POSTPARASITIC MICRONUTRIENT DEFICIENCY IN CHILDREN.

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Summary.
Post-parasitic micronutrient deficiency is an umbrella term for a set of persistent symptoms that can develop in patients who have had intestinal parasites in children.
The purpose of the work is to systematize data on the role of micronutrients in the diagnosis and treatment of intestinal parasitosis in children.

Material and methods. The authors carried out a systematic analysis of foreign (google scholar, ncbi.nlm.nih.gov) and Russian (elibrary.ru) scientific publications. Results. The most common symptoms that can persist for a long time after intestinal parasites in children can be divided into the following groups: 1) macronutrient deficiency; 2) deficiency of trace elements; 3) deficiency of vitamins; 4) gastrointestinal symptoms. The literature review presents generalized data on the content of essential vitamins, macro- and microelements in the body and the provision of children and adolescents at the present time, the most important causes of the development of micronutrient deficiencies arising from intestinal parasitosis in childhood are given. The consequences for the growing organism of the violation of the content of vitamins and macro- and microelements in parasitosis are described, the characteristics of the content of micronutrients in the biological environment of the body of children are given, the relationship between the clinical manifestations of helminthiases with deficiency and imbalance of the vital elemental balance and its effect on clinical manifestations are revealed.

Conclusion. Based on the conducted review studies, it becomes clear that helminthiases alter the levels of various trace elements in children compared to children without parasitic infestation. Therefore, individualized dietary therapy (such as biofortification) is offered to infested children with the addition of possible multimineral supplements to antihelminthic treatment.

Key words: children, intestinal parasitosis, micronutrients, deficiency, vitamins, macro- and microelements.

Helminthiases are an extensive group of parasitic diseases caused by helminths (parasitic worms), which largely determines the state of public health. According to the World Health Organization (WHO), helminthiases are ranked 4th in terms of damage to the health of the Earth's population (after diarrhea, tuberculosis and coronary heart disease). Every year, approximately every second person on the planet becomes infected with one of the 3 main types of helminths, which leads to ascariasis (1.2 billion people), hookworm
(900 million) and trichuriasis (up to 700 million). [12]
Similar trends are observed in Russia, where an increase in the incidence of helminthiases has been registered in recent years. Thus, an increase in toxocariasis (by 64% in 1 year), echinococcosis (by 3 times in 5 years) was recorded, an increase in the incidence among children was noted, with 75% of the incidence of parasitic diseases in the urban population [26]. Intestinal parasitosis and in modern conditions are the most common pathology of the child population and therefore represent a serious socio-economic significance. The performed analysis of literature data shows that in the successful resolution of the problem of intestinal parasitosis and children's health, the following tasks are of paramount importance: rationalization of

approaches for a comprehensive examination of children for the main nosology of intestinal parasitosis; assessment of the incidence of intestinal parasitosis in children; reliable assessment of the impact of intestinal parasitosis on the physical and mental development of children, on their health parameters; identification of epidemiological patterns in the incidence of intestinal parasitosis in children; evaluation of the effectiveness of combinations of the main antiparasitic drugs in the treatment of children with individual and mixed nosological forms of intestinal parasitosis; development of methods for the rehabilitation of the health of children exposed to intestinal parasitosis; approbation of regional epidemiologically substantiated preventive measures to reduce the risk of infection of children with intestinal parasitosis [18].

It is known that in the prevention and treatment of intestinal parasitosis, adequate intake of micronutrients plays an important role in maintaining immunity, growth and development of children, increasing the functional reserves of the body, reducing the risk of infection, the duration and severity of the disease. In this aspect, the scientific literature focuses on the role of vitamins A, B6, B12, C, D, E, folic acid, as well as macro- (calcium, phosphorus, sodium, chlorine, magnesium, potassium) and microelements (iron, selenium, copper, zinc.) [1, 10]

Taking into account the relevance of the problem, the purpose of this work was to systematize data on the role of micronutrients in the diagnosis and treatment of intestinal parasitosis in children.

Material and methods. The authors carried out a systematic analysis of foreign (google scholar) and Russian (elibrary.ru) scientific publications.

