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LEVELS OF CYTOKINES IN CHILDREN OF PRESCHOOL AGE WITH CHRONIC RHINOSINUSITIS

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ABSTRACT

Among the ENT diseases, rhinosinusitis is 29-46%, which is mainly recorded in frequently ill children. From the 180 examined children aged 4-7 years, 120 have been frequently and chronically ill. There were 60 rarely ill children in the control group. Determination of the concentration of cytokines (IL-1ß, IL-4 and TNFα) in blood serum and nasal swabs showed imbalance depending on the stage of the disease.

KEYWORDS: frequently ill children, immunity, cytokines.

INTRODUCTION

The frequency of inflammatory diseases of the nose and paranasal sinuses takes one of the leading places in the structure of ENT diseases, particularly among young people. Thus, according to Russian authors, among patients of ENT clinics, large hospitals the proportion of patients with rhinosinusitis reaches to 29-46%.[1,2,3] It should be noted the high level of this pathology in childhood, mostly recorded in frequently ill children (FIC) and its peak in the first 5 years of life.

According to different authors, FIC are from 20% to 65%[6,7] of children population. Up to 67% of the FIC have the pathology of upper respiratory tract, and 74.3% in its structure accounts for sinusitis (Elagina I.E., 2004). In FIC marked deviation of morpho-functional parameters, forms the prerequisites for the disruption of adaptation and the development of chronic disease. Foci of inflammation of the nose and sinuses are a source of infectious sensitization, especially of the bronchi and lungs, become a cause of pathological reflex impulses, provide severe septic complications, up to lethal.[9,10]

The role of cytokines in acute and self-sustaining a chronic inflammatory process in the mucosa of the upper respiratory tract is evident.[4,5] The manifestation of aggression by infectious agent is only possible on the condition that it would be able to overcome the first supraepithelial level of protection submitted, mainly by non-specific mechanisms of the immune system.

Later comes the activation of the following levels of protection. Thus epithelial cells may cause, spread and modulate inflammation, generating proinflammatory cytokines (IL-6, IL-8, TNFα).[8] The cascade of activation of specific immune response begins with macrophages. The activated macrophages release proinflammatory cytokines (IL-1β, IL-6, IL-8, TNFα), which play an important role in the activation and migration of monocytes, neutrophils, eosinophils, and others into the inflammatory center.[8] The activated vascular endothelium contributes to changing the properties of leukocytes and their adjacency to the vessel wall and migration through the vessel wall into the nidus of inflammation.[2]

In connection with the above, the **purpose of the present study** was to evaluate systemic and local levels of cytokines in children with chronic rhinosinusitis.

MATERIALS AND METHODS

There were 180 children aged from 4 to 7 years who were under the of a dynamic supervision for the year in the clinic of the Tashkent pediatric medical Institute, which included clinical examination, a conversation with the parents, the study of child development card (F 112 / u). Clinical and laboratory examination included a study of ENT organs, blood tests, to determine the concentration of cytokines in peripheral blood and nasal swabs, as well as instrumental methods of study of the paranasal sinuses.

There were 98 (54.5%) boys and 82 (45.5%) girls among the examined children. Depending on the frequency of the incidence the children were divided into 2 groups: 120 frequently ill children (FIC), the main group and 60 rarely ill children (RIC) were the group comparison.

Immunological studies were performed at the Institute of Immunology of the Academy of Sciences of Uzbekistan

and included the determination of levels of (IL-1β, IL-4 and TNFα), IgE and SIgA cytokines in blood serum and nasal swabs, which were determined by ELISA ("Cytokine", St. Petersburg). The statistical analysis of the data was performed by the method of variation statistics of Fischer-Student's.

RESULTS AND DISCUSSION

Analysis of the incidence of upper respiratory tract structure in the examined children indicated that chronic rhinosinusitis was observed in 104 (86.6%) of frequently ill children, and in 23 (38.3%) rarely ill children (Table.1). The curvature of the nasal septum occurred in 96 (80%) children of the main group and in 41 (68.3%) of children of the comparison group. Among the common nasal diseases include allergic rhinitis, are correctly qualified not as a nosological form, but as a symptom, including allergic rhinitis, accompanied by swelling of the mucosa, the expiry of discharge, itching, sneezing. In 25% of the children of the main group allergic rhinitis was observed, whereas in comparison group of children it met in 13.3% of cases.

