FEATURES OF IMMUNITY IN CHILDREN WITH ACUTE DIARRHEA

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Abstract. *The most pronounced changes in the parameters of cellular and humoral immunity were found in patients with acute intestinal infections of unknown etiology, less pronounced in the group of patient children with Escherichia infection.*
Key words: *children, diarrhea, intestinal infections, immunity*

Introduction - Acute diarrhea diseases are one of the priorities in the healthcare system, as they can cause unpleasant and serious complications in children.

The aim of the study was to study the features of the immune status of children with acute diarrhea.

Materials andmethods. We studied the parameters of cellular and humoral immunity depending on bacterial pathogens that caused diarrhea in 76 children, including Salmonella, Shigella, and E. Coli, and separately in children with acute diarrhea of unknown etiology.

Results. A discoordination balance in changes in cellular and humoral immunity was revealed, which was characterized by a decrease in T-lymphocyte counts, T-helper cells, T-killer activity, phagocytic activity, and a deficiency of Ig A and IgM, and an increase in T-suppressors and IgG. In relation to CD_{20}-lymphocytes, their increase was different, especially it was typical for patients with dysentery and acute diarrhea of unknown etiology. There was a deficiency of serum immunoglobulins of the IgA and IgG classes. Serum immunoglobulin IgM in patient tended to increase, but these differences were unreliable.

Actuality. One of the most attention-grabbing tasks that directly affects the interests of doctors of various specialties is the assessment of quantitative and functional indicators that reflect the state of the human immune system at a given time, which allows the doctor to select the most adequate of them for specific diagnostic and prognostic purposes. Currently, the most optimal is a two-stage system for testing immune status. The first level tests are indicative and include: determination of the relative and absolute number of leukocytes and lymphocytes in the peripheral blood, determination of the absolute and relative number of T- and B-lymphocytes ($CD3^+$, $CD20^+$), concentrations of serum IgM, IgA, IgG and determination of the phagocytic activity of leukocytes. Second-level tests are more analytical and include: determination of subpopulations of regulatory T-lymphocytes, assessment of the proliferative activity of T- and B-lymphocytes for mitogens, antigens, allogeneic cells, assessment of the activity of NK-lymphocytes -$CD16^+$, detection of CEC, determination of complement components, determination of mediators immune system, incl. cytokines, as well as analysis of genes responsible for the expression of immunologically significant molecules. In turn, determining the characteristics of the immune status will make it possible to identify defects in cellular and humoral immunity, and the proliferation of pathogenic microorganisms in the macroorganism and theoretically justify the prescription of immunodrugs for the treatment of children with diarrheal diseases.

The purpose of study. To study the features of the immune status of children of a healthy population and patients with acute diarrhea.

Materials and methods. Under our supervision were young children, patients with acute diarrhea (n-76) and healthy children (n-25). The functional state of the B-immune system was assessed by determining serum immunoglobulins of the main classes IgG, IgA, IgM using a set of monospecific sera IgG, IgA, IgM using the generally accepted method of radial immunodiffusion in a gel according to Mancini (1969). The viability of lymphocytes isolated from peripheral blood is determined according to the method described by B.V.Brondz. Determination of immunocompetent cells in the indirect rosette reaction using monoclonal antibodies.

Results and discussions. To assess the immune status, we analyzed the normal indicators of systemic immunity in practically healthy children of two age groups. Since the statistical analysis of the parameters of the average values of the immune status in the two age groups studied did not reveal significant differences, the immunological parameters of the children were combined into one group.

Thus, the indicators of immune status obtained during an immunological study in a population of practically healthy children corresponded to 62.9±0.9% for $CD3^+$ cells, 25.4±1.2% for $CD20^+$ cells, the average values of the T-lymphocyte subpopulation corresponded to T-helper cells 36.8±1.2%, T-suppressors 24.8±0.8%, and for natural killers 15.2±0.9%, for serum immunoglobulins of the main three classes: for IgA 144±6 mg%, for IgM 150±6 mg%, for IgG 1290±23 mg%. Indicators of activation markers averaged 24.3±1.07% for $CD25^+$ cells and 26.1±1.32% for $CD95^+$ cells. Based on studies conducted to study the average values of immune status parameters, average regional indicators were identified that reflect the characteristics of the immunity of a given age period, as well as generalized values taken for the normoimmunogram.

Further, we studied indicators of immune status depending on the bacterial pathogens that caused diarrhea in children, including Salmonella, Shigella, E. Coli, and separately in children with IIUE.

