

DIAGNOSTIC VALUE OF IMMUNOLOGICAL MARKERS IN BRONCHIAL ASTHMA IN CHILDREN

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ABSTRACT

The aim of the study was to study the features of the cytokine profile in patients with bronchial asthma. Immunological research methods were used. In the process of a comprehensive clinical and functional examination of children. Studies have shown that with bronchial asthma in children, hyperproduction of pro- and anti-inflammatory cytokines IL -8, IL -4, and TNF α and a decrease in IFN γ production are determined, contributing to the aggravation of immunodeficiency and possibly the development or aggravation of the course of the disease, dictating the need for immunoprotective therapy.

KEYWORDS: children, bronchial asthma, immunology, cytokines.

INTRODUCTION

Bronchial asthma today is one of the most pressing problems among respiratory diseases. According to the World Health Organization, about 235 million people worldwide suffer from bronchial asthma. Bronchial asthma in children is included in the group of the most frequent chronic diseases with high medical and social significance [1].

Bronchial asthma can develop at any age, but in most cases the first symptoms occur in childhood [5,9]. Despite the successes achieved in the study of the pathogenesis of bronchial asthma, many stages of the formation and modification of the course of this disease are currently not entirely clear.

The theory is generally accepted, according to which atopic diseases are caused by a violation of regulation in the immune system,

associated with the activation of allergen-specific Th2-type clones [4,8]. The functional activity of Th2 is associated with the cytokines secreted by them, mainly with IL-4, IL-5, IL-10, IL-13. Determination of the concentration of cytokines in the blood and other body fluids has a prognostic value. To assess the severity of the disease and predict its course, the concentration of pro- and anti-inflammatory cytokines in the dynamics of the development of the disease is determined [2,3].

One of the main biological properties of IL-4 is its ability to activate the proliferation and functional activity of B-lymphocytes. IL-4 stimulates the production of certain types of antibody - reagents by activated B-lymphocytes. Tumor necrosis factor- α (TNF α) performs a number of important functions during the initiation of inflammation, and also plays a role in the chronization of the inflammatory process, by increasing the adhesion of macrophages. A number of studies have found correlations of TNF α levels with the severity of symptoms of atopic bronchial asthma [4,7]. Many patients with bronchial asthma have decreased and/or delayed response of innate antiviral immunity with deficiency and delayed responses associated with lung interferons IFN- α , IFN- β and IFN- λ [6].

The lack of adequate treatment of bronchial asthma in childhood leads to the progression of the disease over the years. Of course, there is a need for further study of the features of the cytokine profile, aimed at identifying markers of persistent inflammation of the respiratory tract in bronchial asthma, in order to improve methods of diagnosis, treatment and prevention.

The purpose of the study. To study the features of the cytokine profile in patients with bronchial asthma.

MATERIALS AND METHODS

In order to study the features of the cytokine profile, we observed 50 patients with bronchial asthma aged 6 to 15 years who were admitted to the Department of pulmonology and allergology of the RSNPMC Pediatrics of the Ministry of Health of the Republic of Uzbekistan. The comparison group consisted of 30 children with recurrent obstructive bronchitis. The control group consisted of 20 practically healthy children of the same age.

When making a diagnosis of bronchial asthma, the classification adopted by the National Program "Bronchial Asthma in children" was used. Treatment strategy and Prevention", in Russia in 2006, which was supplemented in 2018 by the GINA program. The basis for the diagnosis were: complaints, anamnesis data, results of general clinical, functional and immunological research methods.

Immunological studies were conducted at the Institute of Human Immunology and Genomics of the Academy of Sciences of the Republic of Uzbekistan. The concentration of cytokines: IL-4, IL-8, TNF- α and IFN γ was determined by enzyme immunoassay using reagent kits manufactured by Cytokine LLC (Russia).

The results of the conducted studies were processed on an IBM PC using the EXCEL 5.0 and Statistica for Windows 5.0 application software package using generally accepted statistical methods, the significance of differences in average values was determined using the Student's criterion (t), differences in the variance of samples of random variables according to the Fischer criterion were evaluated.

The results of the study and their discussion. Analysis of anamnestic data showed that of the concomitant and transferred diseases in patients with bronchial asthma, 90.0% of the examined patients had diseases of ENT organs; 68.0% of patients had pollinosis; 18.0% of patients had food allergies. Drug allergy was registered in 4.0% of patients with bronchial asthma. According to X-ray studies of the respiratory organs in 60.0% of patients, emphysematous lung enlargement was observed on both sides with horizontal ribs, pronounced vascular pattern (50.0%). Infiltrative changes in the roots of the lungs with a violation of their X-ray morphological structure were detected in 100.0% of patients.

