

Treatment-prophylaxis measures and their clinical-immunological criteria in children when the Iyambliosis parasite is combined with ascariidosis

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Abstract. Since analyzes of immunological parameters after immunocorrection in children affected by giardiasis and ascariasis revealed significant changes in the immune status of children affected by giardiasis and ascariasis, it is of great interest to study the state of cellular and humoral immunity in these children after immunotropic treatment in comparison with those who received conventional therapy.

1 Introduction

It is known that enterobiosis (up to 65%), ascariasis and opisthorchiasis have the highest rates among human helminthiasis. In recent years, there has been an increase in the incidence of severe mixed helminthiasis among children. Ascariasis is a chronic parasitic disease that develops as a result of parasitism in the human intestine [2,5,8]. Giardiasis is widespread almost everywhere, but among the population of Southern climatic zones, especially in Latin America, North Africa, Italy, Iran, Pakistan, Afghanistan, neighboring countries - Central Asia, Kazakhstan, Moldova, Azerbaijan, Georgia, Armenia and Ukraine. Hymenolepidosis in children was registered in the North Caucasus, Tomsk, Amur and other regions of Russia [1,3,6]. The helminthosis of giardiasis and ascariasis mainly affects urban residents. Children aged 4-14 years are more likely to get sick, which is explained by their insufficient hygiene skills and the characteristics of age-related immunity[4,7]. The main symptoms of the disease are acute abdominal pain, skin rashes, loss of appetite, belching, nausea, vomiting, diarrhea, weight loss, dysbacteriosis, dizziness, headache, asthenia, skin itching, rhinitis, Quincke's edema. In most cases, severe complications such as loss of consciousness, increased body temperature, myocardiodystrophy, seizures, brain tumor, hepatomegaly, anemia and hypovitaminosis are observed in children[9,10,12]. In our region, many measures are being taken to reduce the population's infection with helminths. Today, the actual problem of fighting parasites remains important [11,13,14].

Purpose of work: It consists in the development of treatment-prophylactic measures and clinical-immunological criteria for children infected with giardiasis and ascariasis.

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2 Materials and methods

Scientific work was carried out at the clinical base of the Bukhara Regional Children's Infectious Diseases Hospital, and immunological analyzes were carried out at the Department of Immunology and Human Genomics, Cytokines of the Academy of Sciences of the Republic of Uzbekistan.

In this research, research was conducted in two strategic directions. In each of these directions, the study of epidemiological aspects related to the course of one pathological process was the development of gastrointestinal tract diseases and exacerbation complications due to progressive immunodeficiency.

Detailed analyzes of the structure of children's diseases affected by helminthiasis and the effect of helminthosis on the dynamics of the development of the pathological process were conducted.

Diagnosis and treatment of 114 children aged 3 to 18 years with giardiasis and ascariasis during 2021–2023 were analyzed, and 40 children with hymenolepidosis were examined for the control group. All control patients underwent extensive continuous examination, including clinical and laboratory, biochemical, immunological studies. In this regard, attention was paid to their complaints, past and accompanying diseases, premorbid appearance, causes of the disease, duration of the disease, and the effect of early treatment measures.

In order to study the immunological reactivity of the child's organism in dynamics, 47 children were involved in this study, of which 23 children affected by hymenolepidosis were conventionally treated, and 25 children affected by giardiasis were children who received conventional and immunostimulating therapy.

3 Results and their discussion

Since the analyzes of immunological parameters after immunocorrection in children affected by giardiasis and ascariasis revealed significant changes in the immune status of children affected by hymenolepidosis infection, it is of great interest to study the state of cellular and humoral immunity in these children after immunotropic treatment in comparison with those treated with traditional therapy.

The state of cellular immunity in children during treatment, in children affected by giardiasis and ascariasis the results of the study of the immune status after the traditional treatment and immunomodulating drug therapy are presented.

The patients examined by us were divided into 3 groups:

1. A group of children infected with giardiasis and ascariasis before treatment
2. A group of children affected by giardiasis and ascariasis after traditional therapy
3. A group of children affected by giardiasis and ascariasis after immunocorrective and traditional therapy.

In children infected with giardiasis and ascariasis The results of the study of the values of T-cell immunity are presented in Table 1. According to the data presented in children infected with giardiasis and ascariasis after therapy, a significant decrease in the total number of leukocytes compared to the values before treatment was found ($r < 0.05$). We found that this indicator is close to the value of the norm.

Table 1. Cellular system indicators of immunity after treatment in children (M±m).

