CONTINUING MEDICAL EDUCATION

ZINC—AN UPDATE

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Zinc, a divalent cation, was first isolated in 1509. Its biological importance was first discovered by Raulin[1] in 1869 who showed that it is necessary for the growth of fungus. In man, its essentiality was appreciated as early as 1939 when it was thought that zinc deficiency may contribute to the clinical manifestations of human vitamin deficiency syndromes.[2] In 1973, Moynahan and Barnes[3] established that a genetic disorder called acrodermatitis enteropathica was due to low serum zinc levels and zinc supplementation completely cured the symptoms.

Its importance can be very well judged from the fact that it is a part of over 90 metallo-enzymes. Common enzymes like lactate dehydrogenase, alkaline phosphatase and carboxypeptidase are all zinc metallo-enzymes.

Zinc Physiology

Zinc is available in both animal and vegetable foods, but the former are a better source because of the better bio-availability of the element. Meat, fish, cereals and vegetables are good sources of zinc. Only 20-40% of the ingested metal is available for absorption.[4] Phytates, calcium and phosphate reduce absorption, while chelating agents like EDTA and animal proteins increase it.[5]

Absorption of zinc occurs in the proximal part of the small bowel,[6] and is probably a carrier-mediated process.[7]

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Low molecular weight zinc binding ligands (ZBL) have been demonstrated in the intestine and pancreas of some animals[8] and also human milk[9] Though their exact role is not clear, these almost certainly facilitate zinc absorption from the intestinal lumen. The mucosal ZBL is absent in the new-born rat which is dependent on the maternal milk ZBL for optimun zinc absorption. This dependence is lost after 18 days, by which time the mucosal ZBL has developed and the exogenous ZBL no longer enhances absorption.[10] A similar process may be operable in the human beings also.

The average 70 Kg adult has a body zinc content of 1.4–2.3 gm.[11] Highest tissue concentrations(>500 μg/gm dry weight) are found in the prostate, uveal tract, seminal fluid and skin. About half of the total body content of zinc is found in bones,[12] but this is not readily available for metabolic needs. Movement of zinc between various tissues is limited and as there is no true storage depot, the supply of zinc for tissue growth and repair is dependent on a continued external supply.[4]

The serum zinc levels vary with the technique used for its estimation. The range has been given as 55-160 μg/dl. Serum zinc levels are 16% higher than the plasma levels.[13] Plasma levels fall within hours of stress such as surgery, trauma, myocardial infarction or inflammation.[14] A protein called leucocyte endogenous mediator (LEM) which is released by the activated phagocytes, has been shown to lower the serum zinc levels in such states.[15] Plasma zinc levels are low also in patients with neoplasia.[16]

Assessment of the body zinc status is rather difficult. Serum zinc levels are subject to acute variations. Hair zinc levels correlate poorly with plasma levels, but provide historical information in epidemiological studies. Determination of urinary zinc is also unreliable. Erythrocyte zinc level is reliable but only after the age of 12 years, before that it rises progressively.[17] At present, the best criterion of zinc deficiency is an unequivocal clinical response to zinc administration.[16]

Zinc is essential for the activity of atleast 90 enzymes, which participate in all the major metabolic pathways. Carbonic anhydrase, carboxypeptidases, aminopeptidases, alkaline phosphatase, alcohol, retiol, malate, lactate, glutamate, glyceraldehyde 3-phosphate dehydrogenases, DNA and RNA polymerases are all examples of zinc metallo-enzymes.[16] Poor wound healing has been seen in zinc deficient animals.[18] It is essential for all phases of the cell cycle. In the human lymphocytes, zinc acts as a mitogen though the mechanism is not yet clear.[19] Zinc stabilizes the plasma subcellular membranes, especially the lysosomes.[20] Zinc also appears to influence insulin binding and degradation.[21] It also modifies prostatic androgen metabolism.[22] Hartoma et al[23] have demonstrated improved sperm counts and testosterone levels in hypozincemic oligospermic males as a result of zinc administration. A possible physiological role in taste has also been suggested.[24]

Zinc excretion occurs mainly through the faeces, but small quantities are excreted in the urine and sweat.[25]

Deficiency states

Deficiency of zinc can result from an inadequate dietary intake, increased body losses, malabsorption or intravenous feeding.

For the dietary deficiency; protein calorie malnutrition, vegetarianism, patients on protein restricted diets are a few predisposing factors to the hypozincemic state. Even persons from poor socio-economic status are at risk.[26] Infants on special milk formulae which are deficient in zinc, have also shown low levels and retarded growth rate.[27,28] A self limiting variant of acrodermatitis enteropathica recognised recently[29,30] has also been shown to be the result of less supply in the mother's milk.[31] In a personal series, three sisters had all their offsprings affected and the milk zinc secretion in one of them was low. Such infants recover from the deficiency once they start a normal diet. An exactly similar defect of mammary zinc secretion has been reported by Piletz and Ganschow[32] for a lethal milk mouse mutant where the pups develop acute dermatitis and die within 5-10 days of birth because of zinc deficient milk of the mother.

Any chronic gastro-intestinal disease, prematurity, pancreatic insufficiency and acrodermatitis enteropathica are the few causes of malabsorption of zinc. AE was first shown to be the result of zinc deficiency by Moynahan.[33] This prompted a research into this important trace element. Atherton et al[34] later on, demonstrated a pronounced defect in the in vitro uptake of zinc in jejunal biopsies obtained from patients with AE.

Diarrhoea, burns, excessive sweating, excessive blood loss, parasitic infestation, exfoliative dermatitis, alcoholic cirrhosis, diuretic treatment and diabetes mellitus may all increase the loss of zinc and thus produce a hypozincemic state.[35] Premature infants on parenteral alimentation show a progressive decline in the plasma zinc levels after 14 days of continuous treatment.[36]

A number of signs and symptoms have been seen because of zinc deficiency. Anorexia, pica, growth retardation, hypogonadism,[16] neurological and behavioural changes[37,38] such as mood lability, jitteriness, tremors, dysarthria, impaired taste and smell have also been docu-

mented. Night-blindness,[39] photophobia and blephritis[35] have also been observed.

Cutaneous changes in zinc deficiency include dermatitic patches. These are localised to the peri-oral areas, cheeks, ears, around nostrils, peri-anal areas, dorsa of fingers, hand, toes and heels. Nails show paronychia, growth retardation, Beau's lines and sometimes loss.[40] All these lesions may be complicated by candidiasis. The hair growth is retarded. Sometimes alopecia may develop. Wound healing is also delayed. Low levels of zinc have also been reported in acne.[41]

In addition, impaired cell mediated immunity with poor lymphoblast response,[42] thymic hypoplasia,[43] defective monocyte and polymorphonuclear mobility[44] have been described with zinc deficiency.

Therapeutic role

Zinc can be administered as a sulphate (22.5 mg of elemental zinc/100 mg), acetate (30 mg of zinc/100 mg) or an oxide (80 mg of zinc/100 mg). Sulphate salt may sometimes act as an irritant to the gastro-intestinal tract and may precipitate bloody diarrhoea.[30] Capsulated preparations are better tolerated. Recommended daily allowance of zinc is 3 mg of elemental zinc/day for the first 6 months; 5 mg/day for the recond six months; 10 mg/day, during 1-10 years; 15 mg/day for adolescents and adults and 20-25 mg/day for pregnant and lactating women.

Therapeutically, even higher doses, upto 50-150 mg/day have been given safely. It has been used for the treatment of gastric ulcers[45] and acne,[46,47] apart from AE and other deficiency states.

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