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CLINICAL AND FUNCTIONAL FEATURES AND CYTOKINE PROFILE OF CHILDREN WITH CHRONIC BRONCHITIS

SHAXNOZA XABIBULLA QIZI ARIPOVA
DEPARTMENT OF PULMONOLOGY OF THE REPUBLICAN SPECIALIZED SCIENTIFIC AND PRACTICAL MEDICAL CENTER OF PEDIATRICS,
UZBEKISTAN, TASHKENT
Shahnoza0910@list.ru

FURKAT MUKHITDINOVICH SHAMSIEV
DOCTOR OF MEDICAL SCIENCES, PROFESSOR, HEAD OF THE DEPARTMENT OF PULMONOLOGY OF THE REPUBLICAN SPECIALIZED SCIENTIFIC AND PRACTICAL MEDICAL CENTER FOR PEDIATRICS,
UZBEKISTAN, TASHKENT
Sh.furkat8388@gmail.com

RANO ANVARBEKOVNA MUSAJANOVA
DOCTOR OF MEDICAL SCIENCES, LEADING RESEARCHER DEPARTMENT OF PULMONOLOGY OF THE REPUBLICAN SPECIALIZED SCIENTIFIC AND PRACTICAL MEDICAL CENTER OF PEDIATRICS,
UZBEKISTAN, TASHKENT
RANOMUSAJANOVA@MAIL.RU

NARGIS XAYRULLAEVNA MIRSALIHOVA
DOCTOR OF MEDICAL SCIENCES, HEAD OF THE DEPARTMENT OF 1-PEDIATRICS OF THE CENTER FOR DEVELOPMENT OF PROFESSIONAL QUALIFICATION OF MEDICAL WORKERS,
UZBEKISTAN, TASHKENT
NARGIS080@YANDEX.RU

ABSTRACT

The aim of the study was to study the clinical and functional features and indicators of cytokine status in children with chronic bronchitis. The analysis showed that chronic bronchitis in children develops on a burdened premorbid background, concomitant and transferred diseases. The duration of clinical symptoms was significantly longer in children with chronic bronchitis of school age. With spirography, restrictive and mixed types of bronchial patency disorders are more common in children with chronic bronchitis. In chronic bronchitis in school-age children, it is characterized by disorders of the immune system, which predetermine the need to use more effective immunomodulatory therapies in the treatment process.

KEYWORDS:chronic bronchitis, clinic, cytokine status, spirography, children

INTRODUCTION

Consideration of the problem of chronic bronchitis remains quite relevant recently, especially with the emergence of new data on the etiology, morphology, clinical course and new approaches to the therapy of this nosology [3]. Chronic bronchitis is understood as a diffuse progressive disease of the bronchial tree, which is characterized by the development of an inflammatory process in the mucous membrane, accompanied by hypersecretion of sputum, violation of the cleansing and protective function of the bronchi [6].

Despite the painstaking work of doctors and researchers around the world in the study of chronic bronchitis, the mechanisms of formation and course of these diseases, especially in childhood, are still not fully understood [1].

Progressive deterioration of pulmonary function in chronic bronchitis causes the severity of clinical symptoms, along with which there is a decrease in the quality and duration of life in this category of patients

[11]. A comprehensive study of clinical indicators in conjunction with functional features will contribute to understanding the pathophysiological changes in the respiratory system and will simplify the differential diagnosis of the disease [5,9].

The analysis and synthesis of symptoms of chronic bronchitis is of great practical importance, as it allows you to identify the most frequent and early signs of the pathological process.

The most important and most frequently performed functional diagnostic studies are - spirography. Spirography is a method that allows you to assess the patency of the respiratory tract, identify obstruction (due to lung spasm, tracheal stenosis or other causes), and determine the severity of pathological changes.

