“ZINC “ The Friendly and Forgotten Micronutrient

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Introduction

Zinc is the second most abundant trace mineral after iron, and is important in the protein metabolism and synthesis, in DNA metabolism, and in stabilization of cell membrane [1].

It is essential for functions of various cellular metabolisms, and it acts as a cofactor for more than two hundred enzymes [1]. Also, zinc has its crucial role during periods of growth and tissue proliferation (immune system, wound healing, skin, and GIT integrity). Furthermore, zinc has its own vital physiologic role in immune function, sexual maturation and normal growth [1].

Animal products including human milk are considered the best dietary source of zinc. In addition, whole grains and legumes contain moderate amount of zinc. Globally, poor bioavailability of zinc secondary to phytic acid, which inhibits zinc absorption from its sources, is considered more important factor than low intake in many cases of zinc deficiency [1].

A syndrome called Zinc Deficiency Dwarfism was first described in a group of children in the Middle East with low level of zinc in their hair, poor appetite, diminished taste acuity, hypogonadism, and short stature [1]. In developing countries, zinc supplementation can reduce morbidity and mortality among children from diarrhea and pneumonia, and zinc can enhance growth [1]. Prevalence of zinc deficiency is highly noticed in populations with high rates of stunting. Other contributing factors that can lead to zinc deficiency include inadequate zinc intake in complementary feeding or general diet, sever infection, lack of zinc in total parenteral nutrition and in premature infants fed human milk without fortification [1].

Clinical Manifestation of Zinc Insufficiency

In mild cases, poor appetite, growth faltering and immune impairment. Moderate-severe symptoms and signs include, delayed sexual maturation, rough skin and enlarged liver and spleen; whereas, manifestation as mood changes, growth and immune impairment, diarrhea, alopecia, photophobia, night blindness, scaling dermatitis, and acral and periorificial erythematous appear in severe zinc deficiency [1].

Diagnosis of zinc deficiency Is challenging and mainly clinical. In mild zinc deficiency, plasma zinc level is often normal although zinc level is frequently used; levels in moderate to severe deficiency are characteristically less than 60µg/dl. Nevertheless, the response to a trial of zinc supplementation with outcomes such as improved linear growth or weight gain, enhanced appetite, and improved immune function, is the principles for identification of zinc insufficiency [1]. As zinc has no pharmacologic effect on these functions, a positive response to supplementation is considered evidence of preexisting deficiency. Therefore, clinically an empirical trial of zinc supplementation (1µg/kg/day) is a safe and a sensible approach in situations in which zinc deficiency is considered probable.

A specific condition called acrodermatitis enteropathica occurs when there is sever zinc deficiency in which plasma zinc level is markedly reduced and serum alkaline phosphatase activity is low [1]. Clinically, this condition is characterized by acute oral and perianal dermatitis, alopecia, and failure to thrive as a result of lack of intestinal zinc absorption [1]. This is occurring 2-4 weeks after infants have been weaned from breast milk.

Such condition is an autosomal recessive disorder, and it is relatively uncommon due to lack in the secretion of zinc from the mammary gland resulting in abnormally low milk zinc concentration [1]. Hence, this occurs in breast fed infants especially premature present with standard signs of zinc deficiency including growth failure, diarrhea, and dermatitis. Treatment is with high dose of zinc with successful continuous breast feeding.

Zinc is nontoxic element, certain features such as nausea, vomiting, abdominal pain, headache, vertigo and seizures might appear as a result of excessive intake of zinc [1].

Moreover, the main dietary sources of zinc are meat, shellfish, wholegrain, legumes and cheese. In developing countries, due to malnutrition, zinc deficiency is quite common [1].
Zinc dwarfism, hypogonadism, dermatitis and T-cell immunodeficiency are signs of chronic zinc deficiency which often associated with lack of iron micronutrient [1].

People with certain conditions such as Crohn's disease, short bowel syndrome, and sprue are more prone to zinc deficiency as a result of malabsorption of zinc and increased zinc losses in the urine [2,3]. In contrast, persons with mild human zinc deficiency states, the obvious features and laboratory/functional abnormalities of mild zinc deficiency are varied. Such variety is not altogether astonishing in view of the biochemistry of zinc and the ubiquity of this metal in biology with its contribution in an extraordinarily wide range of essential metabolic processes. Impaired growth velocity is a main clinical feature of mild zinc insufficiency and can be corrected with zinc supplementation [4,5]. Pregnancy outcome [6] and the function of the immune system [7] are evident cases that clinically respond to zinc supplementation.