Table 1: The structure of the incidence of upper respiratory tract in the examined children

Deseases	Sick children, n=180	
	FIC, n=120 Abs/%	RIC, n=60 Abs/%
Acute sinusitis	16/13,3	37/61,7
Chronic rhinosinusitis	104/86,6	23/38,3
Nasopharyngeal tonsil hypertrophy	82/68,3	23/38,3
Hypertrophy of tonsils	69/57,5	21/35,0
Chronic tonsillitis	30/25,0	9/15,0
Chronic adenoiditis	18/15,0	6/10,0
The curvature of the nasal septum	96/80,0	41/68,3
Nasal allergy	30/25,0	8/13,3

The study of cytokines in blood serum and nasal swabs was performed in 60 children with chronic rhinosinusitis, including 40 children from the group of FIC, 20 children from the occasionally ill group.

According to some authors, IL-1β and TNFα accumulate in the blood during intense inflammation and adequately reflect the severity of their duration.[9] It was established the regular growth of IL-1β in all the exmined groups of sick children. Moreover, in the group of FIC the level of IL-1β exceeded 2.5 times in comparison with a group of RIC (P <0,001). However, the synthesis of IL-1β in the group of FIC was 1.5 times higher during the exacerbation (P <0,01), than that in rarely ill children (Fig. 1).

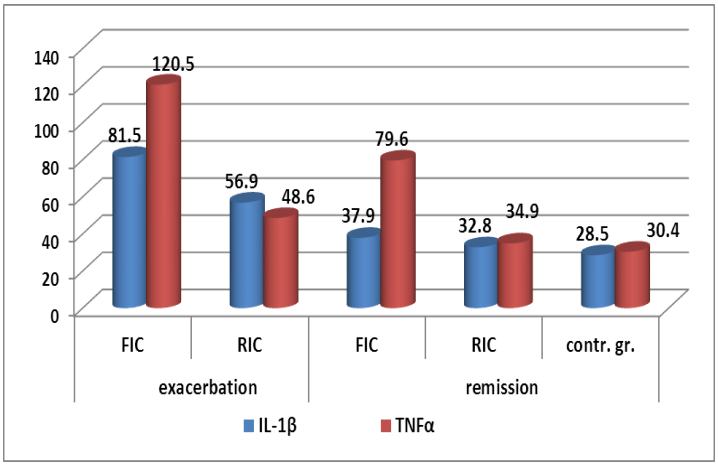

Fig. 1. The concentration of cytokines studied in the serum of children with chronic rhinosinusitis (pkg / ml).

Considering that TNFα produced by monocytes / macrophages and of Th1-lymphocytes, raising its level in the examined sick children apparently activates the cell-mediated immune responses, dysfunction of which occurs frequently in patients with pulmonary pathology.[6] Thus, the increase in the concentration of TNFα was statistically significant in all groups (P <0,01).

The concentration of IL-4 the group of FIC with rhinosinusitis had wide variations - depending on the severity and exacerbation, exacerbation etiologic factor. In remission period in often ill children, and occasionally ill, there was the normal IL-4 (5,6 ± 0,8; 4,8 ± 0,6 pg / ml, respectively). In the period of exacerbation the maximum parameters were in the group of RIC (13,5 ± 1,6 pg / ml) (Figure 2). The concentation of IL-4 in FIC during exacerbation was averaged 18,1 ± 2,4 pg / ml.

The nature of the provoking factor aggravation had expressed influence on the concentration of IL-4. Thus, if the cause of exacerbations was a contact with the allergen, the concentration of IL-4 is increased to the maximum numbers (10-20 pg / ml); during exacerbations caused by a viral infection, parameters were within 8.5 pg / ml.

