

Zinc

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Indications

Zinc is a trace mineral, second only to iron in its concentration in the body. Adult humans contain 2 to 3 grams of zinc, but it is difficult to measure an individual's zinc status, particularly during acute illness.[1] Zinc is necessary for the immune system to function correctly. Zinc is involved in cell division, cell growth, wound healing, break down of carbohydrates, enhancing action insulin, and it is necessary for the sense of smell and taste. During pregnancy, infancy, and childhood, zinc is a requirement for proper growth and development.

While severe zinc deficiency is a rare occurrence in developed nations, mild or moderate deficiency may be common. Severe zinc deficiencies are most common in the developing world. Zinc deficiency is the fifth leading cause of loss of healthy life years in developing countries.[2] The World Health Organization includes zinc as an essential medicine for diarrhea treatment.[3] There have been proposals to add zinc to oral rehydration therapy (ORT; the current formula for ORT includes sodium chloride, trisodium citrate dihydrate, potassium chloride, and anhydrous glucose per liter of fluid). Zinc supplementation may be able to reduce global child mortality by 4%.[4] In Africa and Asia, zinc deficiency was responsible for over 260000 and 182000 deaths, respectively, in 2004. Zinc deficiency was responsible for 10.4% of malaria deaths, 14.4% of diarrhea deaths, and 6.7% of pneumonia deaths for children between 6 months and five years of age.[5] A meta-analysis of 33 prospective intervention trials regarding zinc supplementation and its effects on the growth of children in many countries showed that zinc supplementation alone had a statistically significant effect on linear growth and body weight gain, indicating that other deficiencies that may have been present were not responsible for growth retardation.[6]

Zinc deficiency results in rapid and marked atrophy of the thymus, lymphopenia, and reduced primary and secondary antibody responses.[7] Research has demonstrated zinc supplementation to reduce the incidence of childhood pneumonia, but the effect of zinc as adjunctive therapy in the course of pneumonia is unclear.[8] Severe zinc deficiency states, such as acrodermatitis enteropathica, are associated with a variety of skin manifestations, including perioral, acral, and perineal dermatitis.[9] Zinc, if taken regularly, may reduce the risk of developing the common cold, and zinc lozenges can reduce symptoms. Zinc deficiency of hereditary or dietary cause can lead to pathological changes and delayed wound healing.[10] Oral zinc may be useful in treating zinc-deficient patients with leg ulcers. Topical zinc appears to be superior to oral zinc in wound healing. Zinc decreases the amount of copper in the body, which is why it is used to treat Wilson disease.[6]

Zinc transporters, such as ZIP4, have been shown to have an essential role in cancer development and proliferation.[2] Zinc deficiency also has correlations with depression, schizophrenia, and multiple sclerosis. Zinc has a function in the formation of insulin crystals in beta cells of diabetic patients. On the other hand, zinc plays a substantial role in the prevention of metabolic syndrome. Numerous studies have supported the use of zinc to improve blood pressure, glucose, and LDL cholesterol levels in the serum.[11]

In sepsis patients, zinc gets redistributed from the serum into the liver, and several studies point to a correlation between zinc and sepsis outcomes.[12] Further research into zinc's role in sepsis could elucidate a possible role for zinc monitoring or supplementation in the treatment of septic patients.

Mechanism of Action

Research has recognized over 300 catalytically active zinc metalloproteins and more than 2000 zinc-dependent transcription factors involved in gene expression of various proteins.[6]

Zinc can treat acute and chronic diarrhea by inhibiting three out of the four main intracellular pathways of intestinal ion secretion, including cyclic adenosine monophosphate (cAMP), calcium, and nitric oxide.

The biochemical, immunologic, or virologic basis for the mechanism of action of zinc in the treatment of the common cold remains unclear. A leading hypothesis is that Zn^{2+} is a competitive inhibitor of ICAM-1 in both rhinovirus particles and the nasal epithelium.

