ZINC DEFICIENCY

Zinc is one of the trace metals essential for human and animal health. The importance of zinc for growth of rats and mice was first described as early as in 1934(1). Its significance to human health however, was identified only 3 decades later, when Prasad and his colleagues(2) held zinc deficiency as the causative factor for the syndrome characterized by dwarfism, anemia and hypogonadism in young Iranian adults.

Biological Significance of Zinc

Zinc is present in all organs, tissues, fluids and secretions of the body. More than 95% of zinc is intracellular while only 0.1% is present in plasma. Zinc is probably a major regulatory ion in the metabolism of the cell and its deep involvement in biology is becoming apparent in the recent years. Being a cofactor for over 200 enzymes in the body, zinc plays a vital role in controlling several cellular metabolic processes. Its involvement in gene expression in terms of induction of the enzymes for DNA synthesis prior to entry into S phase of the cell cycle and induction of new proteins during tissue differentiation is now clearly demonstrated.

Bioavailability of Zinc from Diets

Zinc is present in the Earth's crust to the extent of about 0.02% and is 23rd in the order of abundance of the elements in nature. Despite its abundance and its requirement to the human body in relatively small quantities, populations subsisting on cereal diets are potentially susceptible to develop zinc deficiency. Bioavailability of zinc from cereal diets is poor and is due to the presence of factors like phytate and fibre which form insoluble complexes with zinc. High concentration of other cations like iron and calcium also interfere with the absorption of zinc from the gut. Although protein in the diet influences zinc absorption favorably, this factor is not exploited because of the suboptimal protein content of the diets of the populations in developing countries. Nevertheless, the body is equipped with efficient homeostatic mechanisms for the control of body zinc levels and despite the complexity of problems involved in absorption, overt zinc deficiency or excess is relatively rare in man and animals.

Zinc Deficiency

Specific disease syndromes due to severe zinc deficiency have been reported. Clinical syndrome of zinc deficiency characterized by dwarfism, hypogonadism, anemia and hepatosplenomegaly were described in young adults of Arab countries (2,3). Such severe acquired zinc deficiency has not been documented in India. But, the existence of milder grades of zinc deficiency cannot be ruled out in malnourished populations subsisting on rice based diets which could be quantitatively poor in
meeting with the zinc requirements. Because of its importance in protein synthesis, adequacy of zinc status particularly acquires clinical significance in populations where malnutrition is widespread. Besides its potential to aggravate severe protein-energy malnutrition (PEM), zinc deficiency could precipitate severe vitamin A deficiency by interfering with retinol binding protein (RBP) synthesis. Although, the clinical syndrome of severe zinc deficiency is well defined, the manifestations of milder grades of zinc deficiency are non specific. Growth retardation is commonly attributed to zinc deficiency. However, the extent to which zinc deficiency per se contributes to growth retardation is difficult to define, as it is invariably associated with PEM. Lack of suitable, simple parameters to assess zinc status also contributes to the paucity of information on the zinc status of the population.

**Assessment of Zinc Status**

*Plasma Zinc:* Plasma zinc levels obtained following overnight fast are unequivocally low (≤10.5 mmoles/L) in severe zinc deficient states. The levels are less definitive in assessing milder grades of zinc deficiency. Plasma zinc levels depend upon several factors, like pre or post prandial state, serum albumin levels, presence of infection, etc. Further, homeostatic mechanism tend to maintain plasma zinc levels even in the presence of severe dietary zinc restriction. Despite these limitations, plasma zinc estimations are carried out in many laboratories to assess zinc status because of the ease of determination and availability of the sample. Cautious interpretation of data obtained from carefully collected samples is required when this parameter is used to assess zinc status.

*Tissue Zinc:* Zinc assays from tissues are useful as research tools rather than for diagnosis of zinc deficiency in individual cases. Hair zinc, though subject to several limitations still finds a place in assessment of zinc status of the populations. Leukocyte zinc is a useful parameter reflecting tissue zinc status. Determination of zinc from homogeneous populations of leukocytes and platelets appears to be more useful. Erythrocytes tend to conserve their zinc even when severe dietary zinc restriction is imposed and total erythrocyte zinc is not decreased even in severe zinc deficient states. However, the erythrocyte membrane bound zinc appears to vary with dietary zinc restriction and hence assay of zinc in red cell ghosts is suggested as a useful index of zinc status.

