Consequences of zinc deficiency in selected diseases-literature review

Alicja Płaczek, Dominik Machaj, Filip Białas, Katarzyna Cyboran, Monika Kuc

Alicja Płaczek, alicja60@poczta.onet.pl ; Medical Faculty, University of Rzeszow, Pigiona Street 6, 35-310 Rzeszow, Poland

Dominik Machaj, dominik5a4@tlen.pl ; Faculty of Medicine, Medical University of Lublin, Chodźki 19, 20-093 Lublin, Poland

Filip Białas, filip.bialas@op.pl ; Medical Faculty, University of Rzeszow, Pigiona Street 6, 35-310 Rzeszow, Poland

Katarzyna Cyboran, katarzyna_cyboran@o2.pl ; Medical Faculty, Institute of Medical Sciences, Collegium Medicum, Oleska Street 48, 45-052 Opole

Monika Kuc, kuc.monika96@gmail.com ; Medical Faculty, Institute of Medical Sciences, Collegium Medicum, Oleska Street 48, 45-052 Opole

Summary:

Zinc is one of the most important micronutrients. It is essential for maintaining health. It is supplied with food, therefore an appropriate diet is the basis for maintaining its appropriate level in the body. The cause of the deficiency may be insufficient supply or malabsorption. [2] Deficiency symptoms manifest themselves in the form of ailments from various systems. A relationship has been shown between zinc deficiency and the occurrence of certain diseases, e.g. cardiovascular diseases, diabetes and depression. Supplementation has a beneficial effect in the prevention and alleviation of the course of certain diseases. [1]

Key words: zinc; deficiency; supplementation
INTRODUCTION AND PURPOSE

Zinc plays an important role in maintaining health and preventing many diseases. The aim of this study is to summarize the current knowledge on the relationship between zinc deficiency and the prevention and pathogenesis of various diseases. Systemic and intracellular zinc homeostasis is essential to health. [9]

The zinc content in the body is 2-3 g, of which 57% is in skeletal muscles, 29% in bones, 0.4% in the heart, and 0.1% in plasma. [1] The risk of deficiency of this element increases if the diet is rich in phytates, strong chelators, and low in protein, which binds biogenic zinc. Such diets consist of a large amount of grain proteins [2,3,4]. Deficiency may also be caused by chronic diseases, including malabsorption syndrome, liver disease or kidney disease.[8]

The literature review shows that the deficiency of this element is associated with many diseases. Zinc deficiency is manifested by disorders of the central nervous system, digestive, skeletal, reproductive, immune and skin barrier systems. [2,7] There are studies confirming its involvement in the metabolism of lipids and glucose, and thus its association with diabetes and cardiovascular diseases [5].

DESCRIPTION OF THE STATE OF KNOWLEDGE

Free zinc ions (Zn2 +) constitute <0.0001% of cellular zinc. [9] Most remain bound to zinc-binding proteins, i.e. serum albumin and metallothionein proteins in cells. [9][14] Its transport takes place with the help of two proteins: the ZIP family, which transports zinc to the cytoplasm, and the ZnT family, associated with the solute 20 (SLC30A), which is responsible for the outflow of zinc outside the cell or the inflow into the organelle. [9]

Zinc plays a catalytic, cocatalytic and structural role in the body. The catalytic role is involved in the activation of over 300 enzymes, an essential process of substrate transformation, the formation of hydroxide ions and gene regulation. [1][2][11] There is usually one zinc atom per subunit of the enzyme, which is bound to 3-4 ligands. The ligands are amino acids, most often histidine, glutamic acid, aspartic acid and cysteine. [2][10] The universal ligand is water. [10] Cocatalytic zinc atoms influence the catalytic function together with another zinc atom in the same enzyme, but are not essential for this process. [10] The structural function is to ensure the structural stability of the protein and to stabilize the quaternary structure of oligomeric holoenzymes. [2] The ions of this metal can also directly influence the activity of channels, phosphatases and kinases. [12]

Zinc deficiency in the body is determined by measuring plasma zinc levels or controlling the amount taken with a meal, which is imprecise. [13] Elderly people, sick people and vegans / vegetarians are particularly vulnerable to zinc deficiency. The vast majority of cases of nutritional deficiency occur in the developing countries of Africa and Asia, where cereal proteins, rice and corn are the main components of the diet. [8][9]

