

## MODERN PERSPECTIVES ON MICRONUTRIENT STATUS AND ALOPECIA

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**Abstract:** The article presents data on the current state of the problem of the use of trace elements in the treatment of various types of alopecia, provides data on clinical research in the use of zinc, selenium, copper, manganese and other trace elements in the treatment of alopecia. Besides, the review reveals pathogenetic mechanisms of hair loss development in the deficiency, imbalance and overabundance of microelements in the organism.

**Keywords:** focal alopecia, diffuse alopecia, trace elements

### СОВРЕМЕННЫЕ ВЗГЛЯДЫ НА МИКРОНУТРИЕНТНЫЙ СТАТУС И АЛОПЕЦИЮ

**Аннотация:** В статье представлены данные о современном состоянии проблемы применения микроэлементов в лечении различных видов алопеции, приведены данные клинических исследований применения цинка, селена, меди, марганца и других микроэлементов в лечение алопеции. Кроме того, в обзоре раскрываются патогенетические механизмы развития облысения при дефиците, дисбалансе и переизбытке микроэлементов в организме.

**Ключевые слова:** очаговая алопеция, диффузная алопеция, микроэлементы.

### INTRODUCTION

Hair loss is one of the most common problems that patients present to dermatological institutions. Several studies have shown that almost half of all men and women experience this condition by the age of 50, causing psycho-emotional discomfort and decreased self-esteem, thereby reducing patients' quality of life [1]. The global market for alopecia services and medications was \$2.6 billion in 2019, with an average annual growth rate of 9.5%. Key to the growth in demand for these types of services has been the increasing prevalence of androgenetic and focal alopecia, which is due to changing lifestyles around the world, including tobacco smoking, excessive alcohol use, and increased stressors as strong triggers for these conditions. In addition, the fashion and societal trend towards aesthetics is the reason for this, which is the incentive to use this kind of service [1]. Due to the variety of forms of alopecia and etiological factors, as well as pathogenetic mechanisms, the range of treatments and methods used is broad and varied, ranging from conservative to hair transplantation. In spite of this the results of treatment still remain disappointing, which is the reason for further search and scientific researches in this field.

### MATERIALS AND METHODS

Currently, there is no single approach to the treatment of alopecia, as in each case of the disease its tactic is determined individually, taking into account a number of factors. One of the important components of the treatment of dermatological diseases in general and alopecia in particular is the use of vitamins and micronutrients, as well as the correction of the diet. Vitamins and trace elements are widely used in the conservative treatment of alopecia, but the application of most micronutrients is done empirically, without taking into account the quantitative and qualitative content of microelements in the body. In addition, research in the field of studying ways to correct micronutrient deficiencies is also scarce. It should also be noted that the irrational use of trace elements can adversely affect not only the state of the body, but also the hair, causing

microelementosis, which is a prerequisite for studying and developing scientifically sound approaches to the use of trace elements in alopecia. Micronutrients despite their ultra-low content in the body, play important roles in many biochemical processes, such as action on specific receptors, influence on the activity of enzymes and hormones, protein-transporters, etc., which is reflected in the functional state of the immune, endocrine and many vital systems. Tamsen-Jones K. et al. back in 1987 identified 15 of the most important trace elements, 5 of which are non-metals, such as iodine, selenium, fluorine, silicon and possibly arsenic, while the remainder relate to metals-copper, iron, manganese, zinc, cobalt, nickel, chromium, vanadium, molybdenum and tin. The cause of alopecia can be both deficiency and imbalance, as well as an overabundance of trace elements, due to its toxic effect.

Despite their effectiveness, most recommendations for the use of trace elements in the treatment of hair loss are often scientifically unsubstantiated, and the number of works is limited. The average scalp contains about 100,000 hairs, 90% of which are in the anagen phase. Normal hair growth requires sufficient protein, vitamins and micronutrients.

