GLOBAL IMPORTANCE OF ZINC DEFICIENCY IN HUMANS: ITS RELATION TO MALNUTRITION AND STRATEGIES FOR ITS PREVENTION

Gibson, R. S.
Department of Human Nutrition, University of Otago, Dunedin, New Zealand

Keywords: Zinc, deficiency, malnutrition, trace-elements, nutrition, phytate, developing countries, bioavailability, diet, growth, deficiency, supplementation, fortification

Contents

Summary

In most developing countries, staple diets are plant-based and consumption of cellular animal protein such as meat, poultry and fish is low. Consequently, intakes and bioavailability of zinc are often poor, resulting in widespread zinc deficiency, especially during childhood and pregnancy. Even mild zinc deficiency has far reaching consequences on maternal, infant and child health, contributing to pregnancy complications, low birth weight, increased susceptibility to infections, maternal and infant mortality and growth failure during childhood.

Zinc deficiency can be alleviated in developing countries by using a combination of targeted supplementation and fortification programs, together with dietary modification/diversification strategies. The latter can be used to improve the content and bioavailability of zinc either in plant-based staples *per se* and/or in plant-based diets used in developing countries. Such strategies range from those based at the household level where no additional inputs are required, to genetic engineering. All these strategies should be integrated with ongoing national food, nutrition and health

education programs to enhance their effectiveness and sustainability, and implemented at the household level using education and social marketing techniques. Ultimately the success of any approach for combating zinc deficiency depends on a political and policy leadership in a country that recognizes that zinc deficiency is a serious public health problem and that is committed to developing an acceptable, equitable and sustainable solution.

1. Introduction

There is increasing evidence that zinc deficiency may be widespread in many developing countries where staple diets are predominantly plant-based and intakes of animal tissues are low. Until recently, however, the potential impact of dietary-induced zinc deficiency on maternal, infant and child health in less industrialized countries has not been recognized. Indeed, until 1997, zinc was not included amongst the micronutrient deficiencies listed as a priority by the United Nations. However, in the UN Third Report on the World Nutrition Situation, zinc was featured alongside iodine, vitamin A, iron and folic acid.

Zinc is a constituent of over 300 metalloenzymes that participate in carbohydrate, lipid and protein metabolism, nucleic acid synthesis and degradation. It is an essential trace element for optimal human growth and development, normal reproduction, immune and sensory function, antioxidant protection, the stabilization of membranes and gene expression.

Zinc was shown to be essential for animals in the 1930s, but it was only in the 1960s that a study of adolescent males from the Middle East led to the first description of nutritional zinc deficiency in humans. In industrialized countries, overt and severe nutritional zinc deficiency was first recognized in patients receiving prolonged parenteral nutrition without a zinc supplement.

Later, conditioned zinc deficiency was described in malabsorption syndromes, chronic renal and liver disease, and alcohol abuse. Two genetic disorders, acrodermatitis enteropathica and sickle cell disease are also associated with suboptimal zinc status. Since these early reports, zinc deficiency has been described in various population groups in industrialized countries, including apparently healthy infants and children, pregnant and lactating women, some vegetarians, especially vegans, and the elderly. In the latter, certain disease states and/or the use of certain medications and supplements may exacerbate conditioned zinc deficiency.

Since the mid 1990s, there have been several reports of zinc deficiency in developing countries, some of which have used carefully designed, double blind placebo-controlled zinc supplementation studies. This article describes the etiological factors associated with zinc deficiency, and summarizes some of the recent studies that have confirmed the existence of zinc deficiency in a wide range of developing countries and its consequences on growth, reproductive function, immune competence, mental, cognitive and psychomotor development. Finally, a brief discussion of possible intervention strategies for alleviating zinc deficiency in developing countries is included, with emphasis on food-based strategies.

2. Etiology of Zinc Deficiency in Developing Countries

The etiology of zinc deficiency in developing countries has been associated with low intakes and poor bioavailability of dietary zinc; with certain environmental and disease states that induce excessive losses of endogenous zinc; and physiological states that increase requirements for this micronutrient. These three major factors are reviewed briefly below.

2.1. Low Intakes and Poor Bioavailability of Dietary Zinc

Dietary-induced zinc deficiency occurs when the content and/or bioavailability of zinc in habitual diets is poor, and homeostatic mechanisms fail to acquire sufficient exogenous zinc and fail to conserve endogenous zinc. Rural diets in developing countries are predominantly plant-based; consumption of cellular animal protein foods such as meat, poultry and fish is often small because of economic, cultural and religious constraints. As a result, the content and/or the amount of zinc available for absorption from such diets is often low.