RESULTS AND DISCUSSION

The results of the analysis of indicators of the function of external respiration according to spirometry data in patients with bronchial asthma recorded a violation of bronchial patency. With exacerbation in children, the obstructive type of respiratory dysfunction was significantly more common – in 72.0% of children.

A study of the results of the cytokine profile data analysis is presented in Figure 1. As can be seen from the figure, we found that in children with bronchial asthma in the phase of exacerbation of the disease, the IL-4 production index was increased to 26.7 ± 1.4 pg/ml, exceeding the norm by 5.8 times ($p < 0.001$). In patients with recurrent obstructive bronchitis (comparison group), the IL-4 production index was significantly increased to 21.3 ± 0.3 pg/ml, which was 4.6 times higher than the norm.

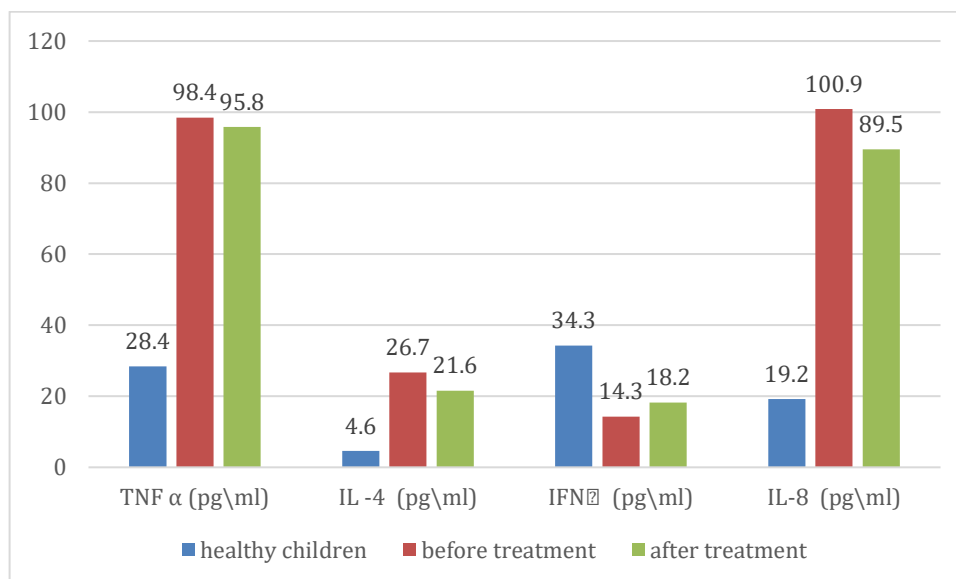


Fig.1. Cytokine content in the examined children, (M±m)

There is a regular increase in the anti-inflammatory cytokine IL-4 in all the examined groups, but it is more pronounced in bronchial asthma. IL-8 is a powerful inflammatory mediator belonging to the chemokine group. This cytokine is an important mediator of the inflammatory process in the lungs. In patients with recurrent obstructive bronchitis, the IL-8 production index was significantly increased to 89.5 ± 3.9 pg/ml, which was 4.7 times higher than the norm. In patients with bronchial asthma, the IL-8 production index was increased to 100.9 ± 7.7 pg/ml ($p < 0.01$). There is a regular increase in the anti-inflammatory cytokine IL-8 in all the examined groups, but it is more pronounced in bronchial asthma, exceeding the norm by 5.3 times.

Shortly after the first cycles of reproduction of the pathogen in cells, the expression of a large family of interferon genes is activated, accompanied by the appearance in the blood of both serum interferon and leukocytes activated for interferon production. Our studies on the level of interferon - γ in the examined patients showed a deep deficiency in their content.

Thus, in children with recurrent obstructive bronchitis, the serum IFN γ level averaged 21.4 ± 1.7 pg/ml and in bronchial asthma – 14.3 ± 1.9 pg/ml, respectively, which is 1.6-2.4 times lower than the values of practically healthy children ($p < 0.01$). A more significant increase was determined in patients with bronchial asthma. Violation of IFN γ production, which plays an important role in maintaining homeostasis, is characteristic of the examined patients.

The reduced production of IFN γ leads, apparently, to a long-term recurrent course of the disease. The increase in IL-4 concentration established in our study with persistently reduced levels of IFN γ determines the predominance of Th2-type immune response, which may indirectly indicate immunopathological shifts that determine inadequate differentiation of T-helper cells and the development of immunosuppression. Such suppression of IFN γ with a high content of proinflammatory cytokines initiates a polyclonal reaction of T-lymphocytes, then hyperproduction of cytokines and apoptosis.

