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Essentials of zinc: Focus on sickle cell disease

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RESUMEN

El cinc es un micronutriente que juega un papel importante en la salud, crecimiento y desarrollo del hombre. Es un antioxidante que mejora la inmunidad. La deficiencia de cinc se relaciona con múltiples enfermedades, por ejemplo: diarrea en niños, retraso en el crecimiento y exposición a varias enfermedades. También tiene una participación decisiva en la enfermedad de células falciformes y en las talasemias. Las carnes rojas tienen alto contenido de cinc, y las verduras carecen de éste. En el mundo se han realizado varios estudios donde se demuestra la correlación de este metal con diversas enfermedades. El propósito de esta revisión es tomar en cuenta los estudios internacionales y sus descubrimientos en el papel del cinc.

Palabras clave: cinc, enfermedades por deficiencia de cinc, antioxidante.

ABSTRACT

Zinc is an important micronutrient, which plays a key role in human health, growth and development. It is a potent antioxidant that improves immunity. Deficiency of zinc is related to various disease i.e. diarrhea in children, slow growth and exposure to various infections. It also plays an important role in sickle cell disease and thalassemia. Red meat is a rich source of zinc, where as vegetables are a poor source of zinc. There are extensive studies carried out across the world and correlation is established with various diseases. The aim of this review is to account the various international and national studies and their findings in the role of zinc.

Key words: Zinc, Zinc deficiency diseases, Antioxidant.

Zinc is an essential micronutrient and an important nutrient for growth and development, which plays an extensive role in immune functions and resistance to infections in children. It is the most abundant trace mineral in the body after iron.[1] It is stored primarily in muscle, and also found in high concentrations in red and white blood cells, retina of the eye, bones, skin, kidneys, liver, and pancreas. It has also been reported that the prostate gland stores high amounts of zinc.[2]

It is essential for reproduction in both males and females.[3] Zinc has antioxidant properties, which help protect cells in the body from potential damage caused by free radicals. Free radicals found naturally in body, as well as ultraviolet light, radiation and air pollution that increase the initial damage.[4] Free radicals contribute to the aging process, development of heart disease and cancer. Zinc as an antioxidant can neutralize free radicals and reduce or help prevent some of the damage they cause.[5] Zinc is essential for more than 300 enzymes, structural proteins and hormones. Deficiency of zinc is associated with atrophy of the thymus, reduction in delayed type hypersensitivity and immune responses mediated by T cells.[6] Mild to moderate Zinc deficiency is common in the low-income countries and increased risk of illness and death from infectious diseases.[7] Zinc is essential for the activity of a large number of enzymes and recently its role in fibroplastic proliferation and collagen synthesis has been recognized.[8,9] Few reports indicate that zinc is required for deoxyribonucleic acid synthesis and DNA-dependent RNA polymerase.[10-12]

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Prasad et al first reported zinc deficiency in adult patients with sickle cell disease.[13] Deficiency of zinc in sickle cell patients' result in growth retardation (dwarfism), hypogonadism in males, rough skin, poor appetite, mental lethargy and recurrent infections.[14]

Symptoms of zinc deficiency

Loss of appetite, poor growth, weight loss, impaired taste or smell, poor wound healing, skin abnormalities, hair loss, night blindness, hypogonadism, delayed sexual maturation, white spots on the fingernails and feelings of depression.[15]

Importance of zinc in child health

Studies showed the strong association of diarrhea and zinc deficiency in children. A study from India found that children with acute diarrhea were cured sooner, when they received a zinc supplement, compared to children that did not. Similar results have been found in studies of children with persistent diarrhea, including a study undertaken in Lima.[16,17] Studies in Vietnam, Mexico, Guatemala, India, Jamaica, Papua New Guinea and Peru concluded the impact of daily oral zinc supplements benefits in diarrhea fewer episodes of respiratory illness and less visits to the health center for malaria attacks.[6,18-25] A recent study in northern India indicated significantly reduced mortality by 67%.[16] There are studies that report severe zinc deficiency resulting in dwarfism and delayed sexual maturation in Iranian and Egyptian youths. These studies suggested that zinc supplementation might have a significant role to play in improved child growth. Zinc deficiency as early as intrauterine may influence the dynamics of physical and intellectual development in humans.[26-28] A studies from Latin American showed increased weight gain in low birth weight infants receiving daily supplement of 5 mg zinc. Responses in linear growth have been less consistent; increased growth was noted in the study in Chile but not in Brazil.[29,30] A studies carried out in Jamaica showed that zinc supplementation increased weight gain in children recovering from severe malnutrition.[31] Another trial in Bangladesh reported similar findings.[32] However, excessive zinc supplementation may increase the risk of severe complication in malnourished children.[33] A meta-analysis of 33 randomized intervention trials showed that zinc supplementation produced highly significant positive response in weight gain as well as linear growth.[34] A controlled trial in zinc deficiency children resulted in increased dietary intake of energy after zinc supplementation.[35]

