

Clinical-Neurological and Immunological Indicators Children with Helminth Infusion

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ABSTRACT

A detailed analysis of the main clinical and laboratory parameters in groups of children suffering from allergic rhinitis (AR) with concomitant hymenolepiasis in the course of antiallergic, antiparasitic and complex therapy is presented. Patients with AR with hymenolepiasis were divided into three groups: 21 patients received antiallergic, 22 patients - antiparasitic and 24 patients - complex therapy. The maximum clinical effect was achieved by us with the use of complex treatment, which included antiallergic and antiparasitic therapy.

The dynamics of immunological parameters after treatment of AR patients with hymenolepiasis only with antiallergic or antiparasitic drugs shows that, despite a positive result, it is insufficient and does not normalize immunological parameters. Complex antiallergic and antiparasitic treatment has a pronounced immunological effect, activates the severity of the immune response, switches the nature of the immune response to suppressive and thereby contributes to a more rapid relief of the allergic process in the body.

Relevance

Uzbekistan is among the countries with a hot climate, where helminthic and protozoal diseases are endemic [1]. Currently, the number of infected individuals is approximately 200,000, with children under the age of 14 constituting 70% of the cases. The most widespread protozoal invasion in Uzbekistan is giardiasis, while hymenolepiasis is the most common helminthic invasion [5, 8]. The wide distribution of parasitic invasions and the severity of the associated internal organ pathologies have not only medical but also socio-economic significance [4, 7, 12].

Parasitic diseases are characterized by relatively slow development, a chronic course, and often prolonged compensation. It is precisely these characteristics that mainly contribute to the underestimation of the medical and social importance of these diseases [2, 7, 9]. Parasitic diseases are the cause of delayed mental and physical development in children [10], reduce resistance to infectious and somatic diseases [1], decrease the effectiveness of vaccination [3], induce organism allergization, and induce secondary immunodeficiencies [11]. The presence of helminths and protozoa disrupts homeostasis in the body, leading to pathological and immunopathological processes that are adaptive in nature. The nervous system is the most sensitive to pathological shifts in homeostasis. At the same time, according to many researchers,

the restoration of bodily functions and human recovery also depend on the state of the nervous system. The composition of the organism determines the possibility of development and life activity of invasive agents, their activity, the extent of intraorgan changes, and the neurological complications they cause, while the activity of parasites and their ability to alter the physiological state of a person determine the severity of pathological shifts [2, 6]. Currently, research results show that combined forms of invasions, rather than isolated forms, have become more common. The main reason for this is the common routes of penetration of helminths into the human body, a decrease in the immune status of the body, and pathology of the gastrointestinal tract.

Thus, the relevance of studying neurological complications in the combined course of hymenolepiasis and giardiasis has increased in recent years due to the tendency of these parasitic diseases to increase in prevalence throughout the territory of the Republic of Uzbekistan, as well as the insufficient study of this problem and the ineffectiveness of existing drug therapy regimens.

Materials and Methods

The study presents an analysis of the results of dynamic observation of 120 pediatric patients aged 5 to 14 with central nervous system (CNS) intoxication due to giardiasis and hymenolepiasis infestations. Careful selection was conducted to form groups, with the aim of excluding the possibility of remote consequences of perinatal factors, previous cranial-cerebral traumas, infectious and viral diseases with high fever, which could potentially lead to CNS damage and autonomic disorders. In the presence of chronic foci of infection, a differential diagnosis of possible neurological complications was performed, with the mandatory condition of compensating the process during the study period. Subsequently, based on the obtained coprological data on the presence of protozoal and helminthic invasions, the examined children were divided into two groups. The first group (main group) consisted of 70 children (58.3%) with combined giardiasis and hymenolepiasis infestation, with a mean age of 9.7 ± 0.35 years. The second group (comparison group) comprised 50 children (41.7%) with isolated giardiasis infestation, with a mean age of 9.2 ± 0.6 years.

As a control, 40 children of similar age (mean age 9.1 ± 0.6), who had not experienced acute illnesses for 3 months, without chronic foci of infection that could affect the research results, and without neurological complaints, were selected. The study utilized clinical-neurological, clinical-laboratory-immunological, neurophysiological (EEG), and neurovisualization (CT and MRI examination) methods of investigation.

Results and Discussion: The main complaints of the patients and the primary reason for seeking medical attention were not the clinical signs of infestations but complaints of asthenoneurotic nature (48.4%), as well as seizure syndrome (30.8%) and tic hyperkinesias (20.8%). The clinical manifestations of combined hymenolepiasis and giardiasis infestations represented a combination of symptoms from each infestation. In the main group of children, the clinical presentation of hymenolepiasis infestation significantly prevailed, while the clinical presentation of giardiasis was more pronounced in the comparison group with isolated infestation. It should be noted that in our study, the examined children exhibited a dominance of signs of nervous system involvement over clinical symptoms of infestations.