TNF α is known to be a pluripotent cytokine, which is mainly produced by monocytes and macrophages and performs the most important functions. During the start of inflammation, it activates the endothelium, increases the expression of adhesion molecules on endothelial cells and promotes the adhesion of leukocytes to the endothelium, activates leukocytes (granulocytes, monocytes, lymphocytes), induces the production of other pro-inflammatory cytokines having a synergistic effect with TNF α .

In our studies, the TNF α level was more significantly increased by 3.5 times in children with bronchial asthma compared to children of the control group ($p < 0.001$). In patients with recurrent OB - 62.7 ± 3.2 pg/ml versus 28.4 ± 1.5 pg/ml in the control ($p < 0.001$), which reflects the increased activity of macrophages involved in maintaining the inflammatory process.

The dynamics of cytokine production after basic treatment are presented in Fig.2.

Analysis of the data obtained when studying the concentration of cytokines showed that during the basic treatment of children with bronchial asthma, there was a decrease in elevated levels of IL-8, IL-4 and TNF α , but these indicators remained higher than the baseline values. IFN γ production after therapy was 18.2 \pm 2.3% in bronchial asthma versus 14.3 \pm 1.9%.

Thus, the data obtained indicate an increase in the serum content of sick children with bronchial asthma, accompanied by pronounced changes in intercellular immune mechanisms, which are manifested by a violation of cytokine production, which determines the course of the disease.

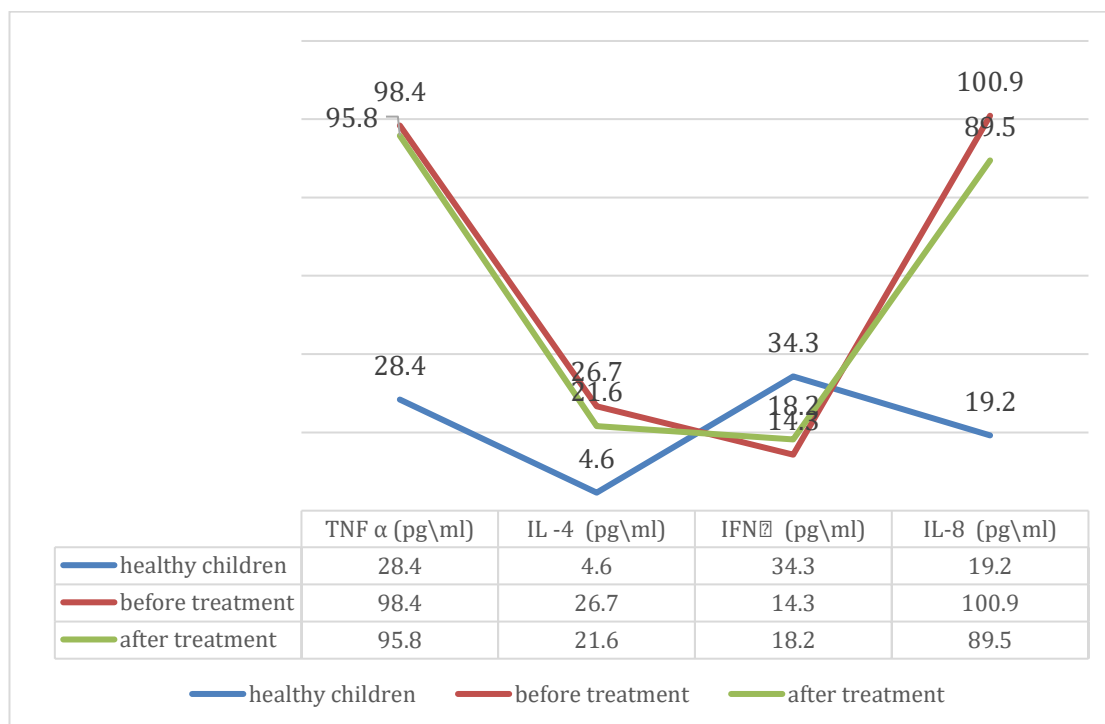


Fig.2. Dynamics of cytokine status in children with AD, (M \pm m)

Hyperproduction of cytokines indicates serious violations in the work of all parts of the immune system, suppression of nonspecific protection and specific immunity, negatively affecting the course of the underlying disease, requiring appropriate correction.

CONCLUSION

1. With bronchial asthma in children, hyperproduction of pro- and anti-inflammatory cytokines IL-8, IL-4, TNF α and a decrease in IFN γ production are determined, which are a diagnostic marker of an inflammatory reaction in hypoxia.
2. The studies carried out in dynamics after basic therapy, the cytokine profile indicators did not recover, in some cases even decreased from the initial value during the year, which contributes to the aggravation of immunodeficiency and possibly to the development or aggravation of the course of complications, which dictates the need for immunocorrective therapy.

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