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FEATURES OF ZINC METABOLISM IN NEWBORN AND INFANT CHILDREN

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Abstract. The child's body is in the process of continuous growth and development, and the violation of its normal course is regarded as an indicator of ill health. An important role is given to the deficiency of essential micronutrients, among which zinc is of particular importance. This trace element is necessary in the antenatal and postnatal periods, since it affects cell division and differentiation, neurogenesis, osteogenesis, is involved in cell metabolism, is an antioxidant protection factor, and also maintains homeostasis in the body. Zinc deficiency is associated with the development of immunopathological reactions that underlie the development of allergies, a decrease in the regenerative capabilities of the skin and mucous membranes. This article will consider the main aspects of the clinical significance of the trace element in newborns and young children.

Key words: *newborn; zinc; microelementoses.*

ОСОБЕННОСТИ ОБМЕНА ЦИНКА У НОВОРОЖДЕННЫХ И ДЕТЕЙ РАННЕГО ВОЗРАСТА

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Резюме. Организм ребенка находится в процессе непрерывного роста и развития, и нарушение его нормального хода расценивается как показатель неблагополучия в состоянии здоровья. Важная роль при этом придается дефициту эссенциальных микронутриентов, среди которых особое значение отводится цинку. Данный микроэлемент необходим в антенатальный и постнатальный периоды, поскольку он оказывает влияние на деление и дифференцировку клеток, нейрогенез, остеогенез, участвует в обеспечении клеточного метаболизма, является фактором антиоксидантной защиты, а также поддерживает гомеостаз в организме. С дефицитом цинка связано развитие иммунопатологических реакций, лежащих в основе развития аллергии, снижения регенераторных возможностей кожи и слизистых оболочек. В данной статье будут рассмотрены основные аспекты клинического значения цинка у новорожденных и детей раннего возраста.

Ключевые слова: *новорожденный; цинк; микроэлементозы.*

LONG-TERM EFFECTS OF ZINC DEFICIENCY DURING PREGNANCY

In recent years, the problem of macro- and microelementosis in various pathological conditions remains very controversial. This is due to the fact that most of these elements are part of biologically active substances or influence them, thus participating in most metabolic and immune processes in the child's body and determining the functional state of its various organs and systems [1]. Micronutrient deficiencies are dangerous because they do not clinically manifest for a long time, thus causing a period of «hidden hunger». In addition, it should be noted that deficiency of essential elements, such as zinc, has the most severe consequences for health [2].

Unbalanced nutrition, considered by the World Health Organisation (WHO) as a problem of starvation, and, in particular, mineral deficiencies are often observed in the majority of the population (including pregnant women and lactating mothers), which, in turn, has a direct impact on morbidity and mortality. In addition, during pregnancy, the need for minerals increases significantly, and nutrition determines both the health of the mother and the full health and development of her future baby. In foreign studies it is noted that zinc deficiency increases the risk of pathological course of pregnancy and childbirth, uteroplacental circulation disorders, which, in turn, can cause chronic placental insufficiency, which leads to impaired nutrition of the foetus, the emergence of chronic hypoxia and delay in its intrauterine development. The impact of malnutrition during pregnancy may be comparable to the role of genetic factors and active chemical or infectious teratogens.

Normally zinc is actively transported through the placenta and accumulates in the organs and tissues of the fetus, mainly in the brain, liver, pancreas and bone tissue. Disturbances in homeostasis in the intrauterine and antenatal period can lead to the development of malformations, signs of dysadaptation, hypothorphy, anaemia and other nutrient-dependent diseases, disorders of physical and psychomotor development of the baby, as they and the mother represent a single biological system in which changes in the state of one of the links are reflected in the functional activity of the other. Analysis of zinc content in umbilical cord blood revealed zinc deficiency in preterm newborns compared to term infants. At the same time, in about one in ten of very low birth weight infants the concentration of zinc in cord blood did not differ from that in preterm infants with normal body weight. It was found that newborns with zinc deficiency more often had an unfavourable course of the period of early neonatal adaptation. Such indicators as the child's condition at birth, Apgar score, degree of weight loss, severity of borderline conditions and morbidity were significantly different [3, 4].

EFFECT OF TRACE ELEMENTAL NUTRITION ON METABOLIC PROCESSES IN A CHILDREN

Children with zinc deficiency are significantly more likely to have dry skin, perioral and periorbital dermatitis, pathological changes in skin derivatives in the form of dystrophic changes in the nail plate, hyperkeratosis of the nail bed, impaired hair growth and structure, as well as the development of eczema, psoriasis and furunculosis [5, 6]. Skin injuries in children with microelementosis heal much slower than in healthy babies. Atopic dermatitis is accompanied by more pronounced hyperproduction of IgE, increased number of eosinophils, decreased number of lymphocytes in peripheral blood, increased ratio of CD4+/CD8+ immunophenotypes of lymphocytes in blood. The obtained data are probably related to the fact that the deficiency of zink leads to atrophy of the thymic-lymphatic system (manifested by atrophy of thymus, tonsils, lymph nodes, spleen), decreased function of macrophages and T-lymphocytes, and, consequently, to depression of cellular immunity, decreased level of immunoglobulins and formation of allergic reactions of the reactive type. In childhood, at the stage of formation of specific defence mechanisms, these changes may contribute to the development of allergic reactions of both general and local nature [7].