Information on zinc intakes in developing countries is limited because of the paucity of data on the zinc content of local staple foods. Substitution of zinc values for staple foods grown in western countries is not advisable because the zinc content of plant-based foods tends to reflect local soil zinc levels. Diets based on cereals tend to have a higher zinc content than those based on starchy roots and tubers which are lower in zinc. Such differences in the major food sources of zinc have an important impact on the amount of dietary zinc available for absorption. Cereals contain high levels of phytic acid (myo-inositol hexaphosphate), a potent inhibitor of zinc absorption, which forms insoluble zinc-phytic acid complexes in the intestine (see *Genetic Improvement of Cereals with low Phytic Acid Content*). A measure of the negative effect of phytic acid on zinc absorption is the phytate-to-zinc [Phy]/[Zn] molar ratio of a diet; ratios above 15 have been associated with suboptimal zinc deficiency in humans. Note the high phytate:zinc molar ratios of unrefined maize, wheat, barley and some of the legumes compared to the ratio for leaves and starchy roots/tubers shown in Table 1.

Food Group	Staple	Zn (mg/100g)	Phy (mg/100g)	(Ph:Zn)
Ceareals	Maize flour (refined)	1.0	234	23
	Maize flour (unrefined)	2.5	880	35
	Sorghum	1.3	490	37
	White rice	1.6	192	12
	Wheat	2.7	824	29
	Millet	1.7	480	28
Legumes	Groundnuts	2.8	990	35
	Soya beans	4.9	193	39
	Kidney beans	3.2	1160	36
	Pigeon peas	2.5	690	27
Leaves	Pumpkin leaf	0.7	34	5

	Okra leaf	1.8	97	5
Roots, tubers,	Sweet potato	0.3	12	4
and plantains	Cocoyam	0.5	37	7
	Banana	0.9	80	9
	Plantain	0.2	0	0
	Cassava	0.3	54	18

Table 1. Zinc, phytic acid (Phy), and phytate:zinc molar ratios (Ph:Zn) of selected staples foods consumed in Ghana and Malawi

Consequently, population groups consuming diets based on cereals, especially unrefined corn, have higher intakes of phytic acid and phytate: zinc molar ratios than those consuming starchy roots and tubers. Exceptions are persons living in countries (e.g., Egypt) where diets are based on leavened bread or fermented corn products (e.g., Ghana). During leavening and fermentation, phytic acid is broken down by hydrolysis.

Country	Age (yrs)	Zn (mg/day)*	Ca (mg/day)*	Phytic acid (mg/day) *	[Ph]:[Zn]
PNG (67)	6-10	4.4 ± 1.3	359 ± 160	646 ± 663	12
Ghana (148)	3-6	4.7 ± 1.1	344 ± 145	591 ± 153	13
Malawi (67)	4-6	6.6 ± 1.7	413 ± 189	1899 ± 590	25
Canada (106)	4-6	6.9 ± 2.3	702 ± 249	300**	5
Egypt (96)	1.5-2.5	5.2 ± 1.6	218 ± 89	796 ± 249	16
Kenya (100)	1.5-2.5	3.7 ± 0.9	210 ± 99	1066 ± 324	28
Mexico	1.5-2.5	5.3 ± 1.3	735 ± 199	1666 ± 650	30
Nigeria	1-10	3.6 ± 0.9	-	-	-
Guatemala	6-8	9.0 ± 2.7	621**	962	11
The Gambia	1.2-1.5	4	284 ± NA	-	-

* Mean ± SD **Median NA = not available

Table 2. Dietary zinc and phytate intakes of children

Table 2 presents a compilation of data on intakes of zinc, phytic acid, and the molar ratios of phytate:zinc in children from several less-industrialized countries, as well as from Canada. Calcium intakes are also given in Table 2 because high concentrations of calcium exacerbate the inhibitory effect of phytate on zinc absorption in humans. Calcium forms a calcium-zinc-phytate complex in the intestine that is even less soluble than phytate complexes formed by either ion alone. In general, the calcium content of most plant-based diets in less-industrialized countries is too low to potentiate the negative effect of phytate on zinc bioavailability. Notable exceptions include the diets of lactoovovegetarians, diets based on tortillas prepared with lime-soaked maize, and possibly in the diets of people who chew betal nut with lime.

Several other dietary components inhibit zinc bioavailability. Of these, the amount and type of dietary fibre may be additional inhibiting factors, especially in the diets of less-industrialized countries. The relative importance of dietary fiber compared to phytate in

compromising zinc absorption is controversial, in part because these two anti-nutrients generally coexist in plant-based diets, making it difficult to establish independent effects. Notable exceptions are diets based on sweet potatoes, taros, bananas, and sago in Papua New Guinea, and diets based on cassava and plantains in the forest regions of Ghana. Such diets have a relatively low phytate, but high dietary fiber, content. It appears that in the rural diets of less-industrialized countries where protein intakes are generally low, insoluble cereal and vegetable fiber (i.e., cellulose and lignin) probably exacerbate the adverse effects of phytate on zinc absorption to some degree.

The amount and type of protein also impacts on zinc bioavailability. For example, inclusion of small amounts of animal and fish protein can increase the apparent absorption of zinc, and counteract the negative effect of phytic acid, even when the levels of zinc in the diet are only modestly increased.