Zinc is widely used in people with common cold. However, the clinical consequence of zinc lozenges in dropping the duration of flue is still unclear [8].

In patients fed intravenously with no addition of enough zinc to the infusates [9] and in cases of the autosomal recessively inherited disease such as acrodermatitis enteropathica, severe zinc deficiency is documented [10]. Because of association of zinc micronutrient in so many core areas of metabolism, the features of zinc deficiency are basic and nonspecific, including growth retardation, alopecia, diarrhea, delayed sexual maturation and impotence, eye and skin lesions, and impaired appetite. Therefore, clinical features and laboratory criteria are not always reliable. As a result, certain potentially useful laboratory indicators such as alkaline phosphatase activity can be used clinically to validate reliable, sensitive clinical or functional indicators of zinc status in the body.

**Zinc and Neurodevelopment**

In addition to studies on the clinical impacts of low-dose zinc supplements on individuals with pneumonia, diarrhea [11] and on nonspecific laboratory functional tests of zinc status such as tests of neuro- cognitive function [12] or immune status [13], research results including the effects of zinc supplementation on physical growth velocity in children are helpful to assess the dietary zinc intake for many causes. 1st, approved clinical evidence of zinc supplements on growth velocity (linear growth and weight) in children with variable degrees of growth delay has been documented [14,15]. 2nd, because an adequate figure of these studies has been done in North America, growth is appropriate as a functional/clinical indicator of zinc requirement in North American children [5,16-18]. Finally, database involved in these studies are adequate to use for cohort analysis.

**Average Zinc Consumption from Human Milk During the First 12 Months of Feeding**

In order to match the zinc intake of the infant in early weeks (Figure) the adequate intake is set at 2.0 mg/day (2.5mg/L × 0.78L/day). Interestingly, similar clinical results have been obtained concerning weight gain and body length or height at ages four-six months when evaluated by zinc intake from human milk and complementary foods at this age [19]. Consequently, a helpful connection between zinc content of human milk at five months and improvement in the weight-for age Z scores for the five to seven months interval have been documented [20]. However, that growth-limiting zinc deficiency can occur in infants mainly fed human milk after the age of four months [21].
Factorial estimates of requirements (i.e., 2.1mg/day at one month and 1.54mg/day at five months) are consistent with this adequate intake for infants from birth to six months. Such evaluations are based on amount of zinc ingestion of infants fed human milk, fractional absorption, and endogenous losses [22]. Skin and urine losses are from available estimations [23]. In addition an earlier report that physical growth of male infants fed a zinc-fortified cow milk formula (5.8mg/L) was superior to that of infants receiving the same formula but with a zinc concentration of 1.8mg/L, which provided about 1.4mg/day of zinc [17].

Zinc intake from Human Milk. Zinc nourishment in afterward infancy varies quietly from that in the younger infant. It is likely that neonatal hepatic stores, which may contribute to metabolically usable zinc pools in early postnatal life, have been degenerated [24]. Human milk provides only 0.5mg/day of zinc by seven months postpartum [120], and the concentration drops even further by twelve months [25]. Consequently, human milk alone is an insufficient source of zinc after the first six months. Hence, extrapolation from human milk intake during the 1st six months after birth, which yields 2.4mg/day, does not reflect adequate zinc intake during the 2nd six months.

Zinc consumption from Human Milk and Complementary Foods. According to the Third National Health and Nutrition Examination Survey, the median intake of zinc from complementary foods is 1.48mg/day (n = 45) for older infants consuming human milk. So, the average zinc intake from human milk and complementary foods is estimated to be approximately 2mg/day (0.5 + 1.48).

Requirements of zinc for Growth. These requirements have been estimated from chemical analyses of infants and adults, which give an average concentration of 20μg/g wet weight of zinc [26]. It is assumed that each gram of new lean and adipose tissue requires this amount of zinc. The average amount of new tissue accreted for older infants and young children is thirteen and 6g/day, correspondingly [27].

Therefore, the total amount of absorbed zinc required for infants ages seven to twelve months is 836μg/day (Table 1), while for children ages one to four years is 74μg/kg/day (Table 2).

GIT (Gastrointestinal tract) losses vary directly with the amount of zinc absorbed (see "Adults Ages 19 Years and Older"). The average gut excretion of endogenous zinc in infants aged two-four months who receive human milk is approximately 50μg/kg/day [22]. This risk is in adults as the amount of absorbed zinc is equal to the total endogenous zinc losses. This critical level, derived from all available sets of data for adult men, yields an average emission of 34μg/kg/day of zinc and is used for children beyond one year of age and adolescents. Consequently, 50μg/kg/day is used for infants and 34μg/kg/day for children aged one to three years.

