Discussion on Vitamin A Supplementation in Childhood

Vitamin A deficiency (VAD) is a very common public health problem in more than half of the world, especially in Africa and Southeast Asia, with young children and pregnant women in low-income countries being hardest hit. The WHO estimates that 250 million preschool children have VAD and that a substantial proportion of pregnant women in VAD geographic areas is vitamin A deficient. Globally, between 1995 and 2005, ~5.2 million preschool children and ~9.7 million pregnant women were affected by night blindness. If retinol concentrations <70 μmol/l are reviewed, 190 million children have low levels of retinol compared to 19 million pregnant women. For children, VAD significantly increases the risk of severe illness, and even death from common illnesses such as diarrhea and measles. For pregnant women, VAD occurs during the last trimester and the mother presents with night blindness. The relationship or association of VAD and vertical transmission of HIV remains to be clarified.

Dietary deficiency can begin in the neonatal period due to lack of breastfeeding and continue into adulthood due to diets deficient in vitamin A-containing foods such as liver, cheese, milk, eggs, fruits and vegetables and fortified foods. Randomized controlled studies of vitamin A supplementation in women before, during or after pregnancy have yielded conflicting results. West et al. [1] in a double-blind, placebo controlled study in Nepal, demonstrated that weekly 7,000 retinol equivalents as vitamin A or provitamin A β-carotene were associated with a 44% reduction in maternal mortality. In the SUMMIT trial conducted in Indonesia, early infant mortality was reduced in infants born to mothers receiving micronutrient supplementation including 800 μg of retinol (35.5/1,000 vs. 43/1,000, RR 0.82, 95% CI: 0.70–0.95), but there was no effect on maternal mortality [2, 3]. More recently, Kirkwood et al. [3], found no significant effect on pregnancy-related mortality or on all-cause mortality with vitamin A supplementation. There were no effects on the rate of still birth, perinatal, neonatal or infant death.

The effect of VAD on all cause and diarrheal mortality remains controversial. In one study of over 200,000 children, vitamin A supplementation decreased
mortality, whereas in the DEVTA study from India, no differences in mortality were observed [4]. Further, a question raised was whether vitamin A supplementation would still have a beneficial effect on mortality in countries with a high measles immunization rate. In 1995, Ramakrishnan and colleagues found that respiratory and diarrheal morbidity were similar in children less than 3 years of age who were vaccinated against measles but were not severely malnourished, suggesting that overall nutrition is a very important confounding factor. There appears to be an inverse relationship between vitamin A supplementation and all-cause mortality with declining mortality with increased number of doses per child per year. On the other hand, vitamin A supplementation in doses ranging from 1,000 to 9,000 IU/kg per day for 28 days increased markers of oxidative stress in animal models.

In children, protection from VAD comes from breastfeeding in the neonatal period, and later providing a periodic supply of high-dose vitamin A has demonstrated a reduction in mortality. Since breast milk is a good source of vitamin A, and its level can be influenced by supplementation of the lactating mother, promoting breastfeeding is a good strategy to prevent VAD. For deficient children, a periodic supply of high doses of vitamin A has been demonstrated to reduce mortality by 23% and up to 50% in those with measles. The exact number of doses and the dose itself is still not clear. Overall, in an analysis by Kirkwood et al. [3], there was a favorable trend towards reduced mortality in boys, but not in girls. However, of the 6 studies used in the analyses for boys, the confidence interval crossed 1 in 5 of the 6, whereas they crossed 1 in all 6 studies for girls. There were no significant differences in outcomes that included infant mortality, newborn mortality, respiratory or diarrheal morbidity [5]. Vitamin A supplementation during infancy does not appear to adversely interact with common immunizations with no differences in mortality in the first year in supplementation vs. placebo and DPT/polio vaccination [6].

Control of VAD can be done by different approaches: improving the availability and intake of vitamin A through dietary intake of vitamin A-rich foods; increasing the dietary intake through fortification of foods as has been done in Central and South America; periodic delivery of 200,000 IU of vitamin A in preschool children with half the dose given between 6 and 11 months of age appears very successful [7, 8]. The periodic approach to supplementation has been shown to reduce the risks of xerophthalmia by ~90% and mortality by up to 23% in young children [9]. Many high-risk countries have also adopted the WHO policy of supplementing mothers within 6 weeks after delivery to increase vitamin A content of breast milk.

There appear, however, to be geographic differences with trials in Africa of vitamin A supplementation in infants that did not alter mortality, and those in Asia that did. In infants between 1 and 5 months of age, there was no effect on mortality. In infants >6 months of age, vitamin A supplementation decreased all-cause and diarrhea-specific mortality in some studies, but not others.
Thus, for the continuum of vitamin A sufficiency, one would include breastfeeding for 6 months, appropriate timely vitamin A supplementation between 6 months and 6 years of age, and food fortification after that (Guatemala, for example, where sugar is fortified). For specific vulnerable populations, growing fruits and vegetables complements dietary diversity and food fortification.

These three approaches combined with other public health initiatives to promote breastfeeding, oral rehydration therapy, vaccination and birth spacing can all lead to significant reductions in VAD and related morbidities.

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**References**