**Zinc Metallothionein and Zinc Containing Biomolecules:** Data on zinc metallothionein concentrations and serum thymulin activity which appear to detect early zinc deficiency are limited. These parameters need further validation.

**Stable Isotopes:** Usage of stable isotopes of zinc (67Zn, 68Zn and 70Zn) in the kinetic studies of zinc metabolism is the most recent, promising and safe research tool in estimating zinc status (4).

**Zinc Supplementation and Measurement of Parameters like Growth:** Supplementation of zinc and measurement of certain functions like growth, immune response, etc. are often practised to infer the existence of subclinical zinc deficiency. The results of such studies need to be interpreted cautiously because of the complex and multifactorial regulation of human physiology.
**Zinc Supplementation in PEM**

Despite the lack of information on the magnitude of zinc deficiency, and its functional significance, zinc supplements are often prescribed to children to improve growth and immune function. While zinc supplements confer no additional benefits to an individual whose zinc status is already normal, inadvertent usage of zinc is known to disturb the homeostasis of trace element nutriture. Several investigators observed the close association of impaired zinc status with the coexistent PEM. Children with kwashiorkor and marasmus have severe zinc deficiency, while the mild-moderately malnourished children suffer from subclinical zinc deficiency as detected by estimation of serum thymulin activity and its activation in vitro(5). Daily supplementation of zinc along with the high calorie and high protein diets failed to enhance clinical recovery in children with kwashiorkor and marasmus. Food intake, disappearance of edema and weight gain were comparable to those children who received only diet. However, the supplemented children had better zinc status at the end of rehabilitation period(7). There is also evidence to suggest that the zinc supplements, though failed to accelerate clinical recovery, caused alterations in body composition in favor of muscle tissue deposition. This indicates that the energy cost of tissue deposition is less in the supplemented children(8). In view of these observations routine supplementation of zinc to severely malnourished children may be advocated. However, the need for routine zinc supplements to apparently normal children is not established.

**Zinc Status of Pregnant Women and Newborns**

Zinc status of pregnant women and its relation to the zinc levels in the newborn were not well defined till recently. With the help of leukocyte zinc levels it is now observed that there is no evidence of zinc deficiency in pregnant women. Maternal zinc status had no effect on birth weight. Zinc status of the new born infants also had no relation to their birth weight. Gestational age appears to influence the zinc status of the newborns with preterm infants having higher leukocyte zinc at birth(9). The higher leukocyte zinc concentration coupled with higher levels in breastmilk of preterm mothers probably meet the zinc needs of the rapidly growing preterm infants(10).

Zinc status of breastfed infants declines progressively during early infancy to reach significantly low values at the time of weaning. Based on such observations routine supplements to breastfed infants are suggested to prevent growth faltering that may occur at the time of weaning. However, it has been observed that the zinc levels improved to normal following appropriate weaning, thus suggesting the need for proper weaning rather than to administer routine zinc supplements to breastfed infants(12). The situation with formula-fed infants is, however, different. The zinc status of these infants declines to very low levels till weaning is initiated. The functional significance of this transient, yet severe zinc deficiency of formula fed infants needs to be investigated(10).

**Zinc Administration in Diarrhea**

There is lot of information on the
beneficial effects of zinc supplements in the management of childhood diarrhea. Zinc supplementation reduced mean duration and frequency of purging in diarrhea, probably by improving the water and electrolyte transport across the intestinal mucosa (13-15).

Thus, zinc plays a vital role in human physiology. Available information does not identify isolated zinc deficiency as an important health problem in the Indian population. While routine zinc supplements to enhance normal physiological functions is not recommended, judicious administration of zinc supplements in zinc depleted individuals plays an important role in reducing the morbidity.

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