In recent years, mechanisms of intercellular interactions, especially cytokines, have been given special importance in the formation of the inflammatory bronchopulmonary process and the body's response to the introduction of a foreign agent [7]. An imbalance in cytokine production leads to the formation of a chronic inflammatory process, the early diagnosis of which is quite an urgent problem, especially in children [10]. IL-1ß is a pro-inflammatory cytokine and is directly involved in the formation of inflammatory reactions, as well as the entire complex of protective reactions of the body, i.e. acute phase response. IL-4 is involved in the activation of B-lymphocytes activated by a specific antigen. An increase in the immune status of IL-6 contributes to the development of autoimmune and inflammatory processes. Against the background of an increase in the level of leukocytes, endothelial and pathogenic cells, there is an increase in the production of IL-8 [8].

However, to date, there are practically no comprehensive clinical, functional and immunological studies for chronic bronchitis, and those few works that analyze this problem are contradictory. Therefore, there is a need to optimize the criteria for evaluating the results of modern clinical, instrumental and immunological studies of diseases at early stages.

The purpose of the study. To study the clinical and functional features and indicators of cytokine status in children with chronic bronchitis.

MATERIALS AND METHODS

The study included 54 patients with chronic bronchitis of school age who were admitted to the Department of pulmonology of the RSNPMC Pediatrics of the Ministry of Health of the Republic of Uzbekistan. 40 children with acute bronchitis were examined as a comparison group. Clinical and functional research methods were carried out.

When making the diagnosis, anamnestic data, the results of clinical and functional research methods were taken into account.

The diagnosis was made in accordance with ICD-10 and based on the classification of the main clinical forms of bronchopulmonary diseases in children, adopted at a special meeting of the XVIII National Congress on Respiratory Diseases [2].

The diagnosis of CKD was verified on the basis of comprehensive clinical and instrumental studies: a carefully collected anamnesis, clinical, laboratory and instrumental (chest X-ray, electrocardiography and spirography).

Studies of the function of external respiration (FVD) were carried out on a spirometer of the company "Medicor" (Hungary) and determined the vital capacity of the lungs (FVC), forced expiratory volume (FEV-0.5), forced expiratory volume (FTV-1.0), Tiffno coefficient (FEV1.0/FVC), maximum volume expiratory velocity (PEF), air permeability at the level of small bronchi (FEF 75%), air permeability at the level of medium bronchi (FEF-50%), air permeability at the level of large bronchi (FEF-25%).

The concentration of cytokines -IL-1ß, IL-4, IL-6 and IL-8 in blood serum was determined by enzyme immunoassay on a semi-automatic IF analyzer "Multiskan FC" (Finland) in the laboratory of Biochemistry of the Institute of RSNPMTSP of the Ministry of Health of the Republic of Uzbekistan.

Statistical processing of the obtained results was carried out by a program developed in the Microsoft Office Excel-2010 package. The methods of variational statistics were used with the calculation of arithmetic averages (M), their standard errors (m) and significant differences according to the Fisher-Student criterion.

RESULTS AND DISCUSSION

In children with chronic diseases of the lower respiratory tract, when analyzing anamnestic data, we found the burden of the pre-, peri- and postnatal periods. When analyzing the background condition in children with chronic bronchitis, the most frequent of them were identified: 94.4% had anemia of I-II degree, 53.7% of children had residual rickets, protein-energy deficiency was observed in 24.0% of children. When analyzing concomitant diseases in patients, we found that 100.0% of children had diseases of ENT organs. In 31.4% of cases, children had changes in the gastrointestinal tract. Diseases of the cardiovascular system were observed in 25.9% of children. Of the diseases suffered in children, 64.8% of children had acute respiratory infections. Most of the children had indications of previous pneumonia, 59.2% of children had pneumonia once, 44.4% of children had bronchitis. Subsequently, these children often began to get sick, they had a prolonged cough of a different nature (more than 2 weeks) with sputum separation.