Immunological parameters	Control group (n=15)	Before treatment (n=47)	After traditional treatment (n=22)	After immunocorrective therapy (n=25)
Leukocytes, in 1 μ l	5500±171.9 2	7300±491.8*	5984±315.4 ^	4984±203.2* ^ \ominus
Lymphocytes, %	41.50±0.75	40.72±1.19	38.74±1.65	36.20±0.97* ^
Lymphocytes, in 1 μ l	2241±50.34	2896.7±155.6*	2188.4±77.42 ^	1822.2±81.72* ^ \ominus
CD 3+, %	53.10±2.47	47.40±1.05*	48.82±1.79	50.28±0.99 ^
CD 3+, μ l	1190.3±65.42	1371.72±77.72	990.82±46.05* ^	920.80±48.07* ^
CD 4+, %	27.60±1.51	22.36±0.93*	22.85±0.83*	26.56±0.73 ^ \ominus
CD 4+, μ l	618.52±48.98	647.70±52.35	585.8 ±29.87	483.9 ±19.87 0 * ^ \ominus
CD 8+, %	24.40±1.52	23.04 ±0.70	23.88±0.88	24.28±0.96
CD 8+, μ l	546.8±41.43	667.39±59.1	544.52±34.15	442.38±32.14 ^ \ominus
CD 4+/ CD 8+ (IRI)	1.08±0.06	0.92±0.06	0.99±0.07	1.15±0.06 ^
CD 16, %	15.20±1.60	18.86±0.78*	16.24±0.77 ^	13.16±0.85 ^ \ominus
CD 16, μ l	340.6±32.47	546.32±28.5*	395.82±25.66 ^	239.80±18.68* ^ \ominus

Note: * - significantly compared with the data of the control group, ^ - compared with the data of the group before treatment, \ominus - compared with the data after conventional therapy (P < 0.05)

After treatment, the average value of the relative and absolute number of all lymphocytes in peripheral blood decreased to 36.20±0.97% and 1822.2±81.72 per 1 μ l, respectively, while before treatment this indicator was 40.72±1, 19% and 2896.7 ±155.57 in 1 μ l (r<0.05). Thus, we found a significant decrease in the total number of lymphocytes in the peripheral blood.

A comparative analysis of the total percentage of T-lymphocytes after immunocorrection showed that this indicator significantly increased compared to the values before treatment and was equal to 50.28 ± 0.99% compared to 47.40 ± 1.05%. In the study of a group of sick children after conventional therapy, we found a significant difference between the number of leukocytes and the absolute number of lymphocytes (r<0.05).

The study of the absolute number of T-lymphocytes in 1 μ l revealed a significant decrease compared to the values before treatment, which was associated with a decrease in the total number of leukocytes. Thus, the increase in the total number of T-lymphocytes, the main cells of the immune system, is associated with sufficient immunocorrection. No significant difference was found when studying the expression of CD3+ in T-lymphocytes.

The study of the quantitative properties of the relative and absolute composition of T-helpers/inducers against the background of the use of an immunotropic drug showed the presence of reliable indicators. Thus, the average value of CD4+ in children increased after treatment and was 26.56 ± 0.73% compared to 22.36 ± 0.93% before treatment (r<0.05). The absolute content of CD4+ was also significantly different and decreased, which is associated with a decrease in the inflammatory process and a decrease in the number of leukocytes. In the study of T-helpers / inducers after conventional therapy, we also found a significant difference with the group of children after immunocorrection. These data once again confirm to us the important role of immunocorrection in treatment against the background of antiparasitic therapy. Also, the absolute number of T-helpers was also significantly different from the values of T-helpers/inducers in the group of patients after the use of immunocorrection. Thus, we found significant differences in the number of T-helpers/inducers, which clearly play an important role in the immune response to infection. The obtained data are presented in Table 2. When studying CD8+ expressed in lymphocytes, we found no significant difference between the group of children before and after treatment, but there was a tendency for CD8+ to increase. The absolute CD8+ count showed significant

variation, which again correlated with the total leukocyte count. After conventional therapy, there were no differences in the status of T-cytotoxic lymphocytes in the children's group.

A comparative analysis of the value of the immunoregulatory index (IRI) revealed a significant increase after the treatment, which indicated that the number of CD4⁺ increased sufficiently after the treatment and that a balance was established between the immunoregulatory cells that regulate the inflammatory processes. After treatment, the immunoregulatory index was on average 1.15 ± 0.06 and approached the initial values.

The expression of CD16⁺ in lymphocytes was significantly decreased after treatment compared to pretreatment values. After treatment, the number of natural killers approached the initial value, which indicated a decrease in the inflammatory response process. The absolute number of natural killers also decreased, which stood out significantly.

We saw a significant difference in relative and absolute indicators in the group of children after conventional therapy ($r < 0.05$), which again indicates the presence of infectious pathology.

