Zinc deficiency in neonates

Zinc is a trace metal essential for optimal growth and development. As 70% of the body zinc stores of the fetus are accumulated during the third trimester of pregnancy, prematurely born infants whose body stores are low, postnatal requirements high, and gastrointestinal tract immature, are at increased risk for developing a zinc deficient state. Inadequate zinc supplementation of parenteral nutrition solutions may lead to zinc deficiency at any age. Although human milk is considered advantageous with respect to zinc nutriture, zinc deficiency has been noted in some exclusively breast-fed term and preterm infants. Inability to secrete normal amounts of zinc into the milk has been documented in such cases.[1]

Clinical features of severe acute zinc deficiency in preterm infants have included acro-orificial lesions, diarrhea, jitteriness, behavioural changes and growth retardation.[2] Convincing documentation of milder nutritional deficiency states is a challenging problem due to lack of sufficiently reliable and sensitive indices of zinc nutritional status.

Plasma zinc concentrations in neonates do not differ from those seen in adults. Mean±SD plasma zinc concentration was noted to be 104±28 μg/dl in 48 premature infants less than 28 weeks gestation at the time of the assay.[3] Plasma zinc levels below 65 μg/dl have been considered *diagnostic* of zinc deficiency.[4] However, a low plasma zinc level may not necessarily indicate a zinc deficient state as stress, infection, administration of steroids and low plasma protein levels may lower plasma zinc levels. Hence plasma levels must be interpreted with caution. In addition, the sample must not be hemolyzed as zinc concentration of erythrocytes is approximately fourteen times that of plasma.

As hair and erythrocytes turn over slowly, their zinc levels do not reflect changes with respect to zinc status. Moreover, frequent blood transfusions given to premature infants make interpretation of body zinc status difficult. Leukocyte zinc concentrations and leukocyte alkaline phosphatase activity have been thought to be the best tools for diagnosis of zinc deficiency in adults.[5] In the neonate, however, there is a paucity of data regarding leukocyte zinc concentration. Activities of many zinc-dependent enzymes are depressed during zinc deficiency. Commonly used indicators of zinc nutritional status are serum or leukocyte alkaline phosphatase and leukocyte thymidine kinase. Assay of these enzymes, particularly serum alkaline phosphatase which is easily performed in many laboratories, may be useful in clinical assessment of zinc deficiency, with serial determinations following a trial with zinc therapy. This may provide biochemical confirmation of the adequacy of zinc replacement and may be useful in detection of mild zinc deficiency.[6] Cholestatic liver disease and rickets, both common in preterm infants, may be associated with elevated serum alkaline phosphatase activity.

Zinc balance studies can provide excellent data on net intestinal absorption and body retention of ingested zinc. However, they require skill, are time-consuming and are restricted to special research laboratories. Finally, clinical response to zinc supplementation may be an unequivocal sign of zinc deficiency.

The *in-utero* zinc accumulation rate has been calculated to average 250 μg/kg per day, (increasing from 240 μg/day at 26 weeks to 675 μg/day at 36 weeks. Zinc requirements for tissue growth have been estimated to be 30 μg/kg of fat-free tissue per day. Thus, the estimated absolute minimum daily requirement for zinc in growing premature infants fed parenterally is 350 μg/kg. Renal zinc losses have been reported to be increased when parenteral nutrition solutions, such as Freamin-3 (McGaw) and Vamin (Pharmacia, Montreal) are used, while Aminosyn (Abbot Laboratories) has been noted to have lower renal zinc losses. Thus, the zinc requirements of preterm infants given Freamin-3 or Vamin may be increased up to 500 μg/kg/day. The minimum daily requirement of enterally fed infants in the first two months of life is yet to be established. After this period, total requirement is estimated to be 250 μg/kg per day. Using the special formulas for preterm infants, and 30% zinc absorption rate, the daily intake of a growing preterm infant would be 800 to 1000 μg/kg.[7]

Several studies indicate that the absorption of zinc from human milk is superior to that from formula. However, infants fed pooled donor milk will generally have a lower zinc intake than infants fed their own mother's milk. Results of balance studies in very low birth weight infants fed their own mother's milk indicate a better net zinc absorption and zinc balance despite a much higher zinc intake by formula fed infants.[8] However, infants fed human milk must have their zinc status closely monitored as some mothers may fail to secrete adequate zinc into their breast milk. Soy protein formula have lower bioavailability for zinc. Whey protein formulas, as well as formulas higher in protein content, apparently increase the absorption of zinc, while some studies suggest that iron fortified formulas may impair zinc absorption.

Clinical zinc deficiency may be treated with orally administered zinc salts. One mg/kg of elemental zinc per day is recommended for suspected zinc deficiency. As zinc sulphate is not well tolerated, zinc may be administered as acetate or gluconate (2·8 mg of zinc acetate dihydrate approximates 1 mg of zinc) and may be given in 2-3 divided doses before meals.[4]

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