AMERICAN JOURNALS
Open Access, Peer Reviewed Journals

American Journal of Pedagogical and Educational Research
ISSN (E): 2832-9791| Volume 33, | February - 2025

CYTOKINE PROFILE OF CHILDREN WITH ACUTE PYELONEPHRITIS

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A B S T R A C T

Clinical and immunological examination of 26 children with acute pyelonephritis (P) was carried out. As a control, 17 healthy children of comparable age were examined. It was revealed that in children with OP there is a significant disbalance in the production of proinflammatory (IL-1B, IL-6, IL-8 and IL-18, respectively, in 16,1, in 3,5, in 12,6 and in 6,7 times. INF-y tends to decrease, and IN-a - a tendency to increase) and anti-inflammatory (IL-4 and IL-10 are increased by 3.0 and 2.9 times, respectively) of cytokines.

K E Y W O R D S

Children, acute pyelonephritis, clinic, immunity, cytokines

Introduction

The human immune system is a complex multicomponent mechanism, the functioning of which is provided by specialized immunocompetent cells with various phenotypes and functions, as well as intercellular mediators. functional activity of cells of the immune system, but also belong to trophic factors that stimulate mitotic activity and proliferation of cells of various tissues [1,2,5]. Determining the level of pro- and anti-inflammatory cytokines not only makes it possible to identify the features of the parameters of the immune system in children, but also to determine the role of cytokines in the pathogenesis of pathological conditions [3,4]. patients, when deciding on the need to prescribe immunocorrective therapy and assess its effectiveness.

RESEARCH OBJECTIVE

Determination of the concentration of some cytokines in children with acute pyelonephritis.

MATERIAL AND METHODS

The level of cytokines in the blood serum was determined in 26 children (1st group) with acute pyelonephritis upon admission to the hospital. The control group consisted of 17 healthy children of comparable age.

All clinical, laboratory and instrumental studies and clinical observations of sick children were carried out in the nephrology department of the Children's Road Hospital of Uzbekistan Temir Yollari JSC in Tashkent. The concentration of interleukins and interferons (IL-Iβ, IFN-y IFN-α, IL-4, IL-6, IL-8, IL-

10, IL-18) in the blood serum was determined by the method of enzyme-linked immunosorbent assay using test systems 300 "Vector-Best" (Russia, Novosibirsk). Quantitative assessment results were carried out by constructing a calibration curve or using the commercial computer program "Microplate manager", reflecting the dependence of optical density on concentration for a standard antigen and allowing comparison of the studied samples with it. The sensitivity of the method is 5-30 pg/ml.
Statistical processing of the data obtained was carried out using the Statistica 6.0 computer program. The significance of the differences in the mean values of the compared indicators was assessed according to the student's criterion (t).

RESULTS AND DISCUSSION

Among the children under 6 years of age, 20 (76%) were under 6 years of age, 6 (24) were from 7 to 15 years of age, i.e. acute pyelonephritis was more common in preschool children, among the patients we observed there were more girls (18), corresponding to the literature data on the greater prevalence of microbial inflammatory diseases of the kidneys among women.
As a result of the studies carried out in children with OP, changes in some parameters of cytokines of the immune system were found (Table).

Concentrations of some cytokines (pg/mL) in children with acute pyelonephritis

Cytokine	Control, n=17	Acute pyelonephritis, n=20	p
IL-1β	23,5±1,37	378,5±6,08	<0,001
IL-6	6,3±0,75	22,1±1,31	<0,001
IL-8	12,4±0,77	156,3±2,71	<0,001
IL-18	24,2±1,44	161,8±3,18	<0,001
IL-4	10,7±0,98	32,4±1,41	<0,001
IL-10	9,3±0,96	26,9±1,01	<0,001
INF-α	23,4±1,56	24,8±0,78	<0,05
INF-u	10,1±1,13	8,3±0,59	<0,05

In the processes of immunoregulation, the pro-inflammatory cytokine IL-1 β performs an important physiological role and, initiating inflammation, can become a key link in the pathogenesis of a number of diseases.
It was found that in healthy preschool children, individual indicators of IL-1ß production ranged from 16 to 32 pg/ml, while the average value of this cytokine was 23.5±1.37 pg/ml. In children with acute pyelonephritis, the level of pro-inflammatory cytokine IL-1ß before treatment was 16.1 times higher than in children of the control group ($p<0.001$), on average amounting to 378.5±6.08 pg/ml.
The high level of IL-1ß production in children with OP suggests the presence of a certain dependence of its concentration on the nature of the pathological process.
The pro-inflammatory cytokine IL-6 is a potent pro-inflammatory cytokine, like IL-1 and TNF, but is produced somewhat later than the latter, inhibiting their formation and is believed to be one of the cytokines that complete the development of the inflammatory response. It has been established that IL-6 has a great effect on the regulation of the immune response: it stimulates the proliferation and

differentiation of B cells, enhances antibody formation, participates in the production of multipotent colony-forming factors, and megakaryocytes, can suppress neutrophil apoptosis. The production of IL-6 in children with OP was 3.5 times higher (22.1±1.31 pg/ml) than the control (6.3±0.75 pg/ml).

