

CYTOKINE PROFILE INDICATORS IN SCHOOL AGE CHILDREN WITH RESPIRATORY ALLERGOSES**TURAKULOVA XILOLA ERKINOVNA**

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Introduction

Currently, along with the widespread prevalence of allergies, there is an increase in the number of patients with severe allergic diseases, as well as patients resistant to standard therapy. Changes in the clinical manifestations of allergies, underdiagnosis of a number of nosological forms, and an increase in financial costs for providing adequate medical care are also observed.

Special attention of researchers is focused on the problem of immunological disorders in children with allergic diseases. This is confirmed by the dynamic growth in the number of publications devoted to this topic.

Studies in the field of clinical allergology involve mandatory evaluation of laboratory data in children with allergic diseases, including determination of hypersensitivity to specific allergens. External factors may also influence the prevalence of allergic diseases.

Cytokines are peptide signaling molecules involved in bioregulation, chemoregulation, and immunoregulation. As is known, cytokines include interferons (IFN), colony-stimulating factors, interleukins, chemokines, transforming growth factors, tumor necrosis factor, and others. They are produced by lymphocytes, monocytes, granulocytes, mast cells, endothelial cells, and fibroblasts. Cytokines are produced in very small concentrations (5–10 ng per cell). In essence, they are mediators of intercellular interaction and form a system of initiating, amplifying, and suppressive signals that lead to the formation and integration of physiological and pathological reactions of the body to antigenic exposure, microbial invasion, inflammation, tissue damage, tumor development, and stress. Different cytokines can influence the same target cells, and their effects often overlap.

Interleukin (IL)-1 (endogenous pyrogen, lymphocyte-activating factor) with a molecular weight of 17.5 kDa is produced mainly by activated macrophages and sometimes by epithelial, endothelial, glial cells, fibroblasts, and keratinocytes. Two forms of IL-1 are known—alpha and beta. They are encoded by different genes. An increase in the level of IL-1 β in blood serum is an extremely important indicator in diseases based on inflammatory processes. During exacerbation of bronchial asthma and other allergic reactions, production of IL-1 β by peripheral blood mononuclear cells increases. In various infectious diseases, the severity of the process correlates with the level of IL-1 β production.

IL-4 (B-cell stimulating factor) is produced by activated type 2 T-helper cells. Its main function is to switch immunoglobulin (Ig) synthesis from IgG1 to IgG4 and IgE [13]. In addition to its direct effect on IgE production, IL-4 enhances the Th2 response by modulating T-cell differentiation, promotes proliferation of tissue basophils, and increases proliferation of B-lymphocytes. IL-4 is an antagonist of IFN-gamma and inhibits the production of pro-inflammatory mediators such as tumor necrosis factor-alpha, IL-1, and IL-12, as well as the cytotoxic activity of T-lymphocytes and macrophages.

It has been shown that the level of IL-4 in the blood of children with allergic diseases correlates with clinical manifestations and IgE levels .

IL-8 belongs to the chemokine family and is produced by monocytes, lymphocytes, and granulocytes. The main function of IL-8 is activation of neutrophils, enhancement of chemotaxis, and increased expression of adhesion molecules. In addition, IL-8 enhances exocytosis of lysosomal enzymes and increases the expression of complement receptors .

Particular attention is paid to the study of IFN-alpha, since disturbances in its production lead to the development of recurrent viral infections. Increased levels of IFN in blood serum are accompanied by clinical symptoms of chronic viral infection. During the study of serum, spontaneous and induced in vitro production of IFN-alpha is not always detected, which indicates the most severe degree of impairment of antiviral defense of the body .

KEYWORDS: respiratory allergoses, immunity, cytokines, interleukins.

Materials and Methods

The research work was carried out in the **Laboratory of Pediatric Pathology of the Institute of Biomedical Research of the Vladikavkaz Scientific Center of the Russian Academy of Sciences** and in the **Pulmonology Department of the Republican Children's Clinical Hospital of the Ministry of Health of the Republic of North Ossetia–Alania**.

The study included **70 children with respiratory allergic diseases** who received inpatient treatment at the Republican Children's Clinical Hospital and **22 practically healthy children**.

The aim of the study was to determine the clinical and diagnostic significance of a comprehensive assessment of clinical, laboratory, and immunological parameters and to evaluate local and systemic immunity in children with respiratory allergic diseases.

Statistical data processing was performed using the **Statistica software package** with the **Student's t-test**. The levels of **IL-1 β , IL-4, IL-8, and IFN-alpha** in blood serum were determined using the **enzyme-linked immunosorbent assay (ELISA)** according to the standard method.

General clinical research methods were used, and medical documentation was analyzed.

Цитокины	Группа больных детей (n = 70)	Группа здоровых детей (n = 22)
ИЛ-8	9,89 ± 0,88 p < 0,05	4,36 ± 0,78
ИФН-альфа	7,2 ± 0,45 p < 0,05	10,25 ± 1,27
ИЛ-1-бета	8,75 ± 0,76 p < 0,05	2,24 ± 0,47
ИЛ-4	3,19 ± 0,3 p < 0,05	0,73 ± 0,35

Примечание. p – достоверность различий показателей по отношению к группе здоровых детей.