-
-
-

Bibliography

Black RE. (1998). Therapeutic and preventive effects of zinc on serious childhood infectious diseases in developing countries. *Am J Clin Nutr* **68(S)**, 476S-479. [A critical review of the evaluation of therapeutic and preventive effects of zinc supplementation on acute and chronic diarrhea, preventive effects on acute lower respiratory infections, and clinical attacks of malaria].

Brown KH, Peerson JM, Allen LH. (1998). Effect of zinc supplementation on children's growth: a meta-analysis of intervention trials. In: Role of Trace Elements for Health Promotion and Disease Prevention. Sandstrom B, Walter P (eds). *Bibl Nutr Dieta. Basel*, Karger **54**, 76-83 83. [A meta-analysis of 22 available double-blind zinc supplementation trials of children less than 13 years of age from both industrialized and developing countries. A small but highly significant impact of zinc supplementation was noted on height and weight increments].

Caulfield LE, Zavaleta N, Shankar AH, Merialdi M. (1998). Potential contribution of maternal zinc supplementation during pregnancy to maternal and child survival. *Am J Clin Nutr* **68**, 499S-508S. [A review of the prevalence and consequences of maternal zinc deficiency in animals and humans as it relates to fetal growth and development, pregnancy complications, and maternal and infant health and well-being].

Gibson RS. (1994). Zinc nutrition in developing countries. *Nutrition Research Reviews* **7**, 151-173. [A comprehensive review of the etiology of zinc deficiency in developing countries, with an emphasis on dietary-related factors. Available zinc supplementation studies conducted during infancy, childhood, and pregnancy are summarized].

Gibson RS, Ferguson EL (1998). Nutrition intervention strategies to combat zinc deficiency in developing countries. *Nutr Res Rev* **10**, 1-18. [A review of the advantages and limitations of using supplementation, fortification, and dietary diversification/modification strategies to combat zinc deficiency].

Prasad AS, Miale A, Farid Z, Sandstead HH, Schulert AR. (1963). Zinc metabolism in patients with syndrome of iron deficiency anemia, hepatosplenomegaly, dwarfism and hypogonadism. *J Lab Clin Med* **61**, 537-549. [The first confirmed account of zinc deficiency in adolescent farmers from Iran].

Sandberg A-S. (1991). The effect of food processing on phytate hydrolysis and availability of iron and zinc. In: *Nutritional and Toxicological Consequences of Food Processing* (Friedman M Ed). Plenum Press, New York, pp. 499-508. [A review of the use of soaking, germination, and fermentation to reduce the phytate content of cereals and vegetables, and their impact on *in vitro* iron solubility].

Sandstead HH. (1985). Zinc: Essentiality for brain development and function. *Nutr Rev* **43**, 129-137. [A review of the essential role of zinc for brain maturation and function].

Sandstrom B, Lonnerdal, B. (1989). Promoters and antagonists of zinc absorption. In *Zinc in Human Biology* (International Life Sciences Institute Human Nutrition Reviews), pp. 57-58, ed. C.F. Mills, Berlin: Springer-Verlag. [A comprehensive review of the dietary components known to modify the bioavailability of zinc].

Shankar AH, Prasad AS. (1998). Zinc and immune function: the biological basis of altered resistance to infection. *Am J Clin Nutr* **68**, 447S-463S. [A review which explores the effects of zinc on multiple mediators of host immunity ranging from the physical barrier of the skin to acquired cellular and humoral immunity].

Tamara T, Goldenberg RL. (1996). Zinc nutriture and pregnancy outcome. *Nutr Res* **16**, 139–81. [A critical review of zinc metabolism during pregnancy as well as observational and experimental studies describing the relationship between zinc nutriure and pregnancy in humans and animals].

Biographical Sketch

R.S. Gibson is a professort at department of Human Nutrition, University of Otago, Dunedin, New Zealand. Rosalind Gibson's research involves studies on the aetiology and functional health consequences of mild iron and zinc deficiency in "high risk" population groups (e.g. pregnant women and menstruating women, infants, preschool children and vegetarians). A second research focus is the development of food-based strategies to enhance the content and bioavailability of micronutrients in predominantly plant-based diets consumed in developing countries, and the impact of these dietary interventions on subsequent growth, health, and cognitive development.

Recent Publications

Skeaff SAM, Ferguson E, Valeix P, Gibson R, Thomson CD. Are breast-fed infants and toddlers in New Zealand at risk of iodine deficiency? Nutrition 2005; 21(3): 325-331.

Soh P, Ferguson EL, McKenzie JE, Homs MYV, Gibson RS. Iron deficiency and risk factors for lower iron stores in 6-24 month-old New Zealanders. European Journal of Clinical Nutrition 2004; 58: 71-79.

Green TJ, Skeaff CM, Whiting SJ, Gibson RS. Effect of folic acid supplementation on plasma zinc concentrations of young women. Nutrition. 2003 Jun;19(6):522-3.