#### Micronutrients and Diffuse Alopecia

Today, the micronutrients frequently used in the treatment of hair loss are iron, selenium, zinc and copper. Typical dermatological symptoms of iron deficiency are koilonychia, cheilitis, and glossitis, indicating the effect of iron on epithelial cell growth, division, and maturation. Iron deficiency is often present in telogenic alopecia. Ferritin reflecting iron stores in the body can be considered as an optimal indicator of iron levels in alopecia research. It is well known that serum ferritin concentrations may increase in several clinical conditions such as: inflammatory processes, diabetes, chronic alcoholism, hyperthyroidism and some metabolic syndromes. It should be noted that cells in the hair follicle matrix are among the fastest dividing cells in the body. It should be noted the discordant levels of ferritin and free iron in the matrix of the hair follicle: low level of ferritin, high level of free iron. These cells are highly sensitive to even a slight decrease in the amount of iron in the body. Correction of homeostasis, namely the treatment of iron deficiency anemia allows to achieve better results in the treatment of patients with telogenic alopecia. Selenium is involved in the synthesis of more than 35 kinds of proteins, in addition to the activity of the antioxidant enzyme glutathione peroxidase it serves as a cofactor. Selenium deficiency is more often observed in children with low birth weight, in patients requiring parenteral nutrition, and in populations living in areas with low selenium content (Eastern Finland, Gensu Province in China, etc.) [12]. Venton et al, described hair depigmentation in 4 patients receiving parenteral nutrition without selenium. Serum and hair selenium levels were  $38 \pm 11$  ng/mL and  $0.34 \pm 0.13$   $\mu$ g/mL, respectively. At the same time, therapy with selenium-containing drugs showed efficacy after 6-12 months, which was reflected in the restoration of hair pigmentation. In another study involving the description of a case series of 6 newborns with alopecia and pseudoalbinism who were on artificial absorption, selenium therapy at a dose of 5  $\mu$ g/kg/day, selenium levels recovered to normal values, and the above manifestations were significantly reduced.

A comparative analysis of the development of alopecia among ovarian cancer patients receiving chemotherapy showed a significant reduction in alopecia and gastrointestinal toxicity in the group of patients taking selenium supplements. The authors suggested the use of selenium supplements in accompanying chemotherapy. In the United States, the recommended dietary selenium content for residents over 14 years of age is 55  $\mu$ g/mL. At the same time it should be noted that irrational use of selenium, more than 400  $\mu$ g/ml daily, leads to its overabundance in the body and the associated high toxicity expressed in brittle and altered nails, nausea, vomiting, bad

breath, and pronounced hair loss. Another important micronutrient is zinc, which is found in large quantities in fish and meat. It has been noted that people who eat cereals containing phytinates, which are zinc chelating agents, and those with a low meat diet, parenteral nutrition patients and formula-fed infants are more likely to suffer from zinc deficiency. Anorexia, overuse of laxatives to induce malabsorption, inflammatory diseases of the large intestine, and small intestinal surgery (jejunostomy) also contribute to zinc deficiency. Increased zinc metabolism and excretion are associated with pathological conditions such as: malignant tumors, pregnancy, burns, infection [8]. One of the most well-known signs of zinc deficiency is alopecia. However, the results of studies in this area are inconsistent. A retrospective cross-sectional study of 115 patients with acute and chronic telogen alopecia showed that 9.6% of patients had zinc deficiency. At the time, another study comparing 312 patients with different forms of alopecia with a control group of 32 healthy individuals showed low zinc levels in patients with androgenic and telogen alopecia. The researchers recommended the use of zinc when its level in serum is less than 70 µg/ml. The work of Yavuz I. et al. comparing the data of 40 patients with chronic telogen alopecia and 30 healthy individuals showed no difference in zinc levels between the groups [16]. A number of studies on zinc levels in the body have revealed low zinc levels among patients with androgenic alopecia as compared to the control group. A study by Kil et al, which included patients with androgenic and telogen alopecia, conducting a correlation analysis between zinc levels and the degree of hair loss, revealed a strong relationship between zinc levels below 70 µg/ml and alopecia [7]. In contrast to the above data, in two studies conducted by Dastgheib L et al, and Mussalo-Rauhamaa H et al, no correlation was found between zinc levels in androgenic alopecia and among healthy individuals [2,10]. Also, the role of the use of supplemental zinc application is a matter of debate. A study by Ead R et al, found no positive effect of zinc supplementation in the form of zinc citrate at a dose of 220 mg twice daily, on the degree of androgenic alopecia [4]. While a study by Park H et al, achieved good treatment results in patients with androgenic alopecia who used zinc gluconate at a dose of 50 mg for 12 months compared to a control group [13].

