereditary connective tissue disorder; tuberculosis and other chronic lung diseases, other nationalities.

Diagnosis, severity and indicator of bronchial asthma control level was carried out with criteria of clinical recommendations "Bronchial asthma in children"

(2017) taking into account clinical (detailed anamnesis, a case history), laboratory (clinical blood test, rhinocytogram), functional (results of spirography and daily picflowmetry) and allergic (performing scratch test according to a standard procedure on the inner surface of the forearm, allergen-specific immunoglobulins E in blood serum) examination.

Connective tissue disorder was diagnosed by the external signs of connective tissue involvement (CT) [17]. The criterion for CTD severity was the point assessment of phenotypic signs of CT systemic involvement in children (screening algorithm) according to the classification of T. Milkovskaya-Dimitrova in the modification of L.N. Abbakumova: mild - 0-12, moderate - 13-23, expressed - over 24 points [1].

Two groups were formed due to the severity of CTD external manifestations: 1st (n = 15) - children with bronchial asthma and moderate and pronounced degree of CTD (sum of points over 12), 2nd (n = 18) - BA patients with mild connective tissue disorders (sum of points less than 12). In each BA patient, the level of stigma was determined according to the criteria proposed by V.G. Arsentiev, where a score of 40 or more was considered to be significant for CTD. The result from 30 to 40 points was treated as increased dysplastic stigma [3].

For each child, an individual questionnaire was issued with data from a case history, clinical examination. The BA pattern was evaluated, the level of control of the disease was determined by the asthma control test, the peak expiratory rate was monitored daily with a picflowmeter and the results were recorded in the patient's diary. The identification of possible risk factors determining the course of BA was carried out by analyzing family and allergological history, as well as assessing the quality of anti-inflammatory (basic) therapy, BA frequency per year, the duration of the disease, and the patient's living conditions. All children and parents were given recommendations how to achieve asthma control. Ultrasound examination of organs of the abdominal cavity, kidneys, heart, radiography, as well as specialists' examination was performed to identify clinical-instrumental signs of connective tissue disorders. Body mass index (BMI) was calculated by the formula: body weight (kg)/body length (estimated as normal indicator (18.5 - 30); body weight deficiency (< 18.5); obesity (> 30) [10]. Statistical processing of the material was carried out using a package of SPSS-22 programs using Mann-Whitney U-test, Spearman correlation analysis, differences at $p<0.05$ were statistically significant.

Results and discussion. Clinical and demographic characteristics of BA patients associated with CTD are shown in Table 1.

Boys were dominated in both groups. The groups were comparable in age, the average age in the 1st group was 9.1 ± 3.2 years old, in the 2nd - 8.7 ± 2.9 years old. The vast majority of patients in both groups were characterized by body weight deficiency.

Hereditary predisposition to BA was detected in 38.9% of patients from the 2nd group. Allergic rhinitis is equally common in both groups, in half of cases - from mothers, in 27-28% - fathers. Eczema from both parents was observed more often in the 1st group (46.7%). Atopic dermatitis in Sibs was detected 2 times more frequently in the 2nd group (44.4%) ($p = 0.002$) (Table 1).

Analysis of the structure of comorbid allergic pathology in children of both groups showed that BA was more likely to be associated with diseases such as allergic rhinoconjunctivitis, atopic dermatitis and pollen disease. Less often there were urticaria, Quinke's edema (Table 1).

According to allergotesting, sensitization to household allergens was more often detected in patients of the 2nd group than in the 1st group (Table 1).

The assessment of BA risk factors showed that the majority of children of the 1st group and half of the 2nd group lived in urban conditions (Table 2). There was a residence in a wooden house (barrack) in half of the cases of both groups. 27.8% of patients from the 2nd group and one child from the 1st group grew up in incomplete family. Breastfeeding has been found to prevent the development of atopy. The 2nd group patients were on natural feeding 3 times less often than in the 1st one ($p = 0.03$). The presence of pets was detected with equal frequency in families of the 1st (20%) and 2nd (16.7%) groups. 53.3% of children of the 1st group and 77.7% of children of the 2nd group were subjected to passive smoking by parents, the fathers of the 2nd group smoke most often in families ($p = 0.01$) (Table 2).

