



Features of The Immune Status in Children with Bronchopulmonary Pathologies of The Khorezm Region

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ABSTRACT

The high risk of morbidity in children of all age categories of the Khorezm region also depends on biomedical factors such as nutrition, socio-economic conditions and quality of life. The incidence of bronchopulmonary pathology was 95 children (60%) with acute and recurrent obstructive bronchitis -55 (40%) with community-acquired pneumonia. Some parameters of the immune status were determined - cytokines: interleukin - 1 β (IL-1 β), 8(IL-8), tumor necrosis factor - α (TNF- α). The analysis of the study showed concomitant pathologies from the Central nervous system - PPCNS - 28%, Allergopathology - 46.5% (food allergy, atopic dermatitis, pollinosis), Anemia 56.8%, ENT pathology (otitis, rhinopharyngitis) -44.2%. In preschool children of the Aral Sea region, cytokine status in bronchopulmonary diseases and the influence of concomitant pathology contributes to the severity of the underlying pathology. The high content of interleukins IL-1 β , IL-8, as well as TNF- α is a prognostic unfavorable mediator of inflammation in the dynamics of the disease. A high increase in bronchopulmonary diseases among preschool children is associated with DDU visits, frequent acute respiratory infections and acute respiratory infections, which leads to a decrease in the body's resistance and changes in cytokine status.

Key words: bronchopulmonary pathology, otitis, rhinopharyngitis, respiratory infections, cytokines TNF α , IL-1 β , IL-8, pneumonia

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INTRODUCTION

In the Aral Sea region, due to the drying up of the Aral Sea, the pathology of respiratory diseases is growing steadily and remains one of the urgent problems of modern pediatrics, determining the high level of child morbidity, infant mortality, as well as disability in adolescence [1]. It is worth noting that an important role in the genesis of diseases under the influence of adverse factors is given a special place to risk factors that can be crucial in the prognosis of the pathological process and the prevention of progressive pathology (Baranov A.A., 2005; Samsygina G.A., 2010). Currently, foreign studies conducted in various countries of the world have shown the impact of climate resource changes on the prevalence of a number of diseases [3-5]. The study of the prevalence of acute and chronic respiratory diseases of allergic and infectious-inflammatory nature in children and adolescents does not lose its relevance in this region [1,3,5].

The high risk of morbidity in children of all age categories of the Khorezm region also depends on biomedical factors such as nutrition, socio-economic conditions and quality of life.

The immunological characteristics of the children of the Aral Sea region require constant study of the immune status, since the influence of negative factors contributes to the development of immune shifts and ecopathologies of this region. A violation in the immune system contributes to the development of allergic diseases, infectious and inflammatory complications and the layering of viral infections, which leads to frequent combined pathologies that aggravates the recovery process and further worsens the prognosis of the disease [3,5,12]. To date, the problem of research devoted to the study of the parameters of the immune response in children of all ages is relevant [1,4,9].

In immune reactions, the main regulatory work is performed by cytokines - mediators of intercellular interaction. Cytokines - interleukin -IL-1 α and IL-1 β is a lymphocyte-activating factor produced mainly by activated macrophages, in turn, an increase in the level of IL-1 β in blood serum is an important indicator of allergic diseases [13-14]. Interleukin IL-4 B-cell stimulating factor is produced by activated type 2 T-helper cells. Its main function is to switch the synthesis of immunoglobulin (Ig) G1 to the synthesis of IgG4 and IdE [9-13]. IL-8 belongs to the family of chemokines, is produced by monocytes, lymphocytes, granulocytes.

The main function of IL-8 is neutrophil activation, enhanced chemotaxis, increased expression of adhesive molecules. In addition, IL-8 enhances the exocytosis of lysosomal enzymes and increases the expression of complement receptors. Proinflammatory cytokines are produced and act on immunocompetent cells, initiating an inflammatory response [7,12]. In many studies, the authors show that a high level of cytokines, primarily pro-inflammatory, is a reflection of the activity and severity of the pathological process [2,7-12]. 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 adhesion of leukocytes to the endothelium, activates leukocytes (granulocytes, monocytes, lymphocytes), induces the production of other pro-inflammatory cytokines with synergistic action with TNF α : IL-1, IL-6, IL-8, IFN- β , GM-CSF [6,8]. IL-8 is synthesized mainly by monocytes, macrophages and neutrophils.

