

EDITORIALS

Vitamin A supplementation in children and hearing loss

Long term follow-up suggests a potential benefit only in children with otitis media

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For most clinicians, vitamin A is first and foremost associated with eye disease. Vitamin A deficiency causes a range of ocular manifestations including xerophthalmia, night blindness, Bitot's spots, and keratomalacia. Indeed, vitamin A and the eye provide a well known example of the importance of micronutrients for health, and many children have been told to eat their carrots because it is good for their eyes. In the linked long term follow-up of a randomised controlled trial, Schmitz and colleagues (doi:10.1136/bmj.d7962) assess a different effect of vitamin A—whether vitamin A supplementation in the preschool years can reduce hearing loss.¹

Vitamin A has many important functions in the human body and its role in resistance to infectious diseases has been known for almost 100 years.² However, interest in vitamin A waned with the appearance of antibiotics, to return in the 1980s when a study in Indonesia showed that half yearly high dose vitamin A supplementation dramatically reduced child mortality.³ This brought vitamin A back onto the international public health agenda, with an estimated 600 000 deaths in children each year attributed to vitamin A deficiency.⁴ Half yearly high dose vitamin A supplementation was embraced as a “golden bullet” against child mortality. Unicef distributes around 1.5 billion vitamin A capsules a year in more than 70 countries, and this is thought to prevent about 350 000 child deaths a year.⁵

Schmitz and colleagues report on a long term follow-up of preschool children in Nepal who received five doses of a high dose vitamin A supplement or placebo.⁶ The trial was terminated early owing to a strong beneficial effect of vitamin A on mortality. Hence, all subjects received vitamin A supplements after the first 16 months of the trial. Sixteen years later, about 51% of the participants were traced for hearing assessment. Although overall vitamin A supplementation had no effect on failing the hearing test, in the subgroup of children (20%) with a history of ear discharge, vitamin A supplements significantly reduced the risk of hearing loss by 42% (OR 0.58, 95% confidence interval 0.37 to 0.92). Unfortunately, a weekly recall of ear discharge was recorded during five visits only, hence

morbidity data were available for only five of 64 weeks, and many cases of ear discharge were probably missed.

The effects of vitamin A on morbidity are far from clear. Recent meta-analyses point to a reduction in diarrhoeal disease after vitamin A supplementation, but no effect on, or even an increase in, the incidence of respiratory infections.^{7 8} The current study adds another piece to the big puzzle of how vitamin A may affect morbidity. The authors speculate that vitamin A supplements reduced the severity of ear infections because they had no effect on their incidence. Thus, vitamin A might have led to a more controlled immune response, with less oxidative stress, so that an episode of otitis media caused less damage.

Vitamin A is a strong modulator of the immune reaction, certainly when given in high doses. Because vitamin A modulates the balance between T helper 1 and T helper 2 type immune responses,⁹ the type of pathogen causing the infection is important. For example, vitamin A given to Mexican children reduced the duration of *Escherichia coli* associated diarrhoea but increased the duration of *Giardia lamblia* associated diarrhoea.¹⁰ The modulating effects also depend on the age and sex of the subject and factors such as whether the vitamin A is given together with vaccination, whether other nutritional deficiencies are present, and whether the subject is vitamin A deficient. The results of the study are therefore difficult to extrapolate to other settings.

Although the study's findings are intriguing and original, they will probably not result in a change in practice. More direct evidence for a role of vitamin A in otitis media will be needed before vitamin A is used as a treatment. The modest long term impact on hearing loss in a population that is more severely vitamin A deficient than most is unlikely to result in high dose vitamin A supplementation being taken up by national public health bodies, especially in view of current concerns about sustainability, overall effectiveness, and possible adverse effects of such programmes.^{11 12} Other more immediate outcomes, such as mortality, should guide vitamin A interventions, and other

more direct interventions, such as access to adequate antimicrobial treatment, would be more appropriate for reducing hearing loss.

Instead, the study should inspire further investigations that will help in understanding the role of vitamin A in immune function and how it affects health outcomes. The study underlines the importance of micronutrients in early childhood for health outcomes in the long term and points to a beneficial long term adjuvant effect of vitamin A supplements in certain populations

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