

# Zinc or vitamin A reduced diarrhea in young, poor Bangladeshi children

Rahman MM, Vermund SH, Wahed MA, et al. Simultaneous zinc and vitamin A supplementation in Bangladeshi children: randomised double blind controlled trial. *BMJ*. 2001 Aug 11;323:314-8.

## QUESTION

In young, poor children in Bangladesh, does supplementation with zinc or vitamin A, or both, reduce diarrhea and acute lower respiratory infection (LRI)?

## DESIGN

Randomized (allocation concealed\*), blinded (clinicians, patients, outcome assessors, and statisticians),\* placebo-controlled trial with 6-month follow-up.

## SETTING

Urban slums in Dhaka, Bangladesh.

## PATIENTS

800 children who were 12 to 35 months of age were enrolled. Exclusion criteria were receipt of a vitamin-A capsule in the previous 4 months or severe malnourishment. 665 children (83%) (mean age 24 mo, 53% boys) completed the trial.

## INTERVENTION

Children were allocated to zinc syrup (20 mg of elemental zinc), 5 mL/d ( $n = 170$ ); vitamin A, 200 000 IU ( $n = 159$ ); zinc plus vitamin A ( $n = 175$ ); or placebo ( $n = 161$ ). Zinc or placebo syrup was given for 14 days, and on day 14, patients received a vitamin-A or placebo capsule.

## MAIN OUTCOME MEASURES

Diarrhea ( $\geq 3$  watery stools in 24 h or blood in the stools) and acute LRI (cough, difficult or rapid breathing, and fever).

## MAIN RESULTS

Children who received zinc or vitamin A had a reduced incidence of diarrhea (Table). No interaction existed between zinc and vitamin A in reducing the incidence (rate ratio 1.07, 95% CI 0.91 to 1.277) or prevalence (rate ratio 1.08, CI 0.99 to 1.17) of diarrhea. However, zinc in combination with vitamin A reduced the prevalence of persistent diarrhea (diarrhea lasting  $\geq 14$  d) (rate ratio 0.79, CI 0.66 to 0.94) and dysentery (blood and mucus in stools) (rate ratio 0.80, CI 0.67 to 0.95). The incidence of acute LRI was increased in children who received zinc but not in those who received vitamin A (Table).

The interaction between zinc and vitamin A reduced the prevalence of acute LRI (rate ratio 0.58, CI 0.46 to 0.73) but not the incidence (rate ratio 0.75, CI 0.46 to 1.20).

## CONCLUSIONS

In young, poor children in Bangladesh, supplementation with zinc or vitamin A reduced diarrhea. Zinc increased the incidence of acute lower respiratory infection, but this adverse effect was offset by the interaction of zinc and vitamin A, which reduced the prevalence of acute lower respiratory infection.

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\*See Glossary.

## Zinc or vitamin A vs placebo for incidence of diarrhea in young children†

Outcomes at 6 mo	Comparison	Rate ratio (95% CI)	NNT
Diarrhea (all types)	Zinc vs placebo	0.89 (0.79 to 0.99)	2
	Vitamin A vs placebo	0.84 (0.74 to 0.94)	2
<b>NNH</b>			
Acute lower respiratory infection	Zinc vs placebo	1.62 (1.16 to 2.25)	6
	Vitamin A vs placebo	1.06 (0.74 to 1.53)	Not significant

†Abbreviations defined in Glossary; NNT and NNH calculated from data in article.

## COMMENTARY

The effect of micronutrients, particularly zinc and vitamin A, on morbidity and mortality in children is being increasingly recognized. A combination of zinc and vitamin A was better than vitamin A alone in improving blood levels of vitamin A, suggesting interaction between the 2 micronutrients (1). Whether zinc alone is inferior to the combination is not clear.

Vitamin A has been shown to be responsible for the integrity of the respiratory epithelium through several mechanisms and has a definite beneficial effect in reducing mortality in children with pneumonia (2). The evidence for reducing morbidity is not as clear. Zinc has been found to act on the epithelium and on absorption mechanisms to reduce diarrhea. Zinc supplementation reduces overall mortality and improves growth in high-risk pediatric populations (3).

The findings of the study by Rahman and colleagues show that while vitamin A has limited effects in reducing morbidity from both diarrhea and acute LRI, zinc may actually increase acute LRI morbidity. Another community-based randomized trial in South India has not shown any effect of vitamin A on acute LRI or diarrhea (4).

Clearly, these interventions need to be studied further. The literature is voluminous but inconclusive. A biological basis exists for the reduction in mortality and morbidity with zinc and vitamin A, but the evi-

dence for benefit and harm in sick children remains inconclusive. Diarrhea and respiratory infections have rarely been studied in the same population at the same time. Furthermore, the effect of the simultaneous administration of zinc and vitamin A has not been thoroughly studied. More research is needed before zinc and vitamin A can be accepted as public health intervention measures for childhood illness.

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