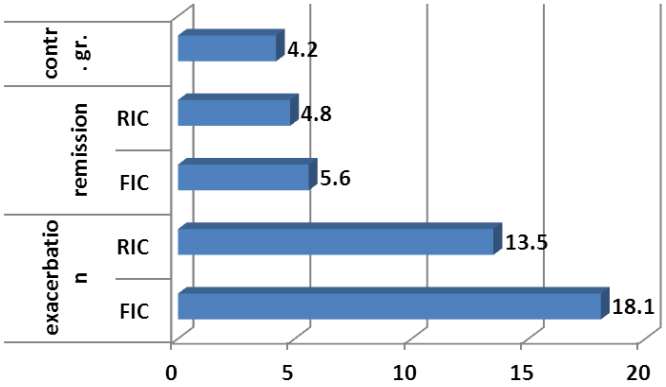

Fig. 2. The concentration of IL-4 in the serum of children with chronic rhinosinusitis (pkg / ml)

During the study of IgE it was found its presence in 56 (46.7%) of the 120 examined FIC. A significant increase in the concentration of IgE in the group of FIC was in exacerbation of chronic rhinosinusitis (up to 330 IU / mL). The content of IgE in rarely ill children during the exacerbation of chronic rhinosinusitis was the same as at an exacerbation in FIC.

We studied the levels of interleukins in the nasal washings, as close as possible to the site of inflammation.

The findings suggest a more expressed activation of T-lymphocyte helper type 2 in often and chronically ill children. In the early stages of inflammation in the microenvironment of Th0-cell cytokines are present, ensure the development of Th2 cell clone, with an important role in this process is played by IL-4, is released by activated mast cells. The inflammatory infiltrate in the mucosa of patients with rhinosinusitis contains large amounts of Th2 lymphocytes and cytokines attract eosinophils in the inflammatory center, basophils and neutrophils.[3,4]

When combining infectious and allergic genesis in children with chronic rhinosinusitis conditions for further activation of Th2 lymphocytes in the microenvironment as Th0 cells along with other cytokines may be present as IL-12 and IFNγ, and IL-4.

Therefore, create complex cause-and-effect relationships between the various effector inflammatory cells and their products - cytokines, as well as the target cells, which, in turn, are also active effectors of inflammation. In the nasal swabs of healthy children and adults were found IL-1, IL-2, IL-4, IL-5, IL-6, IL-8, TNFα, IFNγ, epidermal growth factors and other.[1, 10] The sources of these cytokines may be lymphocytes and helper cells of the immune system, built in mucosal epithelium; their activity is enhanced in various antigenic stimulation, which enter into the nasal cavity in abundance. This is particularly true for the cytokine of growth factors family (epidermal, fibroblast, insulin, etc.).[1] Finally, the cytokines may be the product of mucosal (oral, bronchial) epithelial cells that constitutively (without additional stimulation) and produce a number of cytokines capable of enhancing their secretion upon stimulation, for example, under the influence of the adhesive contact with microorganisms.[9,10] Induced secretion depends on the nature of the stimulus, manifesting differently for different cytokines and epithelial cells of different types.

As seen from the presented data, as the level of proinflammatory cytokines (IL-1ß and TNFα), and anti-inflammatory (IL-4) was significantly higher in the long and often ill children (P <0,01) (Table 2).

Table 2: Indicators of local immunity in the patients examined children in the nasal swabs

Parameters	RIC, n=20	FIC, n=40
IL-1ß (pkg/ml)	16,6 ± 1,12	22,9 ± 1,6*
IL-4 (pkg/ml)	2,06 ± 0,21	3,21 ± 0,15*
TNFα (pkg/ml)	2,34 ± 0,25	4,42 ± 0,3 *
SIg A g/l	0,502 ± 0,02	0,312 ± 0,01*
IgE (pkg/ml)	1,15 ± 0,23	3,29 ± 0,47 *

Note: * values valid in relation the group is rarely ill children (P < 0,05 - 0,001)

The data obtained are developing ideas about that the real state of homeostasis may be an indicator of the distant pathological processes.[2,3,10] In this study, it was showed in the study of cytokine profile (IL-1β, TNFα and IL-4) in the nasal swabs of sick children.

Extremely important in protecting the organism of the child from various types of antigen are specific factors of local immunity.[1] Considering the important role of SIgA in protecting of the organism, and especially of the mucous membranes, it can be stated that the violation of biosynthesis of this class of immunoglobulin may be one of the reasons for the decline of the immune resistance.

In normal immunoglobulin E (IgE) is found in fairly low titer; it is produced by plasma cells of the lymphoid tissue associated with mucosal membranes. In our studies, it has been an increasing level in sickly children with chronic rhinosinusitis ($P < 0,01$).

Thus, the immunological changes observed in the examined children with inflammatory diseases of the paranasal sinuses, can be qualified as secondary immunodeficiency.

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