Thus, when studying the T-cell immune link in the contingent of examined children with ACI, a significant decrease in the average level of the relative content of T-lymphocytes was established, regardless of the bacterial pathogens that caused diarrhea, amounting to 47.5 ± 0.61% for salmonellosis, 48.5 ± for dysentery 0.53%, escherichiosis 52.6±0.6% and CINE 42.5±0.6% compared to 62.9±0.9% in the control ($p<0.001$ in all cases). The T-helper subpopulation expressing CD4+ antigens was characterized by a level of 28.5±0.4% for children with the bacterial pathogen Salmonella, for children with the bacterial pathogen Shigella 28.9±0.47%, for children with the bacterial pathogen E. Coli 30.7 ±0.42% and for children with IIUE 24.5±0.45% compared to 24.4±0.3% in controls ($p<0.001$ in all cases).

The content of the population of cytotoxic T cells expressing CD8+ antigens was also significantly reduced in all groups of children with ACI at 24.8±0.8% in the control ($p<0.05$ for salmonellosis, $p<0.01$ for dysentery, $p<0.001$ with escherichiosis and IIUE).

The results obtained regarding IRI in ACI indicate a decrease in this indicator (1.27±0.02; 1.31±0.03; 1.38±0.03 and 1.04±0.01 compared to 1 .48±0.02 in control, $p<0.001$ in all cases).

Thus, studies of the quantitative parameters of ICC in children with acute diarrhea indicate a decrease in the average level of subpopulations of immunoregulatory T-lymphocytes against the background of a deficiency of the total pool of T-lymphocytes.

The main elements of innate immunity in response to pathogens, including bacterial ones, are natural killer cells. These cells are related to T lymphocytes, but their origin is still a matter of

debate as they have some features of myeloid cells. They make up approximately 10% of all blood lymphocytes.

Thus, in our studies, the content of subpopulations of cells that perform the functions of natural killer cells (Table 1) revealed a decrease in this indicator in acute diarrhea in children with various bacterial pathogens to 10.4 ± 0.3% for the pathogen Salmonella, 10.2 ± 0 .35% with the pathogen Shigella, 10.6±0.42% with the pathogen E. Coli and with IIUE up to 8.8±0.32% (compared to 8.9±0.74% in the control, P<0.001).

Table 1

Natural killer cell counts in some acute diarrheas

Immunological indicators	Control group (n=25)	Escherichiosis (n=16)	IIUE (intestinal infection of unknown etiology) (n=18)
$CD16^+$, %	15,2±0,9	10,6±0,42***	8,8±0,32***
$CD16^+$ (abs)	290±11	196±8***	134±5***
Immunological indicators	Control group (n=25)	Salmonellosis (n=22)	Dysentery (n=20)
$CD16^+$, %	15,2±0,9	10,4±0,3***	10,2±0,35***
$CD16^+$ (abs)	290±11	166±6***	174±6***

Note: * - the differences relative to the control group data are significant (*** - P<0,001).

It should be noted that the most pronounced decrease in natural killer cells was recorded in children with IIUE. B lymphocytes develop in the bone marrow from pluripotent stem cells in response to stromal cell signals (soluble cytokines, cell-cell contact) and express CD20 antigens. The data we obtained on the content of serum B-lymphocytes in children with acute intestinal infections are presented in Table 2.

Table 2

Indicators of humoral immunity in some acute intestinal infections

Immunological indicators	**Control group (n=25)**	**Salmonellosis (n=22)**	**Dysentery (n=20)**
$CD20^+$, %	25,4±1,2	22,6±0,4*	23,2±0,35
$CD20^+$ (abs)	771±18	769±15	817±15*
IgA, mg%	144±6	118±5,1**	121±5,3**
IgM, mg%	150±6	160±5,5	161±5,8
IgG, mg%	1290±23	1086±26***	1066±27,5***
Immunological indicators	**Control group (n=25)**	**Escherichiosis (n=16)**	**IIUE (n=18)**
CD20+, %	25,4±1,2	22,2±0,3*	24,3±0,4

CD20+ (abs)	771±18	783±14	865±16***
IgA, mg%	144±6	127±5,8*	109±5,9***
IgM, mg%	150±6	158±6,9	165±5
IgG, mg%	1290±23	1180±25**	990±29***

Note: * - the differences relative to the control group data are significant (* - P<0,05, ** - P<0,01, *** - P<0,001)

It can be seen that the contingent of children with ACI is characterized by a significant decrease in B-lymphocytes with salmonellosis (P<0.05), escherichiosis (P<0.001) and IIUE (P<0.001), the content of B-lymphocytes with dysentery did not change significantly.

During the immune response, the synthesis of immunoglobulins of various classes occurs. Conducted studies on the content of serum immunoglobulins in sick children with ACI are characterized by the presence of severe disimmunoglobulinemia with an increase in the concentration of IgM and a decrease in the content of serum immunoglobulins of class A and G. It should be noted that disimmunoglobulinemia is most pronounced in the group of children with IIUE.