The main function of IL-8 is to act as a chemoattractant for neutrophils, macrophages, lymphocytes, eosinophils. In addition to this biological action, IL-8 enhances the adhesive properties of neutrophils by altering the expression of integrins and other compounds with adhesive properties. The properties of IL-8 to induce cell migration and promote cell adhesion determine it as an active participant in the acute inflammatory response at the sites of pathogen penetration. In children with OP, the concentration of IL-8 was significantly (12.6 times) higher (156.3±2.71 pg/ml, $p<0.001$) than in the control group (12.4±0.77 pg/ml).

Interleukin-18 occupies a special position among immunoregulatory mediators, as it is one of the key cytokines in the formation of innate and acquired immune responses, differentiation and functional activity of macrophages, dendritic cells and T-lymphocytes.

IL-18 stimulates the production of IFN-y, GM-CSF, TNF, IL-1, IL-2, adhesion molecules and apoptosis factors, which contributes to the activation of cytotoxic T-lymphocytes, NK cells and the formation of an effective anti-infective immune response. IL-18 itself is induced by stress signals (neurogenic or bacterial origin). IL-18 not only stimulates the synthesis of INF-y, but also modulates its functional activity.

In the peripheral blood serum of healthy children, the level of IL-18 ranged from 17 to 35 pg/ml, averaging 24.2±1.44 pg/ml. Study of IL-18 production in children with OP revealed a 6.7-fold increase in its concentration (161.8±3.18 pg/ml, $p<0.001$) compared to the control group.

Increased production of IL-18 causes activation of the expression of Fas proteins (CD95), the stimulation of which leads to apoptosis processes.

An important immunoregulatory role belongs to the anti-inflammatory cytokine IL-4, which inhibits the production of several T-cell cytokines, including pro-inflammatory ones. Determination of the concentration of IL-4 in the blood serum of healthy children showed that its values ranged from 4 to 16 pg/ml, and on average - 10.7±0.98 pg/ml. In children with OP, the production of IL-4 was increased by 3.0 times (32.4±1.41 pg/ml, $p<0.001$) relative to the control group, which indicates a violation of the functioning of the cytokine network.

Anti-inflammatory cytokine IL-10 is an immunosuppressive cytokine that suppresses the proliferation and activity of T-cells, the production of the synthesis of a number of cytokines, the development of delayed hypersensitivity, and reduces the activity of macrophages and monocytes. At the same time, IL-10 stimulates the proliferation of B lymphocytes and the synthesis of IgM and IgA, the proliferation of thymocytes. The production of IL-10 in children with OP was higher (26.9±1.01 pg/ml, $p<0.001$). than in the children of the control group by 2.9 times (9.3±0.96 pg/ml).

An important mediator characterizing the state of the immune system of children is IFN-y, which regulates the intensity of the immune response, increases the bactericidal properties of phagocytes, and has antiviral and immunomodulatory activity. In our studies, the level of IFN-u production in healthy children averaged 10.1±1.13 pg/ml.

In the children of the study group, there was a tendency to reduce IFN-y production compared to the control group to 8.3±0.59 pg/ml ($p>0.05$). The low ability of patients with OP to synthesize IFN-y causes a violation of the immunoregulatory index towards the predominance of the suppressor activity of T-lymphocytes and a decrease in the killer cell activity.

IFN α belongs to type 1 interferons. Almost all types of cells can become producers of IFN-α when stimulated. It plays a key role in local and systemic antiviral protection. The concentration of IFN-α in the peripheral blood in children with OP averaged 24.8±0.78 pg/ml, which was slightly higher than in the control of 23.4±1.56 pg/ml, but did not achieve significant differences. Thus, in children with OP, significant changes in the studied parameters of the immune system were found upon admission. Children with OP develop a significant imbalance in the production of pro-inflammatory (the level of IL-1β, IL-6, IL-8 and IL-18 increases by 16.1; 3.5; 12.6 and 6.7 times, respectively; INF-y tends to decrease, and IFN-α tends to increase) and anti-inflammatory (the content of IL-4 and IL-10 increases by 3.0 and 2.9 times) cytokines.

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