Results. Postparasitic micronutrient deficiency is an umbrella term for a complex of persistent symptoms that can develop in patients after intestinal parasite exposure in children. The most common symptoms that can persist for a long time after intestinal parasites in children can be divided into the following groups: 1) macronutrient deficiency; 2) deficiency of trace elements; 3) deficiency of vitamins; 4) gastrointestinal symptoms. In the last decade, an analysis of the level of achievements shows that the attention of a wide range of clinicians and biomedical researchers is attracted by the study of the content of macro- and microelements in biological structures in pathological conditions. Subsequently, this term was used only to determine the imbalance of chemical elements with low and very low content in human tissues, and the term “imbalance” began to be used to denote violations of the concentrations of the entire complex of chemical elements in pathological conditions [1, 3, 4, 14, 17] .

The problem of microelementoses is very relevant, and the causes that contribute to the occurrence of metabolic disorders of macro- and microelements, according to special literature, are diverse. Microelementosis is a serious health problem in many foreign countries [23, 29]. According to the authors, children are more likely to be deficient in such vital trace elements as zinc, copper, and iron [5, 21, 28].

Low levels of zinc in the hair, recognized as an indicator of zinc deficiency, occur in Russia on average in 20-40% of children, low levels of iron - in 22% of children, copper - in 6-22% of children, selenium - in 98% of children, cobalt - in 75% of children, excess calcium - in 48%, iron - in 22%, copper - in 33% [16].

Most often, violations of the elemental status of children are associated with the influence of such factors as poor nutrition, consumption of poor-quality drinking water, age-related and anatomical and physiological characteristics [31, 32].

Malnutrition (malnutrition) and infections are common health problems in developing countries. Although these diseases may exist independently of each other, they are inextricably linked [21].

Similarly, about 2 billion people worldwide suffer from deficiencies in essential micronutrients such as zinc (Zn) and iron (Fe), as well as 23 vitamins A, C and E. Malnutrition (malnutrition) has been identified as the main cause of immunodeficiency affecting infants, children, adolescents, pregnant women and the elderly [30]. Other mechanisms for the development of micronutrient deficiencies are also discussed, among which malabsorption in the small and duodenal intestines is most often mentioned. An analysis of the literature data shows the scale and significance of the problem of intestinal invasions. The harm caused by intestinal parasites to the developing organism of a child should certainly not be underestimated. The primary condition in solving this problem is the development of modern, complex methods for diagnosing intestinal parasitosis, and also, taking into account the immaturity of the child's immune system, the development of an algorithm for antiparasitic measures before routine vaccinations of children [2].

The cause of micronutrient deficiencies in preschool children is considered to be malabsorption in the small intestine and duodenum due to intestinal helminthiasis. Helminths, penetrating into the human body, have the potential ability to disrupt the microecological balance in the intestinal lumen and cause an imbalance in the microbial flora. Microecological disturbances, in turn, often serve as a trigger for the onset and then maintenance of pathological processes. Among the conditions accompanied by pathological manifestations of microelement deficiency, parasitoses are always mentioned that occur when digestion and intestinal absorption are disturbed, both of exogenous and endogenous origin. First of all, intestinal giardiasis with anemia (iron deficiency), there is a low efficiency of including the missing trace elements in the complex of therapeutic measures due to their poor digestibility [21]. An analysis of the literature showed that the most characteristic conditions for the chronic phase of helminthiases, especially intestinal ones, are iron deficiency anemia, polyhypovitaminosis, reduced resistance and changes in reactivity. The high frequency of anemia in helminthiases is explained by a number of factors: helminths actively use dietary iron to carry out their vital activity [20, 22].

There are very few data on the study of the composition of other minerals in the body of patients infested with helminths. And studies of the mineral profile of children with helminthiases in the available domestic literature are rare [13]. According to A.A. Mochalova (2014), the results of determining the content of microelements in school-age children of the Luhansk region suffering from parasitic invasion showed changes in the microelement composition in blood serum and urine, manifested by a decrease in the content of essential microelements against the background of accumulation of toxic ones. The content of trace elements in the blood depends on the type of parasite carrier. In children with parasitic invasion, a violation of the content of microelements in the blood serum is accompanied by increased urinary excretion of zinc, copper, strontium, chromium and reduced excretion of iron. Iron deficiency conditions have been described in helminthiases, which usually develop gradually and are manifested by pallor, dryness and flaking of the skin, seizures, brittle hair and hair loss, fatigue, and weakness [22].