Research analysis in India

A study conducted in NIN Hyderabad reported formula-fed full term infants had significantly lower leukocyte zinc levels.[36] Another study reported an altered state of zinc nutrition in children with ICC.[37] A Study conducted in KG Medical College, Lucknow showed statistically significantly higher plasma zinc levels in male babies as compared to females. Zinc levels were similar amongst those with and those without breast-feeding.[38] A study conducted in Pune reported; RBCMZn is a more sensitive indicator of long-term zinc status than plasma zinc and SOD.[39] A study of Himachal Pradesh reported statistically significant low zinc levels in SFD babies and their mothers.[40] Study of PGIMER suggest that hypozincemia with low iron levels may be the possible cause of pica and contradict the contention that low levels of plasma Zn and Fe could be secondary to pica.[41] Study conducted in human nutrition unit AIIMS showed; deficiency of zinc during pregnancy affects the outcome of pregnancy. A high prevalence of zinc deficiency (55.5%) has been reported among pregnant women.[42] Another study conduced in the Pediatric Department of AIIMS showed; supplementation of zinc results in clinically important reductions in the duration and severity of diarrhea.[16] Another study of AIIMS showed the zinc supplementation substantially reduced the incidence of severe and prolonged diarrhea.[43] A study of Pediatric Surgery AIIMS; found association between NTD and decreased hair zinc levels.[44] Another study of Pharmacology, AIIMS; reported a significant decrease in zinc levels in newborn babies when the time interval between the previous delivery and the present delivery was less than 3.4 years.[45] A study of hematology, AIIMS; reported the significant lover levels of zinc and an association of clinical complexity in sickle patients.[46]

Dietary Sources of Zinc

Animal foods contain adequate amounts of zinc while vegetables are poor source of zinc. Oysters are greater sources of zinc. Meats (beef, lamb, and pork) and liver is the rich ource of zinc. Egg yolks and milk products are good source of zinc. Fish and poultry also contain fair zinc levels. Whole grains such as whole wheat, rye, and oats are rich in zinc and are good sources for vegetarians.

Table 1. Recommended Dietary Allowances of Zinc for infants, children, adults and Upper Levels for infants, children and adults.

Age	*RDA*					*Upper Levels*				
	Infants/Male female Pregnancy Lactation Children					*Infants/ Male Female Pregnancy Lactation Children*				
7 months - 3 years	3 mg	-	-	-	-	4-7 mg	-	-	-	-
4 - 8 years	5 mg	-	-	-	-	12 mg	-	-	-	-
9 - 13 years	8 mg	-	-	-		23 mg	-	-	-	-
14 - 18 years		11 mg	9 mg	13 mg	14 mg	34 mg	-	-	34 mg	34 mg
19+ years		11 mg	8 mg	11 mg	12 mg	-	40 mg	40 mg	40 mg	40 mg

(Adapted from National Academy Press. Washington, DC, 2001 and Lewis MR et.al.1998)

Pecans and Brazil nuts the highest in zinc. Pumpkin seeds and ginger root is a good zinc source. However fruits and vegetables are not good zinc sources, although peas, carrots, beets, and cabbage contain some zinc.[47]

Inhibitory substances of zinc

Bioavailability of zinc is reduced by the coexistence of inhibitory substances such as fiber and phytates in food of vegetable origin. These substances inhibit the absorption of zinc.[48]

Recommended Dietary Allowance for zinc (RDA)

The 2001 RDAs of zinc for infants, children and adults in mg per day and result of excessive intake of Zinc[49,50]

CONCLUSIONS

Extensive studies are needed to understand the role zinc plays as an antioxidant. There is a lack of data on the deficiency of zinc amongst inherited disorders and their prevalence. The importance of zinc deficiency to the risk of SCD has not better understood. There is a paucity of data on the prevalence of zinc deficiency in SCD patient of the country. Infectious disease in children and the role of zinc can be exploring new therapeutic approaches to manage the disease. Status of zinc is required at the national level.

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