The analysis of laboratory data revealed the increased levels of total IgE serum in patients of both groups, but this indicator was shown 3 times more often in patients of the 2nd group ($p=0,03$). A third of patients in both groups had eosinophilia. An increased number of eosinophils were found 2 times more often in patients of the 2nd group, according to the rhinocytogram (Table 2).

The BA diagnosis was made at the age of 7,4±3,9 years old in the 1st group, in the 2nd group - 6,3±3,2,3 years old. The average duration of the disease in the 1st group was 1,8±2,4,8 years and in the 2nd - 2,4±2,6 years. The BA duration less than 1 year was established in 53,3% patients of the 1st group and 61.1% – in the 2nd group. The duration of the disease from 1 year to 5 years old was determined in 33.3% patients of the 1st group and in 11.1% patients of the 2nd group. The BA duration from 5 to 7 years old was detected in 1 and 2 children, respectively. The BA experience for more than 7 years was in 1 patient of the 1st group and 3 - in the 2nd group.

In the 1st group, a diagnosis of mild BA was established in 1 patient, moderate - in the rest of patients.

In all patients of the 2nd group, BA of moderate severity was stated. No patients with severe BA were recorded in the groups. All patients in both groups received baseline therapy according to the clinical guidelines "Bronchial Asthma in Children" (2017) and were followed up at the place of residence. To correct the therapy, children of both groups were referred to the NCM clinic to a pulmonologist, who revealed that the uncontrolled course of BA was recorded in 80% of patients of the 1st group. In the 2nd group, 50% of patients had partial or complete control over the disease. This circumstance required additional research by narrow specialists, correction of baseline treatment, dynamic control, and increased compliance in this category of patients.

At the 2nd stage, after in-depth multi-specialist study, the prevalence of comorbid diseases was analyzed (Table 3).

Table 3 shows that the musculoskeletal system was affected in all patients of the 1st group and half of the 2nd group. The correlation links between external and internal features were found in the 1st group of patients: scoliosis and flatulence $r = 0.76$, $p < 0.01$, myopia and muscle hypotension $r = 0.50$, $p < 0.05$. 26.7% of children in the 1st and 22.2% in the 2nd group showed cervical spine instability.

Cervical spine instability was revealed in almost a quarter of children of both groups, signs of juvenile osteochondrosis were in one child from the 1st group.

Connective tissue disorder of the heart was diagnosed at the 2nd place. According to ECHO-CG, children in both groups showed additional trabecula, an open oval window, mitral valve prolapse, etc.

The gastrointestinal system pathology

Table 1

Clinical and demographic characteristics of BA patients enrolled in the research

Indicators	1st group (n = 15)		2nd group (n=18)		p
	Абс.	p	Абс.	%	
Средний возраст	9.1 ±		8.7 ±		
Sex					
Male	10	66.7	12	66.7	
Female	5	33.3	6	33.3	
Body mass index (BMI)					
Normal (18.5-30)	1	6.7	4	22.2	
Body weight deficit (<18.5)	14	93.5	14	77.8	
Excess body weight (>30)	0	0	0	0	
Average CTD score					
CTD average score	25.2±7.2*** (14-38)		5.7±2.5 (3-10)		0.0001
Increased stigma from 30 to 40 points	7	46.7	0	0	
Diagnostically significant stigma > 40 points	4	26.7	0	0	
Average Stigma Score	32.2±10.4*** (15-48)		9.5±6.0 (2-27)		0.0001
Hereditary predisposition					
Asthma at Mother	0	0	4	22.2**	0.003
Asthma at Father	1	6.7	3	16.7**	0.027
Atopy in Sibs	3	20	8	44.4**	0.002
Eczema at mother	7	46.7	3	16.7	
Eczema at father	7	46.7	3	16.7	
Allergic rhinitis in mother	8	53.3	8	44.4	
Allergic rhinitis in father	4	26.7	5	27.8	
Concomitant allergopathology					
Atopic dermatitis	10	66.7	10	55.6	
Allergic rhinoconjunctivitis	15	100	16	88.9	
Pollinen disease	5	33.3	4	22.2	
Quinke's edema	0	0	3	16.7	
Urticaria	1	6.7	3	16.7	
Allergoanamnesis					
Home dust	5	33.3	10	56.6	
Library dust	2	13.3	6	33.3	
Mites Pteronissimus. farinea	2	13.3	7	38.9	
Animal allergens	5	33.3	9	50	
Citrus	4	26.7	7	38.9	
Cow's milk proteins	2	13.3	5	27.8	
Chicken egg	3	20	3	16.7	
Birch	2	13.3	1	5.6	
Wormwood	4	26.7	3	16.7	
Other herbs	5	33.3	4	22.3	