The deficiency of zink in early childhood undermines the healthy functioning of the circulatory system and disrupts hematopoiesis [8]. The trace element is part of the enzyme carboanhydrase, which is found mainly in erythrocytes and is directly involved in the transfer of carbon dioxide to the lungs. In addition, the fact that the development of iron deficiency anaemia in zinc deficiency has been established. Zinc-dependent anaemia, the main symptoms of which are taste perversion and muscular hypotonia of the child, has been described. Since zinc is involved in the formation of antioxidant status as a protector of free-radical reactions [9], its deficiency adversely affects the morphofunctional state of the endocrine and reproductive systems and may cause late puberty and pathological disorders in the development of the child's reproductive organs: uterus in girls and testicles in boys.

ROLE OF ZINC IN THE FORMATION MUSCULOSKELETAL SYSTEM OF THE CHILD

When assessing the structure of musculoskeletal system pathology in children with zinc deficiency, it was found to be represented [10]:

- posture disorders — 39%;
- scoliosis — 19%;
- flat feet — 31%;
- flat-valgus or varus position of feet — 42%;
- valgus of knee joints — 22%.

At the same time, more severe forms of these diseases were observed in zinc-deficient young children.

This is explained by the fact that zinc is one of the cofactors of enzymes responsible for the synthesis of collagen and glycosaminoglycans, and participates in the performance of bone-forming cells (osteoblasts) of their main function — the synthesis of bone matrix. Moreover, the trace element is part of bone alkaline phosphatase and is associated with skeletal calcification, formation of hydroxyapatite, which determines its role in the maturation of the bone system.

ZINC IN THE DEVELOPMENT OF CNS STRUCTURES

The unique role of zinc in the development and activity of the central nervous system and behaviour has been proven. Compared to other organs in the baby's body, the highest zinc content is found in the brain (150 μmol/L), ten fold higher than its concentration in serum. The highest concentration is found in the neocortex, hippocampus, striatum and amygdala [11–14]. In zinc deficiency, conditioned reflexes are produced more slowly and learning ability is reduced. It is believed that in conditions of hypocincaemia the nuclear-cytoplasmic ratio of brain cells changes, brain development and structural maturation of the cerebellum are delayed. Deficiency of the mineral is especially dangerous during critical periods of brain development (antenatal stage, age from birth to three years). The child becomes more often ill, capricious, quickly tired [15]. In neglected cases, this can lead to the development of intellectual disability or serious mental illness. Autism spectrum disorders are one of the most complex types of child psychopathology in terms of etiopathogenesis and clinical and diagnostic differentiation. The peculiarity of autism spectrum disorders is the violation of the status of microelements, in particular, zinc deficiency. Intrauterine deficiency of this mineral occupies a key place among the causes of hypocyncaemia in autism spectrum disorders, which contributes not only to complications in pregnancy, but also to defects in fetal development and disruption of the functioning of organs and systems [16, 17].

It is important to note that the metabolism of zinc and vitamin A are closely related. It has been experimentally established that impaired absorption of zinc in the intestine worsens with vitamin A deficiency. In addition, all steps of the vitamin A enzymatic cascade are served by zinc-dependent enzymes. There is evidence that protein and zinc deficiency inhibits the synthesis of retinoic acid-binding protein. Thus, hypocincaemia also affects the baby's vision and may cause the development of myopia.

THE RELATIONSHIP BETWEEN GASTROINTESTINAL PATHOLOGIES AND HYPOCYCAEMIA

The importance of zinc for the normal functioning of the gastrointestinal tract lies in modulating the concentration of intracellular cyclic adenosine monophosphate (cyclic AMP), stimulation of absorption processes in enterocytes, and regulation of intestinal neurons. In addition, zinc as a component of the zinc ring takes part in the formation, migration and specification of cells in the neural crest, which are derived from the enteric nervous system [18].

In animal experiments, it has been proved that hypocincaemia causes the following disorders: significant reduction in the length of the small intestine, morphological changes in the jejunum, shortening and narrowing of villi, decreased absorptive surface, inhibition of mucosal cell proliferation and slower migration, decreased proliferation of crypt cells, ultrastructural changes at the cellular level, such as the appearance of membrane-bound autophagic vacuoles, pycnotic nuclei and enlarged nucleus periphery, as well as impaired intestinal mucin composition, which is accompanied by dysfunction of mucin-secreting goblet cells. Chronic zinc deficiency reduces the activity of disaccharidases, the full functioning of which is necessary for carbohydrate digestion and absorption of saccharides. Thus, zinc deficiency has a negative effect on the structure and function of the intestinal epithelium, characterized by impaired absorption of essential nutrients, malnutrition, diarrhoea and inflammation in the immature gut of the newborn.

Inflammation in the gastrointestinal tract can cause intestinal permeability, commonly referred to as «leaky gut» [19]. Gaps between cells in the small intestine can result in food and other toxins not being fully broken down as they enter the bloodstream, which can trigger an immune system response that triggers antibody production, thereby promoting chronic inflammation. Prolonged inflammation can affect microbial proliferation in the gastrointestinal tract and cause vitamin and mineral deficiencies, food allergies, and the development of autoimmune diseases such as celiac disease [20, 21].

In addition, zinc ions as a cofactor not only participate in insulin processing and storage, but also serve as a signalling molecule for α-cells, being released into the extracellular space after insulin secretion [22]. The discovery of zinc-finger sites in proteins has shown the structural function of zinc. Zinc stimulates insulin synthesis and is a part of its crystals, which are localized in secretory granules of pancreatic islet cells.

Thus, in children with serum zinc deficiency at birth, the deficiency of this trace element persists in early childhood, having a negative impact on growth processes and a harmony of physical and neuropsychiatric development, an allergopathology (among which atopic dermatitis takes the leading place), as well as diseases of the gastrointestinal tract, musculoskeletal and immune systems of the body [23].

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