Zinc deficiency can be mild, moderate and severe. Symptoms of mild zinc deficiency include decreased serum testosterone, oligospermia, decreased lytic activity of NK cells, decreased IL-2 activity of T-helper cells, decreased serum thymulin activity, hyperammonaemia, hypogesis, decreased dark adaptation, and decreased lean body mass. [15][16] Symptoms of moderate deficiency include growth retardation, male hypogonadism in adolescents, rough skin, poor appetite, mental lethargy, delayed wound healing, cellular immune dysfunction, and abnormal neurosensory changes. [8] Severe zinc deficiency includes symptoms such as bullous pustular dermatitis, alopecia, diarrhea, emotional
disturbances, weight loss, cellular immunodeficiency infections, hypogonadism in men, neurosensory disorders, and problems with ulcer healing. [8][15]

There is ample evidence showing a link between zinc deficiency and depression. One study found a relationship between reduced zinc intake and decreased serum levels of zinc and depression in young women. [6] [18] Another study showed a correlation between reduced zinc intake and depressive symptoms and improvement of patients' condition with an adequate supply of zinc in the diet. [17] One of the possible causes is the activation of the hypothalamic-pituitary-adrenal system. [2]

The main cause of CVD is atherosclerosis. Zinc has antioxidant and anti-inflammatory properties, therefore a reduced level of this metal is a serious risk factor for atherosclerosis. [1] Zinc deficiency enhances endothelial cell apoptosis and enhances the damaging influx of oxidized LDL. [1][19] There are studies that show a correlation between low serum zinc concentration and the incidence of postoperative AF in patients after coronary artery bypass grafting. [1][20] Supplementation with numerous micronutrients, including zinc, has a positive effect on the volume of the left ventricle, its ejection fraction, and above all, the quality of life of patients suffering from CHF. [1]

In laboratory studies in rats, an association was found between zinc deficiency in adults and decreased glomerular filtration rate and renal blood flow, and increased renal vascular resistance. These changes are presumed to be due to the increased formation of superoxide anion, a consequence of the low Cu/Zn SOD activity in the kidneys of rats. [2][22] Additionally, zinc deficiency may affect the progression of renal failure. [2][23]

Zinc is essential for the proper secretion of insulin and has an insulinomimetic effect. It affects the synthesis of glycogen and gluconeogenesis. [19] It is essential for the synthesis and storage of insulin. [2] Zinc ions secreted simultaneously with insulin during hyperglycemia may be responsible for the death of β-cells by a paracrine mechanism. [2][21] It is possible that this mechanism may link hyperinsulinism with β-cell necrosis and, consequently, the development of type 2 diabetes. [2] Zinc deficiency affects glucose metabolism and the action of insulin in insulin-sensitive cells such as muscle, adipose tissue and liver. [5] Zinc supplementation has had a beneficial effect in the prevention and treatment of type 2 diabetes, but its effect on type 1 diabetes is still unknown. [5][19] It is known, however, that in both type 2 and type 1 diabetes, hypercincuria and symptoms of zinc malabsorption have been observed. [2]

CONCLUSIONS:

Adequate supply of zinc in the diet is extremely important. While the specific role of zinc in the pathogenesis of many diseases is still unclear, there is ample evidence that zinc deficiency is associated with them. Knowledge of the properties of zinc can broaden the understanding of the pathophysiology of chronic diseases. Zinc is essential for the proper functioning of the nervous, cardiovascular and digestive systems. Proper supplementation can be an important protective factor for many diseases. [2]

LIST OF REFERENCES:

1. Sangyong Choi, Xian Lui, Zui Pan Zinc deficiency and cellular oxidative stress: prognostic implications in cardiovascular diseases. 2018; 39(7): 1120–1132. doi: 10.1038/aps.2018.25
2. Jurowski Kamil, Szewczyk Bernadeta, Nowak Gabriel, Piekoszewski Wojciech. *Biological consequences of zinc deficiency in the pathomechanisms of selected diseases.* 2014; 19(7): 1069–1079. doi: 10.1007/s00775-014-1139-0

3. Tapiero H, Tew K. *Biomed Pharmacother.* 2003; 57:399–411. doi:10.1016/S0753-3322(03)00081-7.

4. Semrad C. *Curr Gastroenterol Rep.* 1999; 1(1999): 398-403. doi: 10.1007/s11894-999-0021-7.

5. Yokonori Tamura. *The Role of Zinc Homeostasis in the Prevention of Diabetes Mellitus and Cardiovascular Diseases.* 2021; 28(11): 1109–1122. doi: 10.5551/jat.RV17057

