

Vitamin A supplementation: A case of not seeing the wood for the trees?

In over 70 countries in the developing world, vitamin A deficiency (VAD) continues to be an important public health problem. It affects about 127 million preschool-aged children, of whom 1.2 - 3 million die unnecessarily and 4.4 million suffer from xerophthalmia that may lead to blindness.¹ Other effects of VAD may be subclinical (impaired iron mobilisation, disturbed cellular differentiation, depressed immune response) or clinical (increased infectious morbidity, growth retardation, anaemia).

The major approaches to combat VAD are vitamin A supplementation (VAS), food fortification, dietary diversification and nutrition education. It is now widely accepted that improving the vitamin A status of preschool-aged children in populations at risk of VAD is an effective, low-cost means of improving child survival.² Vitamin A supplementation to children decreases overall mortality by about 30%, while the mortality reduction in hospitalised children with measles averages 60%.³

Although respiratory illness is responsible for the major part of total child mortality, the effect of VAS has been more on reduction of *diarrhoea-related mortality*. Furthermore, the effect on the latter has not been consistent in all studies. The effect of VAS may also be linked to the aetiology of the diarrhoea. There may therefore be disease- and cause-specific effects of VAS.⁴ This applies to both preventive and treatment regimens.

In this issue of *SAJCN*, Banajeh presents data on high-dose vitamin A supplementation of preschoolers in the Yemen and subsequent diarrhoea mortality rates in hospital.⁵ The study raises several points for debate about VAS and its role in decreasing child mortality and morbidity. It does not, however, refer to the fact that not all trials of VAS have had positive results on mortality and morbidity.^{6,7}

Although the author highlights many reasons as to why the VAS may be linked to the decrease in diarrhoea mortality in this particular study, these cannot be taken as proven because of the nature of the study. One cannot impute causality from an *observational* study such as this one. Information on nutritional status of the children, duration of their illness and hospitalisation before death, and the cause of the diarrhoea may have been relevant to the outcome, but such detail is not provided. Background factors that may have had an effect on the study results (breast-feeding, malnutrition rates, sanitation, and use of oral rehydration therapy) are presented, but these are in fact an indictment of health care and service provision in the Yemen! Efforts to improve the social, economic and health care aspects, as well as the caring capacity of the mothers, are more important than the provision of vitamin A supplements, which is just one means of addressing childhood morbidity

and mortality. Without adequate monitoring and evaluation systems in place, one cannot equate *coverage data* with actual administration of the supplement.

South Africa has implemented VAS of children as part of the Expanded Programme on Immunisation (EPI), as well as medically targeted supplementation. This was largely a result of the South African Vitamin A Consultative Group (SAVACG) Study, which showed that VAD was a problem of public health importance in South Africa.⁸ The Western Cape is the only province that has not implemented VAS with the EPI, although this may change soon. There may be cogent reasons for not going ahead with blanket VAS when one considers the results of recent studies that have shown that VAS may *increase* morbidity in normally nourished children and those unlikely to have VAD.⁹⁻¹² This applies to both hospitalised and community-based populations.

Another reason for caution is the incident, isolated as it may have been, in Assam State in India during a mass VAS campaign. In this campaign a larger dose was administered than was intended, which led to children being hospitalised, and deaths among ill children. The Court's verdict held the State responsible for the deaths due to improper training of the health staff. This led to a loss of confidence of the public in the health system, and attendances at child health clinics for immunisations dropped. According to newspaper reports, UNICEF refused to co-operate with the investigation, claiming it was 'immune to prosecution'. Phrases and words such as '... vitamin A supplementation ... has no adverse effects', 'According to our estimates, administration of 200 000 IU (vitamin A) ... should be perfectly safe', and 'unlikely' are glibly used in the context of safety of VAS.^{13,14} In this regard, a healthy respect for any possible side-effects is what is needed; retinyl palmitate is both a nutrient and a drug depending on the dosages involved. Solomons and Schümann¹⁵ discuss the issue of collateral damage and acceptable tradeoffs in a commentary on the Assam incident. Is there such a thing as an 'acceptable' tradeoff? Irrespective, lessons learned from the Assam incident should be heeded. The unfortunate incident underscores the importance of proper training of health support staff, as well as the need to consider the local circumstances, which may differ vastly between and within regions and countries.

