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The role of zinc in improving weight gain of children with protein energy malnutrition

Amani Abdelrahman Mohamed
Assistant Professor
Department of Pediatrics and Child Health
Alzahari University
Sudan

Abstract

Background

In many developing countries micronutrient deficiencies-including zinc- are prevalent in children. To provide stronger bases for addressing the importance of zinc in growth promotion and weight gain, this systematic literature review was conducted.

Data sources

Studies published in English language were retrieved by searching MEDLINE (1966-2005) as well as manual searching for journals with relevant articles.

Study selection

Only randomized controlled trials with results adjusted for children age, socioeconomic status and nutritional status (according to Z-scores) were included. As well as information on study design, sample size and outcome measures.

Results

Seven studies met the inclusion criteria for the systematic review with regard to the effect of zinc on promotion of weight gain in malnourished children. Five studies showed a significant weight gain after supplementation with zinc, while two studies showed no effect.

Conclusion

Zinc may have a positive effect on weight gain in malnourished children. However, more research is needed to understand the mechanism of zinc on different body systems and functions, its effect on child health and whether, its positive effect holds for its intervention as part of nutritional programs.

Introduction

Malnutrition is frequently part of a vicious cycle that includes poverty and disease. These three factors are interlinked in such a way that each contributes to the presence and permanence of the others. Socioeconomic and political changes that improve health and nutrition can break the cycle; as can specific nutrition and health interventions (1).

Malnutrition usually refers to a number of diseases, each with a specific cause related to one or more nutrients, for example protein, iodine, vitamin A or iron. In the present context malnutrition is synonymous with protein-energy malnutrition, which signifies an imbalance between the supply of protein and energy and the body's demand for them to ensure optimal growth and function. This imbalance includes both inadequate and excessive energy intake; the former leading to malnutrition in the form of wasting, stunting and underweight, and the latter resulting in overweight and obesity(1). Trace mineral deficiencies underlying protein-energy malnutrition (PEM) are being increasingly recognized. These may occur concomitantly with PEM or become overt during the recovery phase. Iron (Fe), zinc (Zinc), and copper (Cu) malnutrition are associated with PEM (2). Increased gastrointestinal losses coupled to greater need for rapid growth are considered important causative factor.

Zinc is an essential nutrient, which is required to maintain the normal structure and

functions of multiple enzymes, including those that are involved in transcription and translation of genetic materials and therefore in cell division (3). Zinc might also influence the growth of young children particularly in resource poor countries where dietary intake or absorption of zinc may be inadequate (4) and excessive zinc loss may occur due to frequent enteric infections(5). Nevertheless, the lack of simple objective biomarkers of zinc status has hindered the ability to implicate zinc deficiency as a cause of growth failure in human.
During the last two decades, Zinc deficiency has been identified in humans with inadequate intake or with various dietary factors that interfere with Zinc absorption. Fiber, phytates, and other minerals such as Cu have been demonstrated to decrease Zinc bioavailability (6). Zinc nutritional status is highly dependant on absorption from diet since body stores of these essential elements are quite small (7). Zinc needs for optimal growth have not been fully defined for either normal or malnourished children. Nevertheless, studies in animals and human suggest that Zinc requirements are increased during rapid growth. Golden has demonstrated that inadequate Zinc intake may be a limiting factor for growth in malnourished infants (8).

Objective

To review the available data on the effect of zinc on the improvement of weight gain in children under five years of age with protein energy malnutrition.

Methods

Identification of studies

A search was conducted in MEDLINE (1966-Feb 2005).
Manual search for journals with relevant articles.

Inclusion criteria

Randomized double blinded placebo controlled trials.
Restricted to studies of malnourished subjects, as evidenced by mean initial anthropometric Z-scores (<-2.0Z).
Subjects age below 5 years of age.

Exclusion criteria

Studies were excluded if there were reports, editorials, or letters to the editor.

- If they did not provide complete data.
- If the subjects were suffering from severe infection or chronic illness.

Results

Table 1 shows the results of the seven included trials which measure weight gain in response to zinc supplementation. Four trials were conducted in Asia: Bangladesh (2 trials), Pakistan, and Vietnam. The other three trials were conducted in Chile, Israel, and Ethiopia.
The trials were different in terms of sample size, age of the patients, duration of zinc supplementation, zinc dose, and primary outcome result.

- Khantun: 20 mg/day in two divided doses
- Roy: 20 mg/day in three divided doses

- Bhutta: 3 mg/kg/day as single dose
- Castillo: 2 mg/kg/day as single dose
- Hershkovitz: 2mg/kg/day as single dose
- Ninh: 10 mg/day as single dose
- Umeta: 10 mg/day as single dose

5 studies found a significantly increased weight gain in zinc supplemented subjects compared with the control.
2 studies concluded that there was no effect of zinc supplementation on weight gain.