Results and Discussion

According to the medical history data, in **62% of cases** relatives of the children suffered from allergic diseases, which indicated a predisposition to the development of respiratory allergic diseases in children from families with allergic pathology.

The main diagnosis of **obstructive bronchitis** was established in **65%** of cases, and **bronchial asthma** in **35%** of cases. Concomitant pathology was also present. Thus, **allergic rhinitis** was detected in **35%** of patients, **atopic dermatitis** in **10%**, and **allergic conjunctivitis** in **1%** of patients.

Evaluation and comparative analysis were carried out between the groups of sick and healthy children. Immunological parameters of healthy children were taken from previous studies.

Assessment of cytokine levels revealed a significant (**p < 0.05**) increase in the levels of **IL-8, IL-1β, and IL-4**, and a decrease in the level of **IFN-alpha** in the group of sick children. Comparative data are presented in the table.

Analysis of the content of pro-inflammatory cytokines in the blood serum of sick children demonstrated a significant increase in the levels of **IL-8 and IL-1β**. A significant decrease in IFN-alpha and a significant increase in IL-4 in the serum of children with respiratory allergic diseases indicated suppression of cellular defense mechanisms and activation of differentiation of **CD4-lymphocytes toward the Th2 pathway**, activation of **B-lymphocytes**, and switching of immunoglobulin synthesis toward **IgE production**.

Thus, impaired immune reactivity, pathological reactions in nonspecific defense mechanisms, and decreased local and systemic immunity in children with respiratory allergic diseases necessitate the introduction of additional treatment methods in pediatric practice.

Conclusion

To improve cytokine profile indicators, it is necessary to use additional correction methods in the treatment of respiratory allergic diseases in children. A comprehensive treatment regimen should include **immunocorrection and evaluation of the effectiveness of therapy**.

References

1. Shamsiev A.M., Yusupov Sh.A., Yuldashev B.A., Mukhamadieva L.A. Immune status in children with chronic bronchitis. *Pediatric Bulletin of the Southern Urals*. 2017;(1):84–89.
2. Vitrishchak S.V., Savina E.L., Zhuk S.V., Klimenko A.K. Influence of industrial pollutants on the immune and metabolic status of healthy children aged 12–14 years living in different industrial zones of the Luhansk region. *Actual Infectology*. 2016;3(12):66–73.
3. Popovich Yu.G. Secondary immunodeficiency in children with heavy metal imbalance. *Pediatrics and Pediatric Surgery*. 2014;2(76):27–31.
4. Popovich Yu.G. Immune status of children with increased sensitization to metal allergens. *Bulletin of the Kyrgyz-Russian Slavic University*. 2014;14(12):117–121.
5. Makieieva N., Malakhova V. Clinical significance of phospholipid levels in exhaled breath condensate in children with wheezing. *Modern Pediatrics*. 2018;4(92):22–26.
6. Umarova Z.K., Mamadzhanova G.S., Rakhimova U.Kh., et al. Experience of vaccination of children with allergic dermatoses in different periods of the disease. *Bulletin of the Pedagogical University*. 2014;5(60):175–179.
7. Saidov M.Z., Amirova P.Yu., Elkun G.B., Jamalutdinov Yu.A. Immunohistochemical indicators of local immunity in frequently ill children. *Immunology*. 2006;27(2):108–112.
8. Ruselevich M.V. The medical and social problem of respiratory allergic diseases in a large city. *Social Aspects of Population Health*. 2018;60(2):5.
9. Vivchar I.S., Zaletsky N.P. Correlation relationships between indicators of immune and cytokine status in children and adolescents with pulmonary tuberculosis. *Modern Problems of Science and Education*. 2013;(6):601.
10. Ruselevich M.V., Malikova L.M., Komarov S.G., Kharina D.V. Medical and social factors in the formation of pollen-induced respiratory allergic diseases in children. *Social Aspects of Population Health*. 2018;59(1):9.
11. Zhernosek V.F., Dyubkova T.P., Sokolov D.V. Interferon preparations in medical practice. *Treatment and Prevention*. 2016;1(17):39–44.
12. Simbirtsev A.S. Cytokines – a new system regulating protective reactions of the body. *Cytokines and Inflammation*. 2002;1(1):9–16.
13. Bacharier L.B., Geha R.S. Molecular mechanisms of IgE regulation. *Journal of Allergy and Clinical Immunology*. 2000;105(2 Pt 2):S547–S558.
14. Namazova L.S., Revyakina V.A., Balabolkin I.I. The role of cytokines in the formation of allergic reactions in children. *Pediatrics*. 2000;(1):56–65.
15. Drannik G.N. *Clinical Immunology and Allergology*. Moscow: Medical Information Agency; 2003.