The general condition was severe in 27.7% of children, moderate in 66.6% of children. Upon admission to the hospital, the main complaints of patients with CKD were cough in 100.0%, shortness of breath in 27.7%, fever in 42.5%, decreased appetite in 92.5%, lethargy in 85.1%, pallor in 92.5% of children.

The main clinical manifestations of the disease were a temperature reaction of varying degrees, which was observed in 40.7% of children with chronic bronchitis, in children with acute bronchitis – in 20.3%. Wet cough with sputum separation was observed in 79.6% of patients with chronic bronchitis. In children with acute bronchitis, the cough was mostly dry - 96.2%. Signs of hypoxia in the form of cyanosis of the nasolabial triangle were observed in 66.5% of patients with chronic bronchitis, hypoxia was observed in 9.2% of children with acute bronchitis. Dyspnea was observed in 33.3% of children with chronic bronchitis, dyspnea was not observed in the comparison group. Chest deformity was observed in 25.9% of children with chronic bronchitis. Percussion changes in the lungs were mainly local in nature in the form of a shortening of the pulmonary sound - in 92.5% of children with chronic bronchitis, in the comparison group - in 12.9%, a boxy shade of percussion sound is determined. During auscultation in 51.8% of children with chronic bronchitis, breathing over the affected area was weakened, in children with acute bronchitis, basically, breathing was hard - 100.0%. Wet multi-caliber wheezing was heard in 92.5% of children with chronic bronchitis.

X-ray examination showed an increase and deformation of the bronchopulmonary pattern, in 62.9% of children with chronic bronchitis, the process was more often localized in both lungs. Most often, the chronic process was localized in the lower lobes of the lungs, which is explained by poor ventilation and reduced drainage function of the bronchi.

Electrocardiographic studies in 31.5% of patients with CKD revealed various disorders (sinus tachycardia, signs of right ventricular hypertrophy, left ventricular hypertrophy, sinus arrhythmia, ventricular extrasystole, violation of the repolarization phase, signs of right ventricular overload), more often these changes were detected in school-age children.

The study of FVD was conducted in the morning on an empty stomach in conditions close to the main exchange. When evaluating the obtained absolute values, they were compared with the norms. The analysis of spirometric data in patients with CKD, regardless of age, revealed various violations of FVD.

The degree and form of ventilation disorders detected during the examination varied from normal indicators to significant ventilation disorders. Studies have shown (Fig.1) that in patients with CKD, FVD disorders were detected by restrictive type – in 46.3% of children, by obstructive type – in 11.1% of children, by mixed type in 33.3% of school-age children. The restrictive type of FVD disorder was more pronounced in the groups of children with CKD of the older age group.

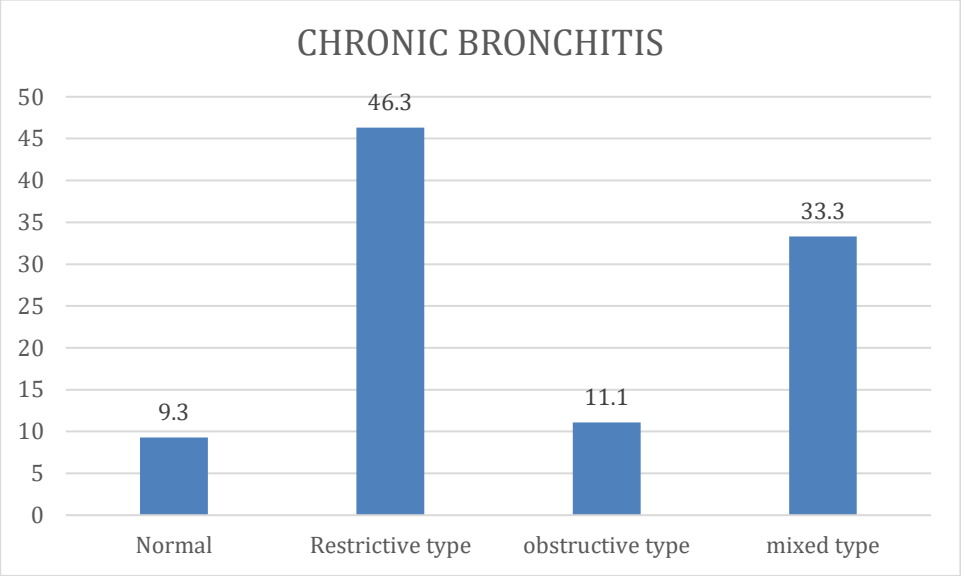

Fig.1. Spirometric parameters in patients with CKD, (%)

