

Issue 54

In a nutshell

Eight recent clinical trials involving zinc in children have had moderate success, but more so in those whose zinc status is low to begin with.

Impacts on growth and intercurrent infection were more impressive than those on mental development, and the results show that dose (at least 5 mg/day) is important.

Zinc in children

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NUTRITION RESEARCH REVIEW

Studies 1 and 2: Zinc and respiratory infection

609 Indian children aged 6-35 months were given either 10 mg of elemental zinc or placebo for 6 months. Before treatment, about a third of these children had zinc deficiency (plasma zinc <60µg/dL). After 4 months, this proportion decreased to 12% in the zinc treated group but increased to 44% in the placebo group. More importantly, lower respiratory infection rates in zinc-supplemented children decreased significantly (by 45% : 95% CI 10%-67%).

Ref: *Pediatrics* 1998; 102:1-5

A trial in Ohio on the other hand failed to yield positive results in treating upper respiratory infections. 249 students in grades 1-12 were randomised to receive either zinc lozenges (10 mg 5-6 times a day depending on age) or placebo within 24 hours of experiencing the symptoms of a cold. There was no significant difference between active and placebo groups in duration of any individual or the cold as a whole. However, there was a higher incidence of side-effects in the zinc-treated group, particularly bad taste, nausea and throat discomfort.

Ref: *JAMA* 1998;279:1962-7

Studies 3 and 4: Psychomotor development

A 10 week double-blind, controlled-trial of zinc repletion was conducted on 740 urban, 6 to 9 year old children from low-income families in China. The three treatment arms were: zinc 20mg/day, the same with additional micronutrients, and micronutrients only. Enhanced neuropsychologic performance and growth was seen after treatment with the zinc and micronutrient combination.

Ref: *Am J Clin Nutr* 1998;68:470S-475S

134 low birth weight infants from a poor area of Brazil were randomly assigned to receive supplements with 1mg/day zinc, 5 mg/day or placebo for eight weeks. At six and twelve months of age there was no significant difference between active and placebo groups in terms of mental or psychomotor development (based on Bayley Scales) However, using a behavioural scale there were significant differences in favour of the infants given 5mg/day of zinc (p=0.042).

Ref: *Eur J Clin Nutr* 1998;52:223-7

Studies 5 and 6: Correcting growth deficits

Two different doses of zinc supplementation were compared in a six month trial of treatment of low-birth-weight babies in Brazil. 205 such babies were randomised to receive either zinc supplementation 5mg/day, 1mg/day or placebo. Home visits were made to assess morbidity and anthropometry. Immune function was assessed at 8 weeks by phytohemagglutinin skin test.

Only the group on the 5mg/day dose of zinc had significant effects - a 28% reduction in prevalence of diarrhoea (p<0.05 after adjustment for confounders), and greater weight gain during the fifth and sixth months (p=0.024 compared to placebo group, analysis of variance).

Ref: *Am J Clin Nutr* 1998;68:418S-424S

Six to 9 month old infants from rural areas in Guatemala who were showing stunted growth were given either 10mg/day of zinc or placebo in a seven

month trial. Zinc supplementation was associated with an overall increase of 0.61 sq cm in midarm muscle area ($p=0.02$), but not with any significantly greater increment in length. The stunted infants given zinc gained 1.40 cm more than those who received the placebo.

Ref: *J Nutr* 1998;128:556-62

Studies 7 and 8: Overall morbidity

61 children aged 6-24 months were randomised to receive either 5mg elemental zinc/day for 12 weeks or placebo. The children's caretakers were interviewed weekly to monitor their morbidity and anthropometric measures were done several times during the trial.

Regression analyses did not show any significant effect of zinc supplementation on length, height or head circumference. There was no significant difference in the incidence of any particular symptom, although the mean duration skin rash episodes was significantly shorter in the zinc supplemented

group ($p=0.02$, ANCOVA) and there was a lower hospitalisation rate (Fisher's exact test, $P = 0.02$). However, episodes of vomiting were longer lasting in supplemented compared with placebo children ($p=0.02$).

Ref: *Eur J Clin Nutr* 1998;52:34-9

141 children aged 6 months to 3 years with severe protein-energy malnutrition were given zinc during a period of nutritional rehabilitation as in-patients in a nutritional rehabilitation unit in Bangladesh. They were randomly assigned to get either a lower or higher dose regimen (elemental zinc 1.5mg/kg for 15 days followed by 6.0mg/d, or 6.0 mg/d throughout the 30 days).

Higher zinc doses were not associated with significant change in any anthropometric measurement, but they were associated with greater mortality. (chi-square $p=0.033$, risk ratio= 4.53 95% CI 1.09-18.8).

Ref: *Am J Clin Nutr* 1998;68:742-8

Comments

At first consideration of some of these results, one might form the impression that the researchers were looking hard for a strong effect of zinc supplementation, but had to be satisfied with subtle, sub-group or borderline results. On closer inspection, however, there are some interesting trends.

1. The best results were seen in those who had, or were likely to have had, serious zinc deficiency and/or significant growth impairment, two things which in fact are likely to be interrelated.

To what extent zinc deficiency is a significant clinical problem requiring supplementation amongst children in Western countries remains to be seen.

2. Impacts were more readily demonstrated on growth and intercurrent infection (respiratory and diarrhoea) than on psychomotor development. Based

on experience in the area of iron deficiency research, however, it may be that when more sensitive measures of psychomotor function are used in studies such as these, we will begin to see more definite results.

3. The studies also show that dose is important - at least 5mg/day of elemental zinc seems to be required, although the last study reminds us that zinc is a toxic as well as essential element.

But perhaps the most encouraging conclusion from this collection of research studies is that they are being conducted in the first place. It has been some time now since we began to see intense interest in studying the impact of vitamin A deficiency on paediatric infectious disease and morbidity rates in the developing world. It seems that we are now beginning to see a similar body of work build up on the impact of zinc deficiency.

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