In the majority of cases in the main group, seizure syndrome was observed (37; 52.9%), while it was absent in the comparison group ($P < 0.001$). Vascular dystonia (VD) predominated in the comparison group, which was detected in 43 children (86%) compared to 15 children (21.4%) in the main group ($P < 0.001$). Tic hyperkinesias were observed in both groups, but there was a significant prevalence in the main group (18; $25.7 \pm 3.2\%$ vs. 7; $14 \pm 4.9\%$; $P < 0.05$). The frequency of complaints related to autonomic disorders in the main group was significantly higher

compared to the comparison group ($P < 0.01$). However, specific complaints specific to the main group were also observed, such as fainting ($5.7 \pm 2.8\%$; $P < 0.001$) and hypersalivation ($80 \pm 4.9\%$; $P < 0.001$), which were characteristic of hymenolepiasis infestations.

Signs of asthenization were more pronounced in the comparison group, which was associated with the toxic effects of *Giardia* on the child's body, while these signs weakened when combined with hymenolepiasis. In the neurological status of children with combined infestation, scattered microsymptomatology was observed, including a uniform increase in tendon reflexes (55; $78.6 \pm 4.9\%$), tremors of eyelids and fingers of outstretched hands (31; $44.3 \pm 5.9\%$), fibrillary twitching of the tongue (26; $37.1 \pm 5.8\%$), pathological dermographism, deviation of vegetative tone indicators, orthostatic and clinostatic tests, and the Danini-Ashner test indicating sympathicotonia.

According to the results of all diagnostic tests, the pathogenesis of the syndrome of vegetative dystonia (VD) is based on parasitic intoxication, causing dysfunction of the vegetative centers in the hypothalamic region, which manifests as sympathicotonia and has a persistent course.

According to our data, tics were observed in 20.8% of all examined children (25 children), most commonly in the facial area - involuntary blinking of both eyes or simultaneous winking, frowning, furrowing of the brow, in the head and neck area - head jerking, shoulder shrugging, and in the limbs - flexion and extension of the foot, knee bending, and so on, which worsened with excitement and agitation in the child. It is worth noting that in children with isolated lamblia infection, tic hyperkinesias were only observed in the facial area (7 children) and were limited to eye blinking. Neurological examination of these children revealed uniform reactivity of tendon and periosteal reflexes (19 children - 76%), fibrillary twitching of the tongue (12 children; 48%), and mild tremor of outstretched fingers (11 children; 44%).

Thus, tic hyperkinesias in children with helminthic and protozoal invasions were functional in nature and correlated with neurological microsymptoms.

In 37 children with combined helminthic and protozoal invasions and seizure syndrome, generalized clonic-tonic seizures were characteristic in 72.9% of cases, with brief duration and no clear distinction between phases. Single seizures were observed in 13.5% of cases.

Unlike seizures of organic origin, there was no aura in parasitic invasions, and the main triggers for seizures were hunger and fatigue. Typical absences with cessation of activity and fixed gaze, without motor disturbances lasting 3-5 seconds, were present in 27.0% of children (10 children). Behavioral characteristics in all children with seizure syndrome included irritability, restlessness, decreased memory and performance, capriciousness, and tearfulness, among others. All children with seizure syndrome reported provocation of seizures by hunger, with patients experiencing pain in the left epigastric region and increased salivation. Neurological status in this group of children was characterized by scattered microsigns, accompanied by reactivity of tendon reflexes.

Rapid recovery of consciousness, absence or a short period after postictal sleep, and the lack of gross neurological symptoms in the neurostatus also distinguished these seizures from organic ones.

Thus, as a result of the conducted studies, signs of autonomic nervous system involvement were detected in all examined children with both combined and isolated forms of helminthic and protozoal invasions. When conducting tests to assess the state of the autonomic nervous system - the Danini-Ashner tests, orthostatic and clinostatic tests - a tendency towards shifting the measurement parameters towards sympathicotonia in the main group of children and parasympathicotonia in the comparison group of children was revealed. We conducted a comparative analysis of EEG studies in 102 children examined with neurological complications,

with 20 practically healthy children taken as controls. In the main group of children with combined helminthic and protozoal invasions, type 1 EEG was observed in 31.4% (22) of children, characterized by a well-formed alpha rhythm with an amplitude ranging from 48 to 100 μV and an index exceeding 87.5%. Observable zonal differences in the distribution of the main EEG rhythms and a moderate amount of slow waves were within the normal range of activity and age.

