

Issue 86

In a nutshell

A meta-analysis of zinc supplementation in children with diarrhoea showed benefit for acute, continuing and persistent diarrhoea.

This is important, because not all trials on this treatment have had positive outcomes. Remaining questions include whether zinc should be given in conjunction with other nutrients, e.g. vitamin A.

Zinc and diarrhoea in children

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NUTRITION RESEARCH REVIEW

Zinc in diarrhoea: a meta-analysis

Researchers from The Zinc Investigators' Collaborative Group conducted pooled analyses of "all available published and unpublished randomised controlled trials" on the effects of supplementary oral zinc in children (under age 5 years) with acute or persistent diarrhoea.

Method: Cox survival regression analysis was used to assess the overall effect on diarrhea duration. The researchers sought sub-group effects based on sex, age, weight-for-height, and initial plasma zinc concentration. Dichotomous outcomes were analyzed by logistic regression.

Results: The pooled results showed that zinc supplementation had statistically significant positive outcomes in acute, continuing and persistent diarrhoea. See Table.

There were no significant paired differences in sub-group analysis, although the researchers reported a greater positive effect in persistent diarrhoea amongst younger subjects (< 12 months), who were male or had wasting or lower initial plasma zinc levels.

Reference: Bhutta ZA et al. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. Am J Clin Nutr 2000;72,1516-1522

Table: Effect of zinc supplementation in reducing diarrhoea

Patient condition	Outcome measure	Probability reduced
Acute diarrhoea (95% CI)	Continuing diarrhoea	15% (5-24%)
Continuing diarrhoea (95% CI)	Continuing diarrhea	24% (9-37%)
Persistent diarrhoea	Treatment failure	

Comments

Zinc is one of those nutrients that keeps cropping up in our Updates. Anything that helps lessen the impact of diarrhoeal disease will be of interest, because this problem causes so much suffering and mortality globally (and suffering that includes so many children).

Zinc and vitamin A are two micronutrients that have attracted particular attention in this situation over the last 5-10 years. Zinc is of interest because diarrhoea causes zinc loss, and because zinc supplementation appears to enhance intestinal integrity and repair. This is seen in the specific zinc deficiency acrodermatitis enteropathica, but it seems that it may also be true of many other forms of diarrhoea.

Some studies have also found zinc supplementation reduces overall mortality and improves growth in high risk paediatric populations, although others have failed to find this benefit.

The meta-analysis summarised above is important because the results of individual trials on zinc supplementation in diarrhoea have also not been consistently positive. The reductions reported in this meta-analysis are certainly clinically as well as statistically significant.

Previous negative trials have included, for example, Pakistani researchers who studied malnourished children hospitalised for persistent diarrhoea. They did not find evidence of accelerated recovery from zinc supplementation, despite a significant improvement in plasma zinc levels in supplemented children ¹. Zinc did not help diarrhoea in AIDS diarrhoea wasting syndrome in Zambia ², although it is not clear how that syndrome is related to more common infective diarrhoeal diseases.

On the other hand, a number of studies over the last 5 years have found benefits from zinc supplementation in diarrhoea (e.g. ³).

In this situation a well conducted meta-analysis can offer guidance in showing the most likely direction in which the overall trend of research results are pointing. At the same time, those reporting a meta-analysis always have a special responsibility to consider carefully the potential pitfalls of putting together data that may have variation in what has actually been measured. Further, when unpublished data are included in the analysis, the authors must make their own assessment of the quality of that data.

Bearing all this in mind, this study does suggest that zinc supplementation is worth pursuing as an option in lowering morbidity and mortality from diarrhoeal disease.

There are some obvious things will need to be clarified in future studies - for example whether zinc alone is the best approach (or for example combinations of zinc with vitamin A). An other question is whether zinc supplementation will help patients in more developed countries where zinc deficiency is more likely to be marginal if present at all.

References:

1. Bhutta ZA et al. Zinc supplementation in malnourished children with persistent diarrhea in Pakistan. *Pediatrics* 1999;103:e42
2. Kelly P et al. Micronutrient supplementation in the AIDS diarrhoea-wasting syndrome in Zambia: a randomized controlled trial. *AIDS* 1999;13:495-500
3. Roy SK et al. Impact of zinc supplementation on persistent diarrhoea in malnourished Bangladeshi children. *Acta Paediatr* 1998;87:1235-9

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