6. Styczeń Krzysztof, Sowa-Kućma Magdalena, Siwek Marcin, Dudek Dominika, Reczyński Witold, Szewczyk Bernadeta, Misztak Paulina, Topór-Madry Roman, Opoka Włodzimierz, Nowak Gabriel. *The serum zinc concentration as a potential biological marker in patients with major depressive disorder* 2017; 32(1): 97–103. doi: 10.1007/s11011-016-9888-9

7. Geiser J, De Lisle R, Andrews K. *PLoS ONE.* 2013; 8(11):1–11. doi: 10.1371/journal.pone.0082149.

8. Ananda S. Prasad. *Discovery of Human Zinc Deficiency: Its Impact on Human Health and Disease* 2013; 4(2): 176–190. doi: 10.3945/an.112.003210

9. Scott A Read, Stephanie Obeid, Chantelle Ahlenstiel, Golo Ahlenstiel. *The Role of Zinc in Antiviral Immunity* 2019; 10(4): 696–710. doi: 10.1093/advances/nmz013

10. Vallee B, Falchuk K. *Physiol Rev.* 1993; 73 :79–118.

11. O’Halloran T. *Nauka.* 1993; 261 :715–725. doi: 10.1126/science.8342038.

12. Pan Z, Choi S, Ouadid-Ahidouch H, Yang JM, Beattie JH, Korchneva I. *Transportery cynku i rozregulowane kanały w nowotworach.* *Front Biosci (wydanie przełomowe)* 2017; 22 :623–43.

13. King JC, Brown KH, Gibson RS, Krebs NF, Lowe NM, Siekmann JH, et al. *Biomarkery żywienia dla rozwoju (BOND) – przegląd cynku.* *J Nutr.* 2016; pii :jn220079.

14. Bozym RA, Thompson RB, Stoddard AK, Fierke CA. *Pomiar pikomolowego wewnątrzkomórkowego wymienialnego cynku w komórkach PC-12 przy użyciu bioczujnika ratiometrycznej fluorescencji.* *ACS Chem Biol.* 2006; 1 (2):103–11.

15. Beck FW, Kaplan J, Fine N, Handschu W, Prasad AS. *Zmniejszona ekspresja CD73 (ekto-5'-nukleotydazy) w podzbiorze CD8+ jest związana z niedoborem cynku u ludzi.* *J Lab Clin Med.* 1997; 130 :147-56.

16. Prasad AS, Meftah S, Abdallah J, Kaplan J, Brewer GJ, Bach JF, Dardenne M. *Tymulina w surowicy w niedoborze cynku u ludzi.* *J Clin Invest.* 1988; 82 :1202-10.

17. Amani R, Saeidi S, Nazari Z, Nemapotour S. *Biol Trace Elem Res.* 2010; 137 :150–158. doi: 10.1007/s12011-009-8572-x.

18. Narang R, Gupta K, Narang A, Singh R. *Indian J Physiol Pharmacol.* 1991; 35 (4):272–274.
19. Foster M, Samman S. Sygnalizacja cynkiem i redoks: zaburzenia związane z chorobami układu krążenia i cukrzycą. *Sygnał antyoksydacyjny Redox*. 2010; 13:1549–73.

20. Yan YQ, Zou LJ. Zależność między stężeniami cynku, miedzi i magnezu po pomostowaniu sercowo-płucnym i pooperacyjnym migotaniu przedsionków u pacjentów poddawanych pomostowaniu aortalno-wieńcowemu. *Biol Trace Elem Res.* 2012; 148:148–53.

21. Mocchegianai E, Boemi M, Fumelli P, Fabris N. *Diabetes*. 1989; 38:932-937. doi: 10.2337/diab.38.7.932.

22. Atlihan F, Soylemezoglu T, Gokce A, Guvendik G, Satici O (1990) Turk J Pediatr 32(1):33-38.

23. Bao B, Prasad A, Beck F, Fitzgerald J, Snell D, Bao G, Singh T, Cardozo L. *Am J Clin Nutr*. 2010; 91 (6): 1634-1641. doi: 10.3945/ajcn.2009.28836.