Another important trace element in the amino oxidase enzyme, which plays an important role in keratin strength, is copper. In addition, there are a number of copper-containing enzymes such as ascorbic acid oxidase and tyrosinase, oxidative processes of connective tissue, skin and its derivatives, which in turn contribute to the process of keratinization and melanin synthesis in the skin, hair pigmentation. Acquired copper deficiency is observed in prematurely born children, artificially fed cow's milk, not received timely complementary feeding or parenteral nutrition and after prolonged therapy with zinc. It is manifested by hypopigmentation of hair, microcytic anemia, leukopenia, and myelopathy. The basic daily dose for adults is 900 mg.

## RESULTS

When the copper content in the body is reduced, growth retardation, disorders of keratinization in the skin, and depigmentation of the skin and its derivatives are observed.

Manganese in the body is contained in fairly low amounts with its deficiency observed in disorders of absorption, characterized by growth retardation, hypogonadism, skeletal bone abnormalities, dermatitis, keratosis, as well as disorders of hair growth and pigmentation.

Jin et al. in their work on the role of micronutrients in patients with male alopecia found lower levels of zinc, copper, iron and manganese in this category of patients compared to healthy controls [5]. Ozturk et al. found an association between low body mass index and low levels of copper in hair, serum and urine among men in the Turkish population with androgenic alopecia, which is due to their important role in cell division processes and other cellular and metabolic

mechanisms. In addition, zinc and copper have antioxidant activity and stabilize the cell membrane thereby preventing oxidative destruction by free radicals [12]. Deshwali et al. in their review showed the great importance of zinc in the functioning of many enzymes. Zinc inhibits hair miniaturization, follicle regression and promotes hair growth. Zinc deficiency is also associated with hypothyroidism and anemia, which are known causes of hair loss [3]. Skalnaya et al. compared the content of trace elements in hair loss from the frontal scalp region with hair growth from the occipital region and found a lower content of copper and zinc in the hair of the first location [15]. These studies demonstrate that maintaining a mineral balance in the body is essential for normal hair growth. Thus, mineral supplements play a well-defined role in preventing hair loss and stimulating healthy hair regrowth.

#### Micronutrients and focal alopecia

There are also a number of studies on the role of micronutrients in focal alopecia.

The work of Waishu J. et al. demonstrated that patients with focal alopecia have significantly lower serum zinc and selenium levels compared to healthy individuals, yet no statistically significant differences were observed between the trace elements copper, iron, ferritin and magnesium among patients and controls [17]. Zinc affects the metabolic function of the hair follicle by inhibiting regression and accelerating its recovery. In addition, zinc plays an important role in the proper functioning of the immune system. Consequently, a significant decrease in zinc levels in patients with focal alopecia can lead to impaired functioning of their immune system.

#### DISCUSSION

Selenium, another important micronutrient with immunomodulatory and antiproliferative properties. It appears that selenium supplementation may enhance cellular immunity through the following mechanisms: enhancing expression of the T-cell high-affinity receptor interleukin-2 and T-cell response, in addition to preventing oxidative stress-induced damage to immune cells. Recent studies have shown that combination therapy with immunomodulators enhances their effect because immunomodulatory therapy promotes zinc redistribution in tissues by reducing the perifollicular infiltrate of CD8+ T cells.

A recent study has shown that copper plays a crucial role in the differentiation and proliferation processes of cells in the papillary layer of the skin, which are represented by specialized fibroblasts that are important in the development of hair follicles. These findings are consistent with a study that showed that serum copper levels were significantly lower in patients with focal alopecia compared with healthy individuals.

#### CONCLUSIONS

Kantor et al. found that serum ferritin levels were lower in patients with focal alopecia. They also suggested that low iron levels in the body play a greater role in the initiation than in the maintenance of this condition. Reduced micronutrient levels were observed more in patients with long duration, extensive lesions, and treatment resistance [6].

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