In the comparison group, this type was encountered in 18.8% (6) of cases. The second type of EEG, hypersynchronous, was observed in 17.1% (12) of children in the main group and 21.9% in the comparison group, characterized by gilasynchronization of burst rhythm. The main activity was absent or represented by isolated oscillations or small groups of alpha waves, both in the comparison and main groups. All children with the second type of EEG exhibited tic-like hyperkinesias. The fourth type of EEG was recorded in the majority of examined children, with 48.6% (34) in the main group and 59.4% (19) in the comparison group. It was characterized by the dominance of irregular theta and alpha activity in terms of frequency and amplitude (alpha rhythm index below 50%). Moderately pronounced diffuse changes in the bioelectrical activity of the brain cortex in both examined groups were statistically significant ($p < 0.01$) compared to the control group of nearly healthy children. It was also found that the prevalence of the fourth disorganized type of EEG in patients in the main group was lower compared to the comparison group, although it was not statistically significant. Immunological studies showed a decrease in CD3+ and CD20+ in children from both examined groups (CD3 - (CI = 1.27 and 1.30, respectively; CD20 - (CI = 1.58 and 1.61, respectively; $p < 0.05$), indicating suppression of phagocytosis, predominantly during combined invasion. CD4 was significantly decreased in both groups compared to the control (CI = 1.38 and 1.41, respectively; $p < 0.05$), which also indicates the suppression of T and B lymphocytes. According to our data, invaded children showed a decrease in CD8+ (CI = 1.14 and 1.18, respectively; $p < 0.05$) in the context of CD4+ suppression, indicating a disruption of the regulatory mechanism of the immune system due to the weakening of the function of the T-helper link.

As a result of the discoordinated decrease in the helper and increase in the suppressor potential, the immunoregulatory index decreased to 1.2 ± 0.01 in the main group (CI = 1.40) and 1.24 ± 0.02 in the comparison group (CI = 1.04), compared to 1.46 ± 0.02 in the control group ($p < 0.05$).

More pronounced changes were observed in the group of children with combined invasion (helminth and protozoan invasions). Against the background of a significant ($p < 0.05$) deficiency of total lymphocytes, CD4+ and CD8+ levels, a picture of immunodeficient state was observed.

Detection of specific IgM antibodies to *Giardia* antigens using the enzyme-linked immunosorbent assay (ELISA) method revealed that in the main group of children, IgM levels exceeded the normative values by nearly 4.5 times, while in the comparison group, it was 1.8 times higher. This indicated an acute course of the disease. According to our data, the level of antigen-binding lymphocytes (ABL) to intestinal antigens was almost 5 times higher in children from the main group and 6 times higher in the comparison group ($8.2 \pm 0.19\%$ and $10.7 \pm 0.2\%$ in the main and comparison groups, respectively, compared to the control value of $1.74 \pm 0.08\%$; $p < 0.001$).

When assessing brain involvement in invaded children, high levels of ABL to brain antigens were detected. In the group with a combination of hymenolepiasis and giardiasis, this indicator exceeded the control values by 5 times, while in isolated giardiasis, it was twice as high (7.0 ± 0.25 and 2.71 ± 0.1 versus $1.39 \pm 0.09\%$; $p < 0.001$).

Functional disturbances of the intestine in examined children, likely resulting from parasite activity, appear to be the main pathogenetic factors contributing to the development of the endogenous intoxication syndrome, as reflected in the levels of medium-molecular peptides

(MMP). The functional influence of the cellular immunity component is directly associated with endogenous intoxication, and its imbalance negatively affects the severity of neurological complications in the form of seizure and hyperkinetic syndromes, manifested by direct and inverse correlation of indicators (ranging from 0.8 to 0.32 and from -0.67 to -0.35). During this period, in addition to specific antigens, pathogenetic mechanisms include immune complexes and autoantigens resulting from the prolonged effects of parasites and depletion of compensatory capabilities of the body.

Conclusions:

1. The involvement of the nervous system due to parasitic intoxication in children with helminth and protozoan invasions manifested as seizure syndrome ($52.9\pm 5.9\%$), tic-like hyperkinesias ($25.7\pm 5.2\%$), and vegetative dysfunction syndrome (VDS) ($21.4\pm 4.9\%$), while in children with isolated giardiasis, these manifestations were observed as tic-like hyperkinesias ($14\pm 4.9\%$) and VDS ($86\pm 4.9\%$).
2. In the combination of giardiasis and hymenolepiasis, neurological complications were accompanied by a sympathetic tonus and reactivity with a higher score for VDS. In children with isolated giardiasis, neurological complications were mostly accompanied by a predominant parasympathetic direction.
3. The formation of secondary immunodeficiency was mainly attributed to the suppression of the T-helper and suppressor components, as well as B-lymphocytes, with more pronounced effects in children with combined giardiasis and hymenolepiasis.

Considering the high levels of antigen-specific lymphocytes (ASL) to brain and intestinal antigens in cases of combined invasion and predominantly ASL to intestinal antigens in isolated protozoan invasion, it can be concluded that the nervous system is more affected in patients with combined helminth and protozoan invasions, which correlated in our research with the results of clinical observations. The presence of endogenous intoxication, confirmed by high levels of medium-molecular peptides (MMP) in both groups compared to the control group ($p < 0.05$), was characteristic of all children with combined helminth and protozoan invasions with neurological complications.

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