

Issue 67

In a nutshell

Previous trials have shown the value of giving vitamin A to populations at risk for vitamin A deficiency in lowering measles morbidity and mortality.

However, trials of vitamin A supplementation have failed to show any consistent benefit in non-measles pneumonia.

Vitamin A and non-measles pneumonia

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NUTRITION RESEARCH REVIEW

Studies one: vitamin A and pneumonia

There is no obvious benefit on clinical outcome in giving children with non-measles pneumonia high dose vitamin A during their illness, according to the results of a new African study.

Subjects: 687 Tanzanian children admitted to hospital with non-measles pneumonia.

Method: Randomised placebo-controlled trial in which active intervention consisted of vitamin A supplementation (200,000 IU for children over 1 year old, and 100,000 IU for infants, given once on the day of admission and again the next day).

Results: There were no significant differences in any of the clinical outcomes reported: duration of hospital stay, number of days of fever, rapid respiratory rate, or hypoxia, and overall mortality. (RR 1.63; 95% CI: 0.67-3.97). This was true regardless of stratification for pre-existing vitamin A dietary status or severity of disease.

Ref. *Am J Clin Nutr* 1998;68:187-92

Study two: Vitamin A and pneumonia: later effects

Another randomised placebo-controlled study from Brazil also failed to find any significant benefit from vitamin A supplementation in children with pneumonia. In this study, it was medium term (16 week) outcomes that were looked at.

No significant positive impact was seen from treatment with vitamin A supplementation (200,000 IU for children 6-12 months of age, and 400,000 IU for those 1-4 years of age) during their initial pneumonia episode. Outcome measures included: prevalence

of morbidity (e.g. wheezing), incidence of clinic attendance and subsequent hospital admission.

Ref: *Trop Med Int Health* 1998;3:661-6

Study three: vitamin A in LRTI

Neither high nor low dose vitamin A supplementation had any impact on respiratory infection, but did significantly impact on associated diarrhoea rates in a recently published study from Africa.

Subjects: 900 preschool-age children from the Democratic Republic of Congo who were hospitalised with acute lower respiratory infection (ALRTI).

Method: A randomised, double-blind, placebo-controlled in which active treatment consisted of two vitamin A supplemented groups: high dose (200,000 IU orally on admission) or low dose (5,000 IU/day whilst in hospital).

Results: There was no significant effect on duration or incidence of either ALRTI or fever from any cause.

There were significant impacts on rates of associated severe diarrhoea, but these differed in different groups of children:

- children receiving the high-dose of vitamin A supplement (who had no oedema) had an increased risk of severe nosocomial diarrhea (RR= 2.42; 95% CI: 1.15- 5.11)
- children in the low dose group who were also severely malnourished had a DECREASED RISK of severe diarrhoea (RR=0.21; 95% CI: 0.07- 0.62)

Ref: *Am J Clin Nutr* 1998;68:1254-60

Study four: Vitamin A prophylaxis in infants

Subjects: 9,424 mother-infant pairs from three countries (Ghana, India, Peru).

Method: A randomised, double-blind, placebo-controlled trial in which the mother-infant pairs received either placebo or vitamin A (200,000 IU vitamin A for the mothers, 25,000 IU vitamin A with each of three immunisations given over the first three 3 months of life).

At 9 months, all children received vitamin A - the placebo group a catch-up dose of 100,000 IU, and the intervention group a further 25,000 IU.

Results: There were no significant differences seen between active and placebo groups in anthropometric status, overall or severe morbidity, and overall mortality at any stage during the study (RR for death= 0.96; 95% CI: 0.73 - 1.27)

There was however a small decrease in the proportion of vitamin A deficiency (serum retinol \leq 0.70 $\mu\text{mol/L}$) in the supplemented children (29.9% vs 37.1% $p < 0.05$) at 6 months of age, but not at 9 or 12 months.

Ref: *Lancet* 1998;352:9136:1257-63

Comments

These trials, particularly the first three, seem to have had disappointing results. None of them has been able to show any convincing benefit in giving vitamin A supplementation to children with non-measles respiratory infection, whether in low or high dose. The main positive outcome was that all except the trial from the Congo found no adverse effects either.

In one way this should not be surprising. The benefits of vitamin A supplementation in populations likely to be malnourished for vitamin A has been convincingly shown for overall mortality and measles morbidity and mortality (e.g. see a meta-analysis in *JAMA* ¹).

But the case for giving it for primary or tertiary prevention of respiratory infection generally not so far been convincingly made. Another meta-analysis from

the mid-1990's failed to show any worthwhile impact on pneumonia morbidity and mortality (based on 12 large-scale field trials in seven countries) ².

That same meta-analysis concluded that there was substantial impact of vitamin A supplementation on all-cause mortality (RR = 0.77; 95% CI: 0.71-0.84) and on diarrhoea- and measles-specific mortality.

The use of vitamin A supplementation, whether using community or hospital-based approaches has been a major reason for excitement in the public health nutrition world for more than a decade. These latest trials, however, show that the full scope of such approaches still needs refinement.

References:

1. *JAMA* 1993;269:898-903
2. *Bull World Health Organ* 1995;73(5):609-19

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