In chronic bronchitis, restrictive and mixed types of bronchial patency disorders are more common. The restrictive type of violation is explained by the irreversible loss of elasticity of the lung tissue in the affected areas and indirectly characterizes the severity of sclerotic processes.

Our studies and analysis of the level of IL-1ß in the blood serum of patients with chronic bronchitis allowed us to obtain interesting results (Table.1). It turned out that in children with chronic bronchitis in the acute phase of the disease, the level of IL-1ß increased by 6.8 times compared to the data of practically healthy children and averaged 189.5±10.8 pg/ml ($p<0.001$), compared to the comparison group it increased by 3.1 times (61.2±4.2 pg/ml, $p<0.001$).

Table 1.

Comparative analysis of cytokine indices in the examined children, (M=m)

Indicators	Control group (n=24) (I)	Acute bronchitis n=40 (II)	Chronic bronchitis n=172 (III)	P	P_1
IL-1β (pg/ml)	27,8±2,6	61,2±4,2	189,5±10,8	<0,01	<0,001
IL-4 (pg/ml)	4,6±0,6	7,2±0,9	18,6±1,5	<0,05	<0,001
IL-6 (pg/ml)	18,7±2,1	26,8±2,4	48,7±2,2	<0,05	<0,001
IL-8 (pg/ml)	19,2±2,4	28,6±2,6	90,2±9,8	<0,05	<0,001

Note: P - the reliability of differences between the indicators of groups I and II of patients; P1 – the reliability of differences between the indicators of groups II and III of patients.

The level of IL-4 increased 4.0 times compared to the data of children in the control group, which averaged 18.6±1.5 pg/ml ($p<0.001$), compared to the comparison group, this indicator increased 3.0 times ($p<0.001$). In patients with chronic bronchitis, the level of IL-6 increased 2.6 times compared to the data of practically healthy children, which averaged 48.7±2.2 pg/ml ($p<0.001$), compared to the comparison group, the indicator increased 1.8 times ($p<0.001$).

IL-8 acts as an inducer of an acute inflammatory reaction, stimulates the adhesive properties of neutrophils. When individually analyzing the content of IL-8 in children with chronic bronchitis, we noted its

increase by 5.0 times compared to the data of children in the control group, which averaged 90.2±9.8 pg/ml ($p<0.001$), in relation to the comparison group, the indicator increased by 4.0 times ($p<0.001$).

Thus, the development of a chronic inflammatory process in the lungs is accompanied by a significant production of cytokines, which indicates a high antigenic stimulation of producing cells. The established violations of cytokine homeostasis confirm the existing position on the role of the cytokine system in the pathogenesis of chronic bronchitis in children and its progression, which predetermine the need to use more effective immunomodulatory agents in the treatment process.

CONCLUSION

1. Chronic bronchitis in children develops on a burdened premorbid background, concomitant and transferred diseases, which can lead to the functional failure of the immune system, contributing to the unfavorable course of the disease.

2. For patients with chronic bronchitis, the degree of bronchial patency disorders is an objective criterion of the severity of the patient's condition and the progression of the underlying disease. Regardless of the nature of lung pathology, the degree of bronchial patency disorders is an objective criterion for the severity of the patient's condition.

3. Patients with chronic bronchitis are characterized by an imbalance of pro-inflammatory cytokines, which determines the need to use more effective immunomodulatory therapies in the treatment process.

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