*p<0.05. **p<0.01. ***p<0.001.

was diagnosed in half of patients from both groups: more often gastroesophageal reflux disease, less often bile dyskinesia.

Visual impairment occurred in patients in both groups, myopia and, less often, accommodation spasm were found with almost the same frequency. Nephroptosis was detected in one child from the 1st group.

The analysis of cumulative pathology of internal organs in the 1st group, damage to three or more systems was noted in 20%, two systems in 40% of patients, one in 26.7%, no visceral pathology was detected in 13.3%. In the 2nd group, involvement of three systems was diagnosed in 11.1% of patients, two in 44.4%, one system in 22.2%, no pathology was detected in 22.2% (Table 3).

Conclusion. Thus, BA patients, regardless of CTD presence, often show hereditary predisposition. Patients with moderate and severe CTD on the maternal line more often had manifestations of eczema (46.7%) and allergic rhinitis (53.3%) than bronchial asthma.

Among the risk factors were the presence of animals at home and smoking parents, which is assessed as lack of compliance leading to uncontrolled asthma type. Patients with mild CTD had a low rate of breastfeeding (p = 0.03).

Most BA patients had a body weight deficit with the same frequency in the study groups (93.5% and 77.8%).

BA associated with a moderate and severe degree of CTD has been found to be characterized by a medium-severe course tendency to lower disease control, a worse prognosis.

BA patients, regardless of the presence of the severity of external signs of CTD had comorbid diseases of the musculoskeletal system, cardiovascular system, digestive organs, pathology of the visual organs, kidneys with almost the same frequency.

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Table 2

Risk factors and clinical-laboratory characteristics of BA patients, included in the research

Indicators	1st group (n = 15)		2nd group (n=18)		p
		%	Абс.	%	
Risk factors					
Accommodation in the city	11	73.7	8	44.4	
Wooden house, barrack	7	46.7	11	61.1	
Incomplete family	1	6.7	5	27.8	
Operative delivery	1	6.7	4	22.2	
Breastfeeding < 6 months	2	13.4*	11	55	0.03
Maternal smoking	2	13.3	4	22.2	
Father smoking	6	40	10	56.6**	0.01
Cat in the house	3	20	3	16.7	
Severity of bronchial asthma					
Mild	1	6.7	0	0	
Average	14	93.3	18	100	
Severe	0	0	0	0	
Level of control					
Controlled	0	0	1	5.6	
Partially controlled	3	20	8	44.4	
Uncontrolled	12	80	9	50	
Laboratory indicators					
Total IgE	341.6±188.3		379.6±202.1*		0.03
Rhinocytogram	8.3±5.7		18.8±13		
Eosinophils in the blood	8.9±3.2		8.9±2.5		

*p<0.05. **p<0.01. ***p<0.001

Table 3

Visceral signs of systemic CT involvement in BA children

Characteristics	1 group		2 group	
	Абс.	%	Абс.	%
Musculoskeletal pathology	15	100	11	55.6
Cervical spine instability	4	26.7	4	22.2
Juvenile osteochondrosis	1	6.7	0	-
Mitral valve prolapse/other MAC	8	53.3	11	61.1
Visual pathology	5	33.3	4	22.2
Reflux Disease	5	33.3	4	22.2
Abnormality of gallbladder development	1	6.7	2	11.1
Nephroptosis and/or ptoses of other organs	1	6.7	0	0

