Vitamin A supplementation and childhood morbidity from diarrhea and respiratory infections: a meta-analysis
Grotto I, Mimouni M, Gdalevich M, Mimouni D

CRD summary
This review assessed the effect of vitamin A supplementation on respiratory tract infections and diarrhoea in children. The authors concluded that high-dose vitamin A supplements are not recommended for routine administration to all pre-school children. The limited literature search and inadequate reporting of study quality weaken the strength of the evidence supporting the authors' conclusions.

Authors' objectives
To assess the effects of vitamin A supplementation on childhood morbidity from respiratory tract infections (RTIs) and diarrhoea.

Searching
MEDLINE was searched from inception to December 2000 using the keywords listed in the paper. MEDLINE was also searched using the names of authors of identified studies and studies listed in bibliographies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion if the individuals were randomised and data for intention-to-treat analysis were presented. The studies had to either report relative risks (RRs) with 95% confidence intervals (CIs), or provide sufficient data for their calculation.

Specific interventions included in the review
Studies of vitamin A supplementation were eligible for inclusion. Studies that used vitamin A as an adjunctive treatment for diarrhoea or RTIs were excluded. The included studies compared vitamin A supplementation with control. The studies were conducted in various countries.

Participants included in the review
Studies of children aged over 6 months, not exclusively infants, were eligible for inclusion. The studies had to be conducted in community-based populations without a specific disease at baseline. The children in the included studies were aged from 6 to 83 months.

Outcomes assessed in the review
It was clear that studies that assessed RTIs or diarrhoea were eligible for inclusion. Studies that assessed the prevention of diseases other than diarrhoea and non-measles pneumonia, or only assessed mortality, were excluded. Diarrhoea was defined as the passage of four or more loose or watery stools over 24 hours. RTI was defined as:

cough, fever or chest retractions plus rapid breathing (more than 40 or more than 50 breaths per minute depending on age), or lower respiratory auscultatory findings;
fever plus respiratory difficulties or runny nose;
rapid breathing alone.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies.
Assessment of study quality
Studies were assessed and scored according to 15 criteria. Higher scores were awarded for the following: sample size greater than 150; exclusion of children older than 7 years of age; previous vitamin A supplementation; underweight or xerophthalmia present; systemic disease or measles identified; good description of randomisation; double-blinding; placebo control; use of 200,000 IU vitamin A; follow-up data from monthly visits; follow-up of 1 year or more; and person-time incidence data either reported, or sufficient data reported to permit its calculation. Two reviewers (one of whom was blinded to author, journal, date of publication and study site) independently assessed validity. Any disagreements were resolved through discussion among all reviewers.

Data extraction
Two reviewers extracted the data using a standardised form. Multiple publications of studies were checked for consistency of data. The extracted data included study location, sample size and age of children. Either reported RRs were extracted, or person-time incidence data were extracted and used to calculate RRs based on intention-to-treat analysis. In one study the data were extracted using disease prevalence rather than incidence.

Methods of synthesis
How were the studies combined?
The studies were combined in a meta-analysis. The pooled RR and 95% CIs were calculated using the fixed-effect model described by Fleiss and Kleinbaum in the absence of significant heterogeneity, and the random-effects model of DerSimonian and Laird when significant heterogeneity was found.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared statistic. Sensitivity analyses were conducted by excluding each study in turn; by excluding the study with the lowest quality score; by excluding the two studies with the lowest quality scores; and by excluding the study reporting disease prevalence rather than incidence.

Results of the review
Nine RCTs (45,468 children) were included.

Diarrhoea prevention: there was no statistically significant difference for diarrhoea between groups receiving vitamin A supplementation and control; the RR (random-effects model) was 1.00 (95% CI: 0.94, 1.07). Statistically significant heterogeneity was detected (P<0.001). The results were similar and heterogeneity remained significant after excluding each study in turn and after excluding lower quality studies. Heterogeneity was no longer significant when only studies reporting incidence data were included (P=0.089); this analysis showed a minimally protective effect of vitamin A (fixed-effect RR 0.97, 95% CI 0.94, 1.00).

RTI prevention: the meta-analysis showed that vitamin A supplementation slightly, but statistically significantly, increased respiratory infections compared with control; the RR (fixed-effect model) was 1.08 (95% CI: 1.05, 1.11). No statistically significant heterogeneity was detected (P=0.539). The results were similar and heterogeneity remained non significant after excluding each study in turn and after excluding lower quality studies.

Authors' conclusions
High-dose vitamin A supplements are not recommended for routine administration to all pre-school children in developed areas. They should only be given to individuals or populations with vitamin A deficiency.

CRD commentary
The review question was clear in terms of the study design, intervention, participants and outcomes. Only one database was searched and this may have resulted in the omission of other relevant studies. No attempts were made to minimise publication bias and it was not stated whether any language limitations had been applied. Two reviewers independently selected the studies, assessed validity and extracted the data, which reduces the potential for bias and errors. Validity
was assessed using specified criteria, but the results were not presented.

Only limited information on the included studies was provided; in particular, there were no details of the characteristics of the participants, such as their vitamin A status. The data were combined in a meta-analysis and statistical heterogeneity was assessed. The finding of significant heterogeneity for diarrhoea suggests that a meta-analysis may not have been appropriate. In addition, it might have been informative had the exploration of heterogeneity sources included population characteristics. Some discussion of specific elements of study quality may have allowed a clearer picture of the strength of the evidence to emerge. The limited literature search and the inadequate reporting of study quality weaken the strength of the evidence supporting the authors’ conclusions.

Implications of the review for practice and research
Practice: The authors stated that high-dose vitamin A supplements are not recommended for routine administration to all pre-school children in developed areas, and should only be given to individuals or populations with vitamin A deficiency. They recommended that a comprehensive nutritional approach be taken since vitamin A deficiency usually accompanies other nutritional deficits.

Research: The authors did not state any implications for further research.

Bibliographic details

PubMedID
12640379

DOI
10.1067/mpd.2003.116

Indexing Status
Subject indexing assigned by NLM

MeSH
Child; Child, Preschool; Diarrhea /prevention & control; Diarrhea, Infantile /prevention & control; Dietary Supplements; Humans; Infant; Respiratory Tract Infections /prevention & control; Vitamin A /therapeutic use

AccessionNumber
12003009516

Date bibliographic record published
30/04/2005

Date abstract record published
30/04/2005

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.