Thus, we found significant differences in the state of immune tolerance in children after immunocorrective therapy, which was manifested by an increase in the content of the main immunoregulatory cells - T-lymphocytes, T-helper / inducers and suppression of the number of natural killers. The index of T-helpers in children affected by giardiasis and ascariasis is a clear example of the balance between immune regulatory cells, which increases after treatment, which is associated with the improvement of the clinical picture of the acute disease in the inflammatory process. It should be noted that before treatment, severe T-cell immunodeficiency in children in the main group was associated with immunodeficiency of immunoregulatory subpopulations of T-lymphocytes, manifested by a clear deficit in the number of CD4⁺ T-cells and CD8⁺ T-cytotoxic lymphocytes. It naturally normalized after therapy.

We found a significant decrease in the content of natural killers, which is explained by the fact that the increase in the expression of natural killers is associated with the presence of an infectious agent and a sharp increase in the response to it in immature forms of lymphocytes, CD16⁺ is a sign of this. It is known that natural killers belong to natural defense factors and provide resistance against non-specific infection, which play a leading role in the detection and elimination of parasitic diseases.

When the status of B-lymphocytes and humoral immunity was studied in the children of the main group after treatment, the study of the level of B-lymphocytes and the humoral connection of immunity after treatment made it possible to determine the characteristic features manifested in a significant increase in B-lymphocytes after treatment, this information is presented in Table 3. As mentioned above, the number of B-lymphocytes decreased in children before treatment, and after treatment this indicator increased to $25.72 \pm 0.98\%$ compared to $22.14 \pm 0.63\%$ before treatment. The absolute values of V-lymphocytes decreased significantly and amounted to 456.48 ± 27.68 in $1 \mu\text{l}$. When studying the relative number of B-lymphocytes, we found a significant increase in the group of children after conventional therapy compared to the group after immunocorrective therapy.

Analysis of the humoral state of immunity showed that in the main group of children there is a tendency to increase all the main classes of immunoglobulins, which are often observed in inflammatory processes. Against the background of therapy, the values of immunoglobulins decreased significantly only in the IgG analysis, which amounted to 0.68 ± 0.03 ME in the blood serum of children after treatment. Other immunoglobulins were not significantly different. Analysis of the humoral state of immunity in the group after conventional therapy did not show significant changes in the group of children before and after treatment.

Table 2. Indicators of B-lymphocytes and humoral immunity (M ± m).

Immunological parameters	Control group (n = 20)	Before Treatment (n =47)	After conventional treatment (n =22)	After immunocorrective therapy (n =25)
CD 20+, %	25.50±2.13	22.14±0.63	23.29±0.66	25.72±0.98 [^] [⊙]
CD 20+, μl	571.30±48.5	641.3±36.2	568.5±29.8	456.5±27.7* [^] [⊙]
IgG, ME	0.93±0.07	1.010±0.06	0.98±0.42	0.68±0.03* [^]
IgA, ME	0.84±0.17	1.26±0.2	1.15±0.12	1.05±0.11
IgM, ME	1.05±0.07	1.11±0.13	1.05±0.08	1.02±0.09

Note: * - control group information within comparison important, [^] - from treatment previous group information with compared to, [⊙] - traditional from therapy next data with compared (r <0.05)

Above, we analyzed the ratio of the main immunoglobulins to each other to assess the direction and stage of immunoglobulin synthesis, which indicates the transition of the B-cell from one class of immunoglobulin synthesis to another. Our analysis showed an increase in the ratio of IgG and IgA to IgM compared to control data, which was manifested by a slight increase in IgG, IgA and IgM in the group of children with acute intestinal infection.

Table 3. Ratios of the main classes of immunoglobulins.

Indicator ratio	Healthy ones	Patients before treatment	Patients after conventional treatment	Patients after conventional and immunotherapy
IgG : IgM	0.88	0.9	0.93	0.67
IgA : IgM	0.8	1.14	1.10	1.03

After treatment, a comparative analysis of immunoglobulin values revealed some changes manifested in the suppression of IgG and IgA synthesis, which clearly showed a decrease in the inflammatory process. This analysis showed that after conventional therapy, we did not observe specific changes, and the data obtained after the use of immunocorrective therapy were close to the norm.

Thus, after treatment in the children of the main group, the number of B-lymphocytes in the peripheral blood serum and the level of basic immunoglobulins were normalized.

The results of studies on the quantitative characteristics of lymphocytes expressing interleukin-2 (CD25+) and FAS/APO-1 (CD95+) receptors, which mediate the physiological apoptosis of lymphocytes, in the analysis of the status of markers of early and late lymphocyte activation (CD25+ and CD95+) in children after treatment are presented in Table 4.

Table 4. Values of markers of lymphocyte activation after treatment(M±m).