The most important biological function of TNF α cytokine is the highest chemoattractant activity selective for neutrophils. IL-4 enhances the adhesion of neutrophils to the endothelium and their degranulation (exocytosis), initiates a respiratory explosion, causes massive infiltration of tissues by neutrophils [2,5,11]. Thus, the level of TNF α and IL-4 can indirectly judge the activity of the inflammatory process as a whole.

MATERIAL AND METHODS

We conducted a survey and analysis of 150 children with various respiratory diseases aged 3-7 years in the Khorezm region. All children were observed and examined in standardized clinical conditions. The children were divided into groups of nosological pathology structure: group I – children with acute and recurrent obstructive bronchitis n=95; group II – with community-acquired pneumonia n=55 children, of which boys accounted for 90 (60%) children and girls - 60 (40%) children, which corresponded to the literature data. The concentration of cytokines was studied: interleukin - 1 β (IL-1 β), 8(IL-8), tumor necrosis factor - α (TNF- α) was determined by enzyme immunoassay using reagent kits manufactured by Cytokine LLC (St. Petersburg Research Institute of Especially Pure Biological Products) in the immunomorphology group of the Institute of Immunology of ANRUz (Head of the gr. – Professor D.A. Musakhodzhayeva, MD.). Statistical processing of the obtained results was carried out using statistical software for statistical data processing Statistica® version 6.0. The reliability of the differences between the compared groups was assessed according to the Student's criteria. The differences of the compared values were recognized as statistically significant at $p < 0.05$.

RESULTS AND DISCUSSIONS

According to the study of morbidity in age groups in preschool children, pneumonia occurred in patients aged 3 years 46.4%, in 4 years 21.6%, in 5 years -12.5%, in 6 years 6.1% and in 7 years -13.4%, pneumonia was more common in children 3 years. Obstructive bronchitis occurred in children aged 3 years – 26.1%, in 4 years -28.9%, in 5 years -36.5%, 6 years -8.5%. At the age of 5, the incidence of obstructive bronchitis was higher than in other groups, this may be the course of bronchial asthma under the mask of obstructive bronchitis. Our research results showed that in children of group 1, concomitant pathologies from the Central nervous system – PCNS - 28%, Allergopathology – 46.5% (food allergy, atopic dermatitis, pollinosis), Anemia 56.8%, ENT pathology (otitis, rhinopharyngitis) -44.2%. In group II children, concomitant pathologies, Allergopathologies–26.5% (food allergy, atopic dermatitis, pollinosis), Functional disorders of the gastrointestinal tract -29.5%, ENT pathologies (otitis, rhinopharyngitis)-32%, Anemia-45%. The dynamics of assessing the clinical picture of acute obstructive bronchitis in preschool age was manifested by the main complaints; prolonged symptoms of intoxication (fever, weakness, refusal of food, emotional apathy) at admission, the temperature in children 3-4 years old was $t=38.5-39^{\circ}\text{C}$ in 100% of patients, in children 5-7 years old $t=37.5-38.0^{\circ}$ 56.5%, and the rest of the children - 43.5% - had a stable temperature. The incidence of catarrhal symptoms was in 100% of children (difficulty in nasal breathing, runny nose, cough). Cough with sputum secretion was 100% in all children at admission in both of their groups. Taking into account the age category in children 5-7 years of age, a prolonged wet cough of more than 4 weeks was observed in group 1 -78.5%, and in children of group 2 from the same category of children, 35.6% also had a protracted nature. In an objective study, dyspnea was observed in all children in both groups, of which a mixed form was found in children aged 3-4 years, 30.5%, expiratory dyspnea-47.5%, inspiratory dyspnea - 22%. Inflating of the wings of the nose and the participation of auxiliary muscles was observed in children aged 3-4 years 24.6%, rapid breathing in children 79.3% in both groups. Signs of respiratory insufficiency of 1-2 degrees were observed in 88.7%, and 3-4 degrees were not observed. In 65.5% of children during auscultation, wet wheezes of various calibers were heard against the background of hard breathing, and in other cases dry whistling wheezes were heard in the main group of 35.5% of children.