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EMOTIONAL DISORDERS IN PATIENTS WITH MOTOR NEURON DISEASES IN THE REPUBLIC SAKHA (YAKUTIA)

The article describes the study of patients with motor neuron disease and their families according to the Hospital Anxiety and Depression Scale (HADS). Motor neuron diseases (MND) are a group of neurodegenerative diseases of unknown etiology and pathogenesis, accompanied by the death of central and / or peripheral motor neurons , steady progression and inevitable death. Objective: To investigate the incidence and severity of anxiety and depression in patients with MND and their families.

Keywords: motor neuron diseases, amyotrophic lateral sclerosis, anxiety, depression, hospital anxiety and depression scale, HADS

Introduction. Motor neuron diseases (MND) are a group of neurodegenerative diseases of unknown etiology and pathogenesis, accompanied by the death of central and / or peripheral motor neurons, steady progression and inevitable death. MND in adults includes: sporadic and familial forms of amyotrophic lateral sclerosis (ALS), progressive muscle atrophy (PMA), progressive bulbar palsy (PBP), primary lateral sclerosis (PBS). Among the scientists of the world scientific community, there are different points of view on the form of diseases from the MND group: is it worth separating them or should it be considered phenotypic variants of ALS? [14,12,16]. The incidence of ALS in the world is 1.89 per 100 thousand of the population, and the prevalence is 5.2 cases per 100 thousand of the population [17]. Among ALS patients, 7% have been ill for more than 5 years. Their average life expectancy is 2.5 years with bulbar and 3.5 years with spinal ALS onset. In recent years, there has been an increase in the incidence of MND in the world. For example, the direct age-standardized incidence in 2016 in Scotland, which maintains a national registry, was 2.89 per 100 thousand population (95% CI 2.50-3.34), which was higher than in previous years ... However, researchers attribute this to improved diagnostics [10]. In Yakutia, the incidence as of 2018. was 0.5 cases per 100,000 population.

The clinical picture of the disease is manifested by the development of paresis and paralysis, atrophy of the muscles of the trunk and limbs, involuntary contractions of muscle fibers. At the onset of the disease or as it progresses, symptoms of pseudobulbar and bulbar syndromes join.

A characteristic feature of the clinical picture of ALS, in contrast to other neurodegenerative diseases, is the absence of oculomotor disorders, dementia (with the exception of some subgroups: the familial form and with the complex "parkinsonism-ALS-dementia'on the island of Guam and ALS-front-temporal dementia syndrome) [1,9], dysfunctions of the pelvic organs and the absence of bedsores, despite the fact that patients are bedridden for a long time.

The main cause of death in ALS is restrictive or restrictive obstructive respiratory failure, which develops due to paresis of the diaphragm muscles, respiratory muscles and aspiration of food and saliva in bulbar disorders. According to Hong Kong researchers, pneumonia (54.8%) and respiratory failure (40.5%) were the main causes of death in patients with MND [5].

Anxiety-depressive disorders can be attributed to the non-motor manifestations of MND. Given the steady progression of the disease and the fatal outcome, a high prevalence of depressive and anxiety disorders can be expected in patients with MND, as well as in their family members or their close associates. Published studies have described the presence of subclinical and clinical manifestations of anxiety and depressive disorders in patients with ALS. Different methods for detecting depressive disorders, together with different representativeness of patient samples used in previous studies, may partially explain the different incidence of anxiety-depressive disorders in this pathology [6].

The aim is to investigate the incidence and severity of anxiety-depressive disorders in patients with motor neuron disease and their relationship with clinical forms and the rate of progression of the disease.

Materials and methods. In our study, we used data from the personalized register of patients with MND of the Center for Neurodegenerative Diseases of the Yakutsk Scientific Center for Complex Medical Problems of the Republic of Sakha (Yakutia). Patients from 1986 were retrospectively included in the register. until now. The register has been maintained since 01.01.2006. As of 01.01.2019. the

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