Zinc aids wound repair by acting as a cofactor in several transcription factors and enzyme systems (i.e., zinc-dependent matrix metalloproteinases) that augment auto-debridement and

keratinocyte migration. Zinc protects against reactive oxygen species and bacterial toxins through the anti-oxidant activity of cysteine-rich metallothioneins.

Zinc decreases the concentration of copper by inducing the synthesis of a copper-binding ligand in mucosal cells; this sequesters copper, making it unavailable for serosal transfer in the GI tract.[13]

Administration

Starting zinc supplements within 24 hours after cold symptoms begin may reduce the symptoms and make the symptoms less severe. Experts do not recommend supplementation beyond the RDA. Food sources include beef, pork, lamb, nuts, whole grains, legumes, and yeast. Zinc is in most multivitamins and mineral supplements. Zinc is present in some over-the-counter medicines, such as cold lozenges, nasal sprays, and nasal gels. The best way to get the daily requirements is to eat a balanced diet that contains a variety of foods.

The recommended dietary allowance (RDA) is the average daily level of intake that is sufficient to meet the nutrient requirements of nearly all (97 to 98%), healthy people. The adequate intake (AI) is the level established when there is not enough scientific research evidence to develop an RDA. The following is the case for zinc:

Infants (AI)

- 0 to 6 months: 2 mg per day (mg/day)
- 7 to 12 months: 3 mg/day

Children (RDA)

- 7 to 12 months: 3 mg/day
- 1 to 3 years: 3 mg/day
- 4 to 8 years: 5 mg/day
- 9 to 13 years: 8 mg/day
- Supplementation Dose: 5 to 20 mg/day[4]

Adolescents and Adults (RDA)

- Males, ages 14 and over: 11 mg/day
- Females, ages 14 to 18: 9 mg/day

- Females, ages 19 and over: 8 mg/day
- Pregnant females, 19 years of age and over: 11 mg/day
- Lactating females, 19 years of age and over: 12 mg/day

Adverse Effects

Zinc taken in large amounts may cause diarrhea, abdominal cramps, and vomiting within 3 to 10 hours of swallowing the supplement. The symptoms usually alleviate within a short period. An excess intake of zinc can result in copper or anemia, iron deficiency, or copper deficiency. [14] Nasal sprays and gels containing zinc may have side effects such as loss of sense of smell.

Contraindications

Zinc supplements above the tolerable upper intake level (40 mg elemental zinc per day in adults) are contraindicated in well-nourished pregnant and lactating women.

Monitoring

Symptoms of zinc deficiency include:

- Frequent infection
- Hypogonadism in males
- Loss of hair
- Poor appetite
- Problems with the sense of taste and smell
- Skin sores
- Slow growth
- Trouble seeing in the dark
- Slow wounds healing

Toxicity

Although zinc is considered relatively nontoxic, extremely high intake of zinc can manifest with nausea, vomiting, epigastric pain, lethargy, and fatigue.[15]

There is no listed treatment for zinc overdose other than to cease using the supplement.

Enhancing Healthcare Team Outcomes

For those working in developing countries, it is crucial to keep in mind that anyone can speak up and suggest zinc supplementation for a child with diarrhea. Many physicians and health-care providers are unaware of the benefits of zinc therapy because of the lack of education on minerals. Zinc is highly cost-effective in treating diarrhea.

When taking a medication history, nurses need to be sure and look for supplements such as zinc and specifically prompt the patient to provide such information, as many patients think they do not need to include OTC supplements in their medication history. Pharmacists need to assist in guiding patients to proper OTC dosing, and the treating clinician can coordinate with the pharmacist in making recommendations where supplementation is necessary and beneficial. While zinc is generally benign and available without a prescription, it merits attention, and the entire interprofessional healthcare team should follow the patient's use of zinc, to avoid interactions as well as optimize the benefit where zinc is beneficial to the patient. [Level V]

Questions

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