According to I.A. Lokhmatova (2018) when examining 43 children aged 7 to 18 years with ascariasis: the content of 19 chemical elements was determined (Ca, Zn, K, I, Cu, Se, Fe, Mn, Cr, S, Br, Cl, Co, Ni, Mo, Sr, Ba, Pb, Cd) in the hair of children. A low content of Zn, Cu, I, Se, Fe and Se, Br, Co, Ni, as well as an increase in toxic Pb and Cd in the hair of younger schoolchildren was established. Infected older schoolchildren showed significantly reduced levels of Ca, Zn, Cu, Fe and Br, Ni, Mo, as well as elevated levels of Ba, Pb, Cd. Based on the data obtained, the author draws the following conclusions: the imbalance of micro- and macroelements in the intestinal stage of ascariasis in children is an important pathogenetic link in the formation of the main clinical syndromes in children: functional disorders of the digestive tact (Fe, Se, Cu), immunological maladaptation (Zn, Ni , Fe, Cd) and asthenic syndrome (Br, N, Mo, Pb). Replenishment of microelement imbalance at the stage of treatment and rehabilitation of children with ascariasis is pathogenetically substantiated and contributes to the speedy restoration of all disturbed functions of the macroorganism. Given the pathogenetic mechanism of intestinal parasites in the child's body, as well as the role of minerals in the formation, functioning and development of a growing organism, the issue of studying the elemental composition in children with ascariasis is extremely relevant. In recent years, it has been established that with helminthiasis, the production of insulin-like growth factor and collagen decreases, the synthesis of tumor necrosis factor increases, which contributes to a decrease in appetite, a decrease in absorption processes in the intestine and, ultimately, a lag in physical development. Intestinal helminths contribute to the activation of T-helper type 2 with an increase in the production of interleukins 4, 5 and 13 and the synthesis of antibodies, including class E [15].

At the same time, ascarone, as a powerful allergen secreted by ascaris, causes thymus hypofunction. And in addition to everything, a deficiency of a number of trace elements (phosphorus, iron, zinc, copper, selenium, silicon) is also capable of causing disturbances in cellular and humoral immunity. For example, thymulin is active only in combination with Zn2+ ions. Zinc is also an important component in the functioning of the antioxidant system. Insufficiency of magnesium ions reduces the differentiation of T-killers, affecting the differentiation of the latter into mature effectors. With copper deficiency, the functions of T-helpers suffer, and the release of lymphocyte activating factors by them is delayed. The development of allergic diseases leads to the influence of toxic metabolic products of ascaris (ammonia, lactic acid, urea), as well as a

consequence of impaired protein breakdown and the formation of large molecular compounds. The connection between the development of allergic diseases and the imbalance of micro- and macroelements has been proven: deficiency of phosphorus, zinc, magnesium and selenium; an excess of nickel, cobalt, lead can lead to the development of allergies. In 75.3% of cases, parasitosis is accompanied by various lesions of the gastrointestinal tract [15].

Deficiency of certain chemical elements leads to dysfunction of the gastrointestinal tract. In particular, bromine is involved in the activation of pepsin, promotes the functioning of amylase and lipase, with its deficiency, the breakdown of proteins, fats, and carbohydrates is disrupted. Cobalt, copper, phosphorus, zinc, and magnesium are involved in protein metabolism, which is disturbed in the absence of such elements [14].

In the assimilation of microelements, changes in the mucous membrane of all parts of the gastrointestinal tract with signs of dystrophy and atrophy of the epithelium play an important role. At the same time, villi and crypts shorten and flatten, the number of microvilli decreases, fibrous tissue grows in the intestinal wall, blood and lymph circulation deteriorates, and intestinal absorption processes decrease. Such changes can reduce the bioavailability of trace elements [14].

An analysis of foreign literature showed that various relationships were registered between helminthiases and a deficiency of vital microelements. Fe and Zn deficiencies have been found to predispose humans to helminth infections, which in turn can also exacerbate nutrient deficiencies, thereby helping helminth survival [6, 25].

Helminthiases worsen nutritional status in several ways. They feed on host tissues (including blood), thereby causing iron and protein loss. They also increase nutrient malabsorption and may compete for vitamin A in the gut. In addition, roundworms can cause loss of appetite. There is evidence to suggest that adding multimineral supplements to deworming programs may offer some benefits [33].

However, these studies are insufficient to make any clear and reliable suggestions. This issue is even more difficult in developing countries (where micronutrients and helminthiases are most common), as there is a limited set of clear treatment recommendations and additional vitamin-mineral complexes that focus on individual micronutrients [19].

