

Should zinc be used the treatment of acute gastroenteritis?

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The World Health Organization has produced guidelines for the management of common illnesses in hospitals with limited resources. This series reviews the scientific evidence behind WHO's recommendations. The WHO guidelines, and more reviews are available at: http://www.who.int/child-adolescent-health/publications/CHILD_HEALTH/PB.htm

This review addresses the question: *Should zinc be used the treatment of acute gastroenteritis?*

The **WHO Pocketbook of Hospital Care for Children** recommends to give zinc supplementation in all severity of diarrhoea once severe dehydration has been corrected. This is given in tablet form (chewed, swallowed or dissolved), dose dependent on age.(Pocketbook chapter 5, page 109).

Introduction:

The case fatality rate for acute watery diarrhoea fell markedly with the introduction of oral rehydration solution. However diarrhoeal disease still results in the deaths of millions of children each year worldwide. Most of these deaths occur because of lack of access to ORS, but diarrhoeal deaths still are a frequent cause of deaths in hospitals, and episodes of acute gastroenteritis often progress to being prolonged or resulting in severe dehydration consuming large amounts of hospital resources in developing countries. Much of this morbidity and mortality is among children with coexisting malnutrition. In the management of acute diarrhoea several adjuvant treatments have been proposed. This review intends to answer the question: Should zinc be used the treatment of acute gastroenteritis?

Methodology

The clinical search strategy employed was follows: zinc AND (acute diarrhoea OR gastroenteritis OR infectious diarrhoea OR acute

gastroenteritis OR diarrhea). Using the clinical filters for both "therapy" and "specific", 67 articles were found; using the same filter but restricting the search to systematic reviews only, 8 further articles were found.

All abstracts were read, if there was any doubt as to the relevance of the article, the complete article was sourced. We excluded articles evaluating whether supplementation with zinc prevents diarrhoea and articles evaluating the empirical use of zinc in children with severe malnutrition.

11 RCT's were found; one was excluded due to methodological flaws and selection criteria. 1 systematic review was sourced but it only included 3 RCT's and hence was sufficiently small and out of date to be excluded. All trials were appraised individually by this review. All included articles were type 1b.

Results

The duration of diarrhoea was the primary outcome for the majority of studies. With the exception of two studies [1, 2], the duration of diarrhoea was decreased by 13-50% in those taking zinc supplementation. [3-11] In the two negative studies [1, 2], the duration of diarrhoea was no different in the zinc and placebo groups, but sample sizes were small and the risk of type II errors considerable. In one study [1], the sample size calculation was not met by recruitment.

Two studies investigated stool output by volume in male children (because in female children it is difficult to measure stool volume independent of urine). These studies found a significant decrease in the boys receiving zinc, the ratio of geometric means being 0.69; 95% CI, (0. 48, 0.99) in one study [5], and stool output difference recorded as 1.5 kg vs 2.4 kg in the other study. [11]

Frequency of stools were studied and recorded in four studies; each found a statistically significant decrease in the children treated with zinc. [1, 3, 6, 10]

The proportion of infants and children with prolonged diarrhoea was the most common secondary outcome measured in five studies [1, 2, 6-8]. The hazard risk ratios for prolongation of diarrhoea were between 0.57 and 0.75 for 3 days, 0.89 for 5 days [12] and approximately 0.5 for 7 days. Three of the five studies [1, 2, 8] found odds ratios of 0.57, 0.87 and 0.83 respectively, but the 95% CI's crossed 1.0. For two studies [1, 2] sample size was not met by recruitment and one study [8] had suboptimal follow-up. No study found statistically significant differences between the groups for the outcome prolongation of diarrhea for 14 days. [6-8]

One relatively small cost effectiveness study found no difference in the following clinical outcomes: duration of diarrhoea, length of hospital stay, diarrhoea for longer than 4 days, or unscheduled intravenous fluid use. This study did however find a small (8%) decrease in the costs associated with children receiving zinc. [2]

One large community study from Bangladesh involving 8000 children, where 14 days of zinc was given during episodes of acute diarrhea, found a 24% lower rate of admission in children treated with zinc, (95% CI .59-.98). Importantly over a follow up period spanning 2 years the non-injury death rate was half in the zinc treatment group compared to the control group (rate ratio .49, 95% CI (0.25,0.94)). [4]

The trials varied in the amount of zinc prescribed, and the duration varied from: time to resolution of diarrhea or a maximum of 5 days, to 14 days therapy, regardless of clinical response.

Two of the trials had factorial designs linked with vitamin A. These did not find clinically significant effect of vitamin A on the course of acute diarrhoea. [6, 7]. In one trial the dose of zinc was either "standard" recommended daily allowance (RDA) or four times the RDA. No clinically significant difference was found between the two dose strategies. [7] The doses of zinc (elemental) ranged from 15 mg to 40mg daily.

Discussion

There may be several mechanisms for the beneficial effect of zinc in acute diarrhoea. Zinc is required for the growth, regeneration and restoration of function of intestinal mucosa and has been shown to improve water and electrolyte absorption. Zinc is also necessary for a functioning immune system, including both cellular and humoral antibody response. There have been few adverse effect evaluations.

Summary

Zinc is an effective adjunctive therapy that decreases the severity and duration of acute diarrhoeal illness in children in developing countries. It decreases the risk of acute gastroenteritis developing into prolonged or severe diarrhoea (Grade A evidence). Medium-term mortality in children from non-traumatic causes may be decreased if zinc is given during episodes of acute diarrhoea in some populations, although further large studies would be needed to confirm this (Grade B evidence).

References

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