Urinary system losses of zinc are concerning 7.5μg/kg/day for both sexes (see "Adults Ages 19 Years and Older"). After early infancy, excretion rates for children on a body weight basis seem to be different from adult values [23]. Yet, no evident database is approved on the skin losses in children, so estimates for children are resulting from statistics in adult men [28], which give an estimation of 14μg/kg/day of zinc. As a result, the estimated figure endogenous excretion of zinc is 6μg/kg/day for older infants and 48μg/kg/day for children aged one to three years. (Table 1 &2).

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<thead>
<tr>
<th>GIT Losses</th>
<th>Essential Absorbed Zinc</th>
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<tbody>
<tr>
<td>50μg/kg/day × 9 kg</td>
<td>836μg/kg/day</td>
</tr>
<tr>
<td>14μg/kg/day × 9 kg</td>
<td>126μg/kg/day</td>
</tr>
<tr>
<td>13 g/day × 20μg/g</td>
<td>260μg/kg/day</td>
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<tr>
<td>6 g/day × 20μg/g</td>
<td>120μg/kg/day</td>
</tr>
</tbody>
</table>

**Table 1: Zinc consumption and need for infants aged seven-twelve months.**

**Table 2: Requirement for absorbed Zinc for children aged one-three years.**

Children Ages 4-8 Years

For this age group, the average intestinal losses are 34μg/kg/day of zinc and the amount of new tissue accreted is 7g/day [27]. Based on the summation of zinc losses and requirements for growth, the required amount of absorbed zinc for this age group is about 1.2mg/day (Table 3). With a fractional absorption of 0.3 based on studies in infants and young children [29,30], the EAR is 4.0mg/kg/day of zinc (Table 3).

**Table 3: Necessity for absorbed Zinc for kids aged 4-8 years.**

**Table 4: Requirement for absorbed Zinc for children aged 9-13 years.**

Children Ages 9-13 Years

Growth. Some dietary data are presented from children aged four-eight years whose growth percentiles were at the lower end of the normal range and who were subjects in placebo-controlled, randomized trials of dietary zinc supplementation. In each of two studies, one in Canada [31-62] and the other in the United States [63-98], zinc supplementation was associated with greater linear growth gain. Mean dietary intakes of the placebo-treated controls in the Canadian and U.S. studies were 6.4 and 4.6 mg/day of zinc, respectively. No growth response was observed with zinc supplementation of healthy children of either gender, unselected for growth, whose average calculated zinc intake was 6.3mg/day [99-156]. The SDs were too large (likely attributable to methodological limitations) to use the se data with any confidence in setting an EAR. Nevertheless, these data are consistent with the EAR derived from a factorial approach.
With use of the same values as for younger children, an average accretion of 10g/day of new tissue [157-187], and a reference weight of 40 kg, the required amount of absorbed zinc is 2.1mg/day (Table 4). Based on a fractional absorption of 0.3 observed in infants and young children [188-227], the EAR is 7mg/day (Table 485).

Table 5: Requirement for absorbed Zinc for adolescent boys and girls aged 14 through 18 years.

<table>
<thead>
<tr>
<th>GIT Losses</th>
<th>Boys</th>
<th>Girls</th>
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<tbody>
<tr>
<td>34μg/kg × 64 kg = 2,176μg/day</td>
<td>34μg/kg × 57 kg = 1,938μg/day</td>
<td></td>
</tr>
<tr>
<td>14μg/kg × 64 kg = 896μg/day</td>
<td>14μg/kg × 57 kg = 798μg/day</td>
<td></td>
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<table>
<thead>
<tr>
<th>Urinary and SKIN Losses</th>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>10g/day × 20μg/g = 200μg</td>
<td>5g/day × 20μg/g = 100μg/day</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Seemen or Menstrual Losses</th>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>100μg/day</td>
<td>100μg/day</td>
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<table>
<thead>
<tr>
<th>Need for Growth</th>
<th>Boys</th>
<th>Girls</th>
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<tbody>
<tr>
<td>3,372μg/day</td>
<td>2,936μg/day</td>
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<thead>
<tr>
<th>Required Absorbed Zinc</th>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.372μg/day</td>
<td>2.936μg/day</td>
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Acknowledgements

None.

Conflict of Interest

No conflict of interest.

References