The cytokine status in bronchopulmonary diseases has not been sufficiently studied in preschool children of the Aral Sea region. Cytokines-interleukins are drawn into the infectious-inflammatory process at the level of their own immune reactions of the link, which contribute to the sequential mechanism of the chain reaction. The infectious-inflammatory process is accompanied by a violation of microcirculation in tissues and leads to their hypoxia, simultaneously to alveolar and interstitial edema, disrupting the metabolic functions of organs and systems, which determines the severity and outcome of the pathological process. According to the data of the immunological study, it was found that in children of group I – 56.8%, the proinflammatory interleukin IL-1 β in the blood was spontaneously produced significantly more than in children from group 2 -25.0% (88.2 \pm 5.1 pg/ml versus 62.5 \pm 2.3pg/ml; $p < 0.001$) (Table No. 1). Hyperactivation correlates with a violation of vascular endothelial thrombosis and this contributes to the procoagulant activity of IL-1 β , which is determined by the ability of the cytokine to enhance the work of tissue factors and reduce platelet expression [2,9,10], which leads to impaired hypoxia and lack of tissue energy supply and further necrotic and apoptotic inflammation processes. The level of interleukin IL-8 in children of group 1, 26.8%, was slightly higher (40.6 \pm 2.0 pg/ml vs. 12.5 \pm 0.6 pg/ml, ($p < 0.001$)) than in children of group 2 -55.8%, a significant increase in the level of IL-8 indicates a bacterial inflammatory process, which is confirmed by literature data. A similar trend is observed when studying the level of TNF- α , $p > 0,001$.

Table-1: Cytokine status of children with bronchopulmonary pathology, M \pm m

Indicator	I group	II group
IL-1 β , pg/ml	88,2 \pm 5,1***	62,5 \pm 2,3**
IL-8, pg/ml	12,7 \pm 0,6**	40,6 \pm 2,0*
TNF α , pg/ml	30,2 \pm 1,1***	33,8 \pm 2,2*

Note: *reliable in relation to the control group – $p < 0,05-0,001$.

Interleukin IL-8, like TNF- α , belongs to proinflammatory cytokines, activates the effect on neutrophils and participates in the intensification of phagocyte migration at the site of the introduction of a foreign microorganism [2,11]. The analysis showed that the high content of IL-1 β in the blood reflects the long-term persistence of infectious pathogens in recurrent respiratory diseases and the allergic process, and IL-8 mainly reflects the course and outcome of pneumonia. A high content of interleukins leads to a restriction of the function of normal neutrophils and secondary phagocytic dysfunction. The analysis showed that the high content of IL-1 β in the blood reflects the long-term persistence of infectious pathogens in recurrent respiratory diseases and the allergic process, and IL-8 mainly reflects the course and outcome of pneumonia. A high content of interleukins leads to a restriction of the function of normal neutrophils and secondary phagocytic dysfunction. The obtained results allowed us to confirm that an important pathogenetic link of the unfavorable course and prognosis in pneumonia is the early hyperactivation of IL-8 cytokine production. Hyperactivation of induced sputum cells, destruction due to increased TNF- α levels, and secondary cell-type dysfunction is formed.

CONCLUSION

It has been shown that the high content of interleukins IL-1 β , IL-8, as well as TNF- α is a prognostic unfavorable mediator of inflammation in the dynamics of the disease. A high increase in bronchopulmonary diseases among preschool children is associated with DDU visits, frequent acute respiratory infections and acute respiratory infections, which leads to a decrease in the body's resistance and changes in cytokine status.

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