In South African terms and in light of the fact that there are such large differences in health and economic status of our people, that fortification of basic staples is in place, and that results of studies caution against the use of VAS in normally nourished groups, it may be prudent to withhold blanket VAS. Furthermore, personal experience has shown that even the

present regimen of administering high-dose vitamin A to mothers during the postpartum period and to targeted children, is not being implemented properly. Mothers are not told what it is they are receiving and there is a lack of social marketing. The present programme of VAS in the country needs to be monitored and evaluated, while considering VAS with EPI in those areas where child health indicators are poor.

The conditions under which vitamin A supplements can be harmful need to be examined further. In light of the findings concerning the 'vitamin A paradox', health care workers in those regions and countries which may have populations that are both vitamin A deficient and sufficient, and with variable degrees of malnutrition, need to be both cautious and vigilant. A single nutrient deficiency is unusual, and concomitant deficiencies of other nutrients need to be considered when implementing VAS as a strategy. In South Africa, plans for the monitoring and evaluation of existing vitamin A supplementation programmes are imperative, especially in light of the food fortification programme now in place. All efforts should be made to strengthen the primary health care system and improve the confidence of the public in the government health care machinery. Unwanted effects of vitamin A supplementation are certainly not going to help!

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1. West KP jun. Extent of vitamin A deficiency among preschool children and women of reproductive age. *J Nutr* 2002; **132**(95): 2857S-2866S.
2. Beaton GH, Martorell R, Aronson KJ, Edmonston B, Mc Cabe G, Ross AC, Harvey B. Effectiveness of vitamin A supplementation in the control of young child morbidity and mortality in developing countries. ACC/SCN State of the Art Series: Nutrition Policy Discussion Paper. United Nations, New York, NY, 1993.
3. Villamour E, Fawzi WW. Vitamin A supplementation: Implications for morbidity and mortality in children. *J Infect Dis* 2000; **182**: Suppl 1, S122-S133.
4. Ross AC. Vitamin A supplementation as therapy - are the benefits disease specific? *Am J Clin Nutr* 1998; **68**: 8-9.
5. Banajeh SM. Is 12-monthly vitamin A supplementation of preschool children effective? An observational study of mortality rates for severe dehydrating diarrhoea in Yemen. *S Afr J Clin Nutr* 2003; **16**: 22-27 (this issue).
6. Dibley MJ, Sadjimin T, Hkjilhed CL, Moulton LH. Vitamin A supplementation fails to reduce incidence of acute respiratory illness and diarrhoea in pre-school age Indonesian children. *J Nutr* 1996; **126**(2): 434-442.
7. Gupta P, Indrayan A. Effect of vitamin A supplementation on childhood morbidity and mortality: critical review of Indian studies. *Indian Pediatr* 2002; **39**(12): 1099-1118.
8. Labadarios D, Van Middelkoop A. South African Vitamin A Consultative Group (SAVACG). Anthropometric, vitamin A, iron and immunization status in children aged 6-71 months in South Africa, 1994. *S Afr Med J* 1996; **86**: 354-357.
9. Grotto I, Mimouni M, Gdalevich M, Mimouni D. Vitamin A supplementation and childhood morbidity from diarrhea and respiratory infections: A meta-analysis. *J Pediatr* 2003; **142**: 297-304.
10. Fawzi WW, Mbise R, Spiegelman D, Fataki M, Hertzmark E, Ndossi G. Vitamin A supplements and diarrheal and respiratory tract infections among children in Dar es Salaam, Tanzania. *J Pediatr* 2000; **137**: 660-667.
11. Griffiths JK. The vitamin A paradox. *J Pediatr* 2000; **137**(5): 604-607.
12. Sempertegui F, Estrella B, Camanero V, et al. The beneficial effects of weekly low-dose vitamin A supplementation on acute lower respiratory infections and diarrhoea in Equadorian children. *Pediatrics* 1999; **104**(1): e1.
13. Schultink W. The use of under-five mortality rate as an indicator for vitamin A deficiency in a population. *J Nutr* 2002; **132**(95): 2881S-2883S.
14. Allen LH, Haskell M. Estimating the potential for vitamin A toxicity in women and young children. *J Nutr* 2002; **132**(95): 2907S-2919S.
15. Solomons NW, Schümann K. Collateral damage in the battle against hypovitaminosis A? *Am J Clin Nutr* 2002; **75**: 659-661.