Table (1): Results of the studies:

Study	Study duration	Sample size	Age of the subjects	Intervention	Primary outcome: *weight gain*	Secondary outcome
Khantun 2001 Bangladesh (9)	1 week	**48** Zinc n=24 Control n=24	6-24 months	-all received dietary supp. (not stated), -Zinc: 20 mg/d in multivitamins in 2 doses, -control: multivitamins	**P<0.045**	-Stool frequency/day) -Stool weight (mg/kg/body wt)
Roy 1997 Bangladesh (10)	8 weeks	**111** Zinc n=57 Control n=54	3-24 months	-all received dietary supp. (670kcal/d, prot. 17g/d) -Zinc: 20 mg/d in multivitamins in 3 doses, -control: multivitamins	**P<0.03**	Stool output
Bhutta 1999 Pakistan (11)	2 weeks	**87** Zinc n=43 Control n=44	6-36 months	-all received dietary supp. (100kcal/kg/d) -Zinc: 3 mg/kg/d once in multivitamins -control: multivitamins	**Not significant**	-Stool frequency/day -IGF-1 level
Castillo 1987 Chile (12)	2 months	**32** Zinc n=16 Control n=16	2-12 months	-all received dietary supp. (150kcal/kg/d, 5g/kg/d) -Zinc: 2 mg/kg/d once in multivitamins -control: received multivitamins	**P<0.05**	Diarrhea episode, RTI, pyoderma
Herchkovitz 1999 Israel (13)	3 months	**25** Zinc n=14 Control n=11	3-9 months	-all received dietary supp. (127kcal/d) -Zinc:2 mg/kg/d once in multivitamins -control: received multivitamins	**Not significant**	IGF-1 level
Ninh 1996 Vietnam (14)	5 months	**146** Zinc n=73 Control n=73	4-36 months	-all received dietary supp. (not stated), -Zinc: 10 mg/d once in multivitamins -control: multivitamins	**P<0.001**	-IGF-1 level -Diarrhea episode, RTI
Umeta 2000 Ethiopia (15)	6 months	**100** Zinc n=50 Control n=50	6-12 months	-all received dietary supp. (not stated), -Zinc: 10 mg/d in multivitamins -control: multivitamins	**P<0.001**	Diarrhea episode, RTI

Discussion

The mechanism by which Zinc supplementation might promote weight gain in malnourished children is unknown. This effect may result from an increased appetite and improved ingestion of energy and protein. Nevertheless, increased appetite is not a consistent clinical finding of Zinc supplementation (16).

Zinc supplementation rapidly improves intestinal transport systems, cellular sodium homeostasis and mucosal integrity. Therefore, adding Zinc to oral rehydration salt might improve both immediate and long-term recovery from diarrhea (17). Golden noted improved efficiency of energy utilization after Zinc supplementation but did not report infectious morbidity before and after Zinc (8).

Zinc supplementation was not effective in two studies. Possible explanation could be the specific characteristics of the study population that may have affected their ability to respond to Zinc. In the study of Bhutta it is likely that the study represented a more severe spectrum of diarrhea, i.e. the rate of Zinc absorption is affected by the rate of enteric infection (11). Moreover the nature of the local diet can affect Zinc status if it contains more phytates which could lead to insufficient absorption (18).

It is as well possible that administering Zinc at an early stage of rehabilitation has a direct detrimental effect on the immune system during an infection and it is better to be administered at a later stage of rehabilitation when it is much less likely that sepsis is ongoing (19). The discrepancy between the absence of weight gain and the significant increase in circulating IGF-1 levels (by more than 60%) is puzzling (13). It is possible that micronutrient deficiency could inhibit the growth promoting properties of the increased blood concentration of IGF-1 level (20).

Again limitations were experienced whether study participants have indeed consumed the recommended amounts since eating problems are not uncommon in this group (21).

Inter-subject heterogeneity of the outcome

In evaluating the effect of Zinc on weight gain, it is important to emphasize the heterogeneous nature of the outcome. Not all malnourished children who had been supplemented with Zinc showed increased weight gain. Some patients showed increased weight gain in the first week while others showed it after 2-3 weeks.

Implications for future research

It is still not clear why weight responses to supplemental Zinc are inconsistent in different studies. Studies have consistently demonstrated a reduced incidence and severity of infections, like diarrhea and acute lower respiratory tract infections following Zinc supplementation, leading to reduced morbidity and mortality among high risk children (22, 23). Studies are needed to look into the different mechanisms of Zinc action on growth promotion. Nevertheless, even if growth is not affected by Zinc supplementation, there are other important reasons to consider intervention to enhance Zinc status in malnourished children.

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