In addition, there is a lack of information on the pattern of micronutrient deficiencies in the most vulnerable group - children, who are more at risk of both malnutrition and helminth infestation. Iron (Fe) is an essential micronutrient whose deficiency most adversely affects infants, children, and women of reproductive age. According to the results of a number of studies, 30%-40% of preschool children 27 have Fe deficiency, which can lead to a decrease in neutrophil activity (with a decrease in myeloperoxidase activity) and impaired cellular immunity [21]. In addition, the results of this study may be a consequence of malabsorption and the systemic effect of invasion, as well as the use of iron (Fe) by parasites for their growth and reproduction. It has also been proven that helminths such as A. lumbricoides can interfere with iron (Fe) absorption in the duodenum and jejunum.

According to O.A. Kuliyev (2019), the significance of micronutrient imbalance in children suffering from helminthiases and their effect on the development of anemia in children showed that the amount of iron (40.9 ± 1.7), manganese (8.1 ± 1.7), chromium (4.1 ± 0.7), iodine (1.9 ± 0.9), antimony (4.3 ± 0.8) in the hair of children with anemia is significantly less than in children with who do not have anemia ($R<0.05;<0.01$). It was found that the difference between the level of copper, zinc, cobalt, selenium, chromium, cadmium is unreliable ($p>0.05$). In cases where anemia in children is accompanied by helminthiases, there is a sharp increase in the level of micronutrients: iron, copper, zinc, and folic acid deficiency is also observed ($p<0.05$; $p<0.01$). Among children suffering from anemia, helminthiases were detected 5 times more often than among healthy children - respectively in 25 and 5% ($p<0.001$), which indicates the presence of a relationship between these diseases..

The content of iron in parasitic infections of the intestine - hookworms closely associated with iron deficiency anemia is described in the works of Hesham M.S. (2004). Hookworm infections cause damage to the intestinal mucosa, which leads to endogenous loss of iron and other trace elements. Parasitic infections leading to bleeding (eg, hookworm and schistosomiasis) are known to be predictors of low iron levels leading to iron deficiency anemia (IDA). A study by the authors of 427 children with the determination of serum hemoglobin and ferritin and their impact on the cognitive function of children showed that there is a significant relationship

between cognitive function and hemoglobin. The adverse effect of iron deficiency on the cognitive function of children can be explained by a decrease in the synthesis, absorption and degradation of neurotransmitters. A study of the relationship between intestinal parasites and nutritional status in northeastern Thailand among rural and urban children aged 3–8 years showed that anemia was more common among infected children (59%) and children infected with giardiasis (61%) than among uninfected children (42%). Daily iron intake, as well as mean hemoglobin, hematocrit and serum ferritin levels, were significantly lower in infected children than in uninfected children. Also, there was a significant decrease in hemoglobin, hematocrit, and serum ferritin with an increase in the number of parasites in children. The study also showed that most of the anemias that occur in children with multiple infections are caused by iron loss due to parasitic hookworm infections. A study conducted among elementary school children in Panama showed that the concentration of hemoglobin in the blood is significantly lower in children with severe trichuriasis. Children with concomitant T. trichiura and hookworm infections also had significantly lower hemoglobin concentrations than children who were uninfected or once infected with one of these helminthiases. A study looking at the association of trichuriasis and iron status among 409 Jamaican children reported that the prevalence of anemia (Hb < 11.0 g/dl) among severely infected children (33%) was significantly higher ($p<0.05$) than the rest of the sample (11%). This study also suggested that iron deficiency anemia is associated with severe trichuriasis in Jamaican children. Studies that have been conducted with a high prevalence of hookworm infection have observed that hookworm infection was a strong predictor of IDA and anemia in school-age children [27]. Enterobiosis is one of the most widespread helminthiases and confirmation of its pronounced impact on the physical development of children is a very serious fact. Poor nutrition and low anthropometry almost always accompanies invasion by intestinal parasitosis. Even mild to moderate infestation affects children's health, with lower weight, weight-for-height ratio, blood hemoglobin levels and blood oxygen saturation and iron deficiency. With a high intensity of ascariasis after treatment with albendazole in children, an acceleration of their growth was observed. A decrease in all anthropometric indicators in children is recorded in almost all intestinal parasitosis. In all cases, when children were dewormed, a rapid increase in their anthropometric parameters was observed, while albendazole, mebendazole, niclosamide, pyrantel, metronidazole, furazolidone, levamisole were used depending on the nosoform of invasions. Almost all children improve intestinal nutrition and absorption of vitamins. A significant relationship was found between a decrease in ascariasis and an increase in body length as early as 3 months after treatment, and after 12 months, the growth of children reached the control values. Even with giardiasis, which for a long time was considered not so pathogenic, a delay in the growth and weight of children was recorded. At the same time, it has been calculated that the cost-effectiveness of treatment far outweighs the damage caused by intestinal parasitosis to the health of children. Therefore, programs of mass treatment of children are proposed as a necessary means of improving their health, as well as the implementation of appropriate preventive measures to reduce the risk of infection of children with intestinal parasitosis [18].