It seems interesting to study regulatory T cells that have a suppressor function (Table 3).

Table 3

Indicators of activation markers of immunity for some acute intestinal infections

Immunological indicators	**Control group**	**Salmonellosis (n=22)**	**Dysentery (n=20)**
$CD25^+$, %	24,3±1,07	27,4±0,75*	27,7±0,84*
$CD25^+$ (abs)	738±18	936±33***	980±23***
$CD95^+$, %	26,1±1,32	31,5±1,01**	30,9±0,42**
$CD95^+$ (абс)	793±16	1076±28***	1094±28***
Immunological indicators	**Control group (n=25)**	**Escherichiosis (n=16)**	**IIUE (n=18)**
$CD25^+$, %	24,3±1,07	28,2±0,68**	29,7±0,49**
$CD25^+$ (abs)	738±18	995±20***	1063±23***
$CD95^+$, %	26,1±1,32	27,4±0,48	32,5±0,92**
$CD95^+$ (abs)	793±16	967±22***	1163±28***

Note: * - the differences relative to the control group data are significant (* - P<0,05, ** - P<0,01, *** - P<0,001)

They represent a small subpopulation of $CD4^+$ T cells that also express CD25+ even without activation. $CD4^+$, $CD25^+$ regulatory T cells have been shown to be responsible for autoimmune responses, as their depletion leads to the development of various autoimmune diseases in mice. A study of the content of regulatory $CD4^+$ $CD25^+$ cells that perform a suppressor function revealed a significant increase in this indicator in acute intestinal infections in children to 27.4±0.75% with the pathogen Salmonella, 27.7±0.84% with the pathogen Shigella, 28.2±0 .68%

with the pathogen E. Coli and with IIUE up to 29.7±0.49% (compared to 24.3±1.07% in the control).

Cells that have apoptosis receptors such as the $CD95^+$ antigen (another name for Fas or APO-1) trigger a cell "suicide" mechanism called programmed cell death, or apoptosis. As can be seen from the information presented in Table 4 on the content of CD95 positive cells in sick children with ACI, this is reflected by a significantly increased number of cells with Fas/CD95 expression on lymphocytes. An unreliable increase in the content of CD95 positive cells was observed in sick children with the pathogen E. Coli.

Conclusion. In general, disorders of the immune system in acute diarrhea in children are manifested by a quantitative deficiency of T-lymphocytes with a change in the ratio of subpopulations of T-helpers and T-suppressors with a predominance of the T-helper effect, a decrease in the content of the population of natural killer cells, hyperproduction of IgM, as well as an increased content number of cells with expression on $CD25^+$ and $CD95^+$ lymphocytes. At the same time, a complex system of interactions between various parts of ensuring the body's immune homeostasis is reflected by multidirectional fluctuations in the main parameters of the immune status depending on the pathogen.

REFERENCES

1. Диарейные инфекции у детей раннего возраста на фоне кандидозной инфекции. Рашидов Ф.А. Мирисмоилов М.,Умаров Т.У.,Рихсиева Г.М.,Алимов М.М.// Вестник - Ташкентской медицинской академии №3/2 2023, С.-88-90.
2. Зайцева Н.В., Хмелевская И.Г., Калуцкий П.В. Клинико-иммунологические особенности течения вирусных диарей у детей // Вестник современной клинической медицины. – Казань, 2017. - Том 10, Вып. 2. – С. 30 – 33.
3. Максудова Л. И. Острые кишечные инфекций у детей. //"EFFECT-D".Ташкент-2023.- С. 155.
4. Руженцова Т.А. Роль пробиотиков в формировании иммунитета //Лечащий врач. - 2018. - №4. - С.27-30.
5. Шаджалилова М.С., Халилова З.Т., Осипова Е.М. // Анализ про- и противовоспалительных цитокинов при некоторых острых диареях. Журнал инфектологии, Том 15, №1, 2023, с 190-191.
6. Шаджалилова М.С., Худойберганова Ч.К. //Острые диареи у детей. Инфектология, эпидемиология ва паразитологиянинг долзарб муаммолари мавзусидаги халкаро илмий-амалий анжумани. Бухара 2022.- 139-140 бет.
7. Шаджалилова М.С., Шаропова Г.М., Осипова Е.М. //Сравнительная оценка клинического течения острых диареи у детей. Тиббиётда янги кун», №2(40) - 2022.- С.- 552-555.
8. Таджиев Б.М., Худайбердиева Ч.К., Ахрарова А.Р. Особенности острых инфекционных диарей у детей в Республике Узбекистан // Science and innovation international scientific journal. Volume 2, issue 5 may 2023.- p 2024-2030.