Immunological parameters	Control group (n=20)	Before treatment (n =47)	After conventional therapy (n =22)	After immunocorrective therapy (n =25)
CD 25+, %	23.8±1.72	19.6±0.66*	19.66±0.92*	22.40±0.60 [^] ⊙
CD 25+, μl	533.4±29.0	625.7±14.1*	518.2±24.4 [^]	408.1±31.2* [^] ⊙
CD 95+, %	23.20±1.31	20.80±0.62	20.15±0.54*	21.72±0.63
CD 95+, μl	566.9±24.0	369.0±16.2*	372.7 ±15.9*	395.7 ±19.0*

Note: * - control group information within comparison important, [^] - from treatment previous group information with compared to, ⊙ - traditional from therapy next data with compared (r < 0.05)

Analysis of the relative and absolute values of activated CD25+ lymphocytes in the main group of children after treatment revealed a significant difference (r < 0.05) compared to the values of the group of children before treatment. We observed an increase in the studied indicator, which indicated the presence of sufficient cellular immunity during treatment. These data can also be described from the point of view of our observation of clinical improvement of the general condition of children during treatment and improvement of cellular immunity value. After treatment, the absolute value of CD25+ decreased, which is associated with the absence of a clear inflammatory process that naturally accompanies leukocytosis. Analysis of the results obtained after conventional therapy showed that CD25 + markers in lymphocytes were significantly different after immunocorrective therapy (r < 0.05).

Analysis of late activation symptoms - CD95+ in children in the main group after treatment did not reveal significant differences. We observed a certain trend compared to the normalization of the content of lymphocytes carrying markers of apoptosis, which increased slightly. Analysis of the absolute values of CD95+ also revealed no significant difference.

Thus, the cellular immune response in children in the main group after treatment is characterized by the normalization of T-cell immunity, as well as humoral protective factors and the state of activated lymphocytes, which are of decisive importance in the development, course and prognosis of pathological processes, which are processes in children with a clear inflammatory process.

The normalization of the pathological changes we found clearly shows that the children in the main group are characterized by a state of immunodeficiency at the level of cellular and humoral protective factors.

In the results of cytokine profiles of children affected by giardiasis and ascariasis after treatment, the study of cytokine profiles after treatment in children affected by giardiasis and ascariasis showed a significant imbalance in the levels of cytokines that naturally affect the course of the disease.

We had the opportunity to compare the status of the main immunoregulatory cytokines in the peripheral blood serum of children before and after treatment.

IFN- γ before treatment against the background of the peak of the disease was 82.80±25.07 pg/ml, which was significantly different from the control group. After therapy, this indicator was 21.93 ± 5.28 pg / ml, which was also significantly different from the values before treatment (r < 0.05). The obtained results are presented in Table 5.

Table 5. Characteristics of the cytokine profile in children after treatment, (M \pm m).

Indicators	Control group	Until the cure	After conventional treatment	After immunocorrective therapy
IFN- γ	23.7 \pm 5.4	82.8 \pm 25.1*	42.8 \pm 6.2*	21.9 \pm 5.3 ^{^\circ}
IL-4	11.0 \pm 3.6	86.1 \pm 25.7*	62.6 \pm 21.1*	52.0 \pm 15.1

Note: * - control group information within comparison important, [^] - from treatment previous group information with compared to, ^o - traditional from therapy next data with compared (r < 0.05)

Examination of IL-4 levels after treatment revealed a significant difference between the values of children before and after treatment. At the same time, IL-4 level before treatment with immunocorrective drug was 86.1 \pm 25.7 pg/ml, and after treatment it was 52.0 \pm 15.1 pg/ml. In the study of IFN- γ , we found that this indicator significantly differed from the indicators of the immunocorrective group (r < 0.05). Thus, we found that the level of IFN- γ was normalized, but the level of IL-4 decreased significantly, but did not approach the values of the control group. In addition, suppression of IFN- γ was observed in the patient group after conventional therapy, but this indicator did not fall to the control level. This once again confirms the presence of an inflammatory process that continued against the background of conventional therapy without the use of immunocorrection. IL-4 did not significantly differ from the indicators in the children's group after the use of immunocorrection, but it was also observed that IL-4 did not decrease to normal values.

Above, we analyzed the IFN- γ /IL-4 ratio, which indicates the existence of an imbalance between pro-inflammatory and anti-inflammatory cytokines. We performed the same ratio analysis after treatment and found that this ratio was maintained in favor of increased pro-inflammatory cytokine production. Thus, in the group of healthy children, the value was 2.2. If the inflammatory process was clear, this indicator was 0.96 before treatment with immunocorrectors in the main group of children. At the same time, there was an imbalance of regulatory cytokines, which was expressed by a sharp increase in anti-inflammatory cytokines and a decrease in pro-inflammatory cytokines, which are the main regulators of inflammatory conditions.

4 Conclusion

Thus, the immunological studies we conducted to study the state of cellular, humoral factors and cytokine parameters of immunity allowed us to identify some changes or features characterized by severe immunodeficiency in children before treatment with immunotropic drugs and after treatment with normalization of the main immunity.

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