Zinc is one of the most important essential minerals necessary for the activity of more than 300 enzymes involved in carbohydrate and protein metabolism, iron biosynthesis, and carbohydrate transport [16].

Zinc plays an important role in the immune response because its deficiency reduces non-specific immunity, reduces the number of T- and B-lymphocytes, and suppresses delayed-type hypersensitivity, cytotoxic activity and antibody production. There is evidence that children of preschool and school age infested with helminthiases have lower levels of zinc (Zn) compared to children without parasitic infestation. The low zinc (Zn) levels that have been observed in children with invasion may be due to poor dietary intake (due to loss of appetite), gastrointestinal bleeding, malabsorption, or diarrhea [24]. . Zinc (Zn) deficiency reduces resistance to infectious diseases by affecting the ability of T cells to form interleukin-4, which is an important component of the cytokine required to lead to an optimal 2nd order helper T cell response, thereby causing a defective immunoglobulin response (Ig) E, which plays an important role in the control of helminthiases [7, 8, 11].

These data allow us to explain why some parasites survive better under Zn-deficient conditions of the host than under conditions of microelement balance. Selenium (Se) is an essential trace element for an effective immune response. It is an integral component of glutathione peroxidase, selenoprotein-P, and thioredoxin reductase. The content of Se depends on its concentration in plant products, which reflects the concentration

in the soil in which the plants were grown. Similarly, Se concentrations in animal foods depend on the Se content of plants used for food. There is increasing evidence that serum levels of selenium (Se) and several other vital trace elements are reduced in helminthiasis [33]. A change in the content in the body of one of the essential, vital trace elements (deficiency, excess or imbalance) disrupts their homeostasis in all living systems, organs, tissues, cells. Many enzymes either contain metals embedded in them or are specifically activated/inhibited in the presence of trace elements. The presented data suggest that the development of new treatment tactics will improve the results of treatment of various microelementoses in the human body that complicate the course of diseases [9].

Studies conducted in different regions of Russia, which is close to us in terms of socioeconomic parameters, testify to the insufficient provision of healthy children of preschool and school age for basic vitamins: 80-90% of children have a lack of vitamin C, 40-80% of vitamins of group B and folic acid. acids, more than 40% - vitamins A, E and carotene. Examination of sick children revealed a deficiency of vitamin C in 60-70% of children, vitamin B1 - in 40-45%, B2 - in 50-60%, E - in 40-60% of patients. An imbalance of chemical elements was found in 76% of healthy and sick children, and a deficiency of zinc, iron, calcium - in 52%. At the same time, the detected deficit is often

nature of combined vitamin deficiency. It is also alarming that vitamin deficiency is found not only in winter and spring, but also in summer-autumn periods, which indicates the formation of an extremely unfavorable year-round type of polyhypovitaminosis in the majority of the population. Data on the prevalence of micronutrient deficiencies in pregnant and lactating women, newborns and infants are alarming [10].

Conclusion.

Based on the conducted review studies, it becomes clear that helminthiases alter the levels of various trace elements in children compared to children without parasitic infestation. Therefore, individualized dietary therapy (such as biofortification) is offered to infested children with the addition of possible multimineral supplements to antihelminthic treatment. At present, the relationship between the clinical manifestations of helminthiases and the deficiency of vital trace elements has already been identified. Among numerous studies in the field of pathogenetic features of helminthiases, single works reflect the imbalance of elemental balance and its effect on clinical manifestations. The use of vitamin-mineral complexes in postparasitic invasions in order to provide the child's body with the necessary micronutrients should be justified, and requires a balanced approach in choosing a specific drug and should not be isolated from attempts to provide the growing and developing child's body with a complete and balanced diet. In published research results, the data presented are insufficient to make any clear and reliable suggestions for micronutrient deficiencies in preschool and school-age children with intestinal parasitosis.

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