Zinc and Childhood Infections

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Background

Zinc deficiency is estimated to be widespread in developing countries, with the result that children are more vulnerable to illness and death from infectious diseases (Black 2003; Bahl 1998, 2002). The low intake of food rich in zinc, consumption of foods containing high phytate levels which impair the absorption of zinc, and frequent episodes of infection might be responsible for the high prevalence of zinc deficiency (Baqui 2003; Bhatnagar, 2004). Zinc is an essential mineral important for proper functioning of the immune system, growth and development, cell division, and differentiation of skin and epithelial cells in the body (Dutta 2000; Ellis 1987). Intervention through clinical trials directed at the correction of zinc deficiency has been demonstrated to lead to a substantial reduction in the severity and duration of acute diarrhoea and a potential for a lowered prevalence of pneumonia in children in developing countries.

Zinc in an acute diarrhoea trial in Bhaktapur, Nepal

Method

A total of 1792 cases of acute diarrhoea in Nepalese children were randomised into four study groups. The first three groups were blinded: one placebo group, one zinc syrup group, and one zinc syrup plus vitamin A group; placebo syrup and zinc syrup were given daily by field workers; vitamin A was given as a single dose at enrolment. The fourth group was open and also received zinc syrup daily, but administered by the child's care giver. The study period was 1997-2000.

Results

The prevalence of zinc deficiency in the study was 84% (plasma zinc <10 μmol/L). The relative hazards for termination of diarrhoea were 26% (95%, confidence interval [CI]: 8%, 46%), 21% (95%, CI: 4%, 38%), and 19% (95%, CI: 2%, 40%) higher in zinc, zinc-vitamin A, and zinc-caretaker groups, respectively, than in the placebo group. The relative risks of prolonged diarrhoea (duration >7 days) in these groups was 0.55 (0.37, 0.84). Thus zinc shortened the duration of acute diarrhoea by 19-26% and reduced the risk of prolonged diarrhoea by 43-47%. Five per cent and 5.1% of all syrup administrations were followed by regurgitation in the zinc and zinc-vitamin A groups, respectively, whereas this occurred after only 1.3% of placebo administrations.

A World Health Organization (WHO) meeting in 2001 (New Delhi) reviewed all the studies evaluating the effects of zinc on the clinical course of acute diarrhoea, including the study carried out in Bhaktapur, Nepal. The report concluded that "there is now enough evidence demonstrating the efficacy of zinc supplementation on the clinical course of acute diarrhoea" (Faruque et. al., 1999). The results of published studies by others on therapeutic effects of zinc on acute and prolonged diahorrea are summarised in Tables 1 and 2.

Table 1: Other studies evaluating the therapeutic effects of zinc supplementation in acute diarrhoea			
Author, year	**No. of subjects zinc/placebo**	**Dose of zinc (elemental)**	**Difference in mean duration of diarrhoea in days (95% CI)**
Sachdev, 1988	25/25	40 mg	-0.4 (-1.4, 0.6)
Faruque, 1999	341/340	14.2 or 40 mg	-1.0 (-1.8, -0.2)
Dutta, 2000	44/36	40 mg	-1.4 (-1.6, -1.1)
Sazawal, 2001	547/547	5 or 10 mg	0.1 (-0.2, 0.3)
			Relative Hazard (95% CI)
Hidayat, 1998	739/659	4.5 mg/kg	0.92 (0.83, 1.02)
Sazawal, 1997	456/481	20 mg	0.79 (0.69, 0.90)
Roy, 1997	57/54	20 mg	0.85 (0.57, 1.28)
Bhatnagar, 2004	132/134	15 or 30 mg	0.77 (0.59, 0.99)
Bahl, 2002	404/401	15 or 30 mg	0.89 (0.80, 0.99)
Strand, 2002	442/449	15 or 30 mg	0.79 (0.68, 0.93)

Table 2: Other studies evaluating the therapeutic effects of zinc supplementation on episodes of prolonged diarrhoea			
Author, year	**No. of subjects zinc/placebo**	**Dose of zinc (elemental)**	**Odds ratio (95% CI)**
Hidayat, 1998	739/659	4.5 mg/kg	0.72 (0.48, 1.07)
Sazawal, 1997	456/481	20 mg	0.85 (0.60, 1.19)
Roy, 1997	57/54	20 mg	0.77 (0.33, 1.79)
Bahl, 2002	404/401	15 or 30 mg	0.61 (0.33, 1.12)
Strand, 2002	442/449	15 or 30 mg	0.57 (0.38, 0.86)

Zinc supplementation as an adjuvant therapy for the treatment of childhood pneumonia

Pneumonia is a major cause of death among children under five years of age in developing countries. Treatment of pneumonia still remains a major challenge in Nepal as elsewhere. A pooled analysis of the results of routine zinc supplementation in the prevention of pneumonia showed a reduction of 41% (95% CI: 17, 69%) (Sazawal, 1997; Strand, 2002). However, the data on zinc as an adjuvant therapy for the treatment of pneumonia are limited. Two small studies that have been published showed no substantial effect of zinc on the prevention of pneumonia. From November 2003, we have been undertaking a clinical trial in Bhaktapur, Nepal, to measure the efficacy of zinc as an adjuvant therapy along with antibiotics on childhood pneumonia.

Effect of zinc supplementation on child mortality

As studies have shown promising results of zinc supplementation for prevention of childhood pneumonia and diarrhoea, the two most common causes of death among children in developing countries, scientists are now evaluating its effect on overall reduction of child mortality. A clinical trial of zinc supplementation among infants born small for gestational age found a substantial reduction in mortality (Hidayat et al. 1998). Currently, large clinical trials in India, Nepal, and Zanzibar are underway to evaluate the effect of zinc on child mortality and hospitalisation for infectious diseases.

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