

Vitamin A Supplements Ameliorate the Adverse Effect of HIV-1, Malaria, and Diarrheal Infections on Child Growth

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Objective. Evidence from animal experiments and observational studies in humans suggests that vitamin A plays a fundamental role in physical growth. However, results from vitamin A supplementation trials in children are inconsistent; whereas some did not find an overall effect on growth, others found benefits only among specific groups, including children with low concentrations of serum retinol or short duration of breastfeeding. The apparent lack of an overall effect of vitamin A on growth could be attributed to context-specific distribution of conditions that affect both growth and the response to supplementation, eg, baseline vitamin A status, deficiency of other nutrients (fat, zinc), and the presence of infectious diseases. Human immunodeficiency virus (HIV) infection, malaria, and diarrheal disease adversely affect growth and are associated with increased prevalence of vitamin A deficiency. We hypothesize that vitamin A supplementation could ameliorate the adverse effect of these infections on child growth.

Methods. We conducted a randomized, clinical trial among 687 Tanzanian children who were 6 to 60 months of age and admitted to the hospital with pneumonia. Children were assigned to oral doses of 200 000 IU vitamin A (half that dose if <12 months) or placebo on the day of admission, a second dose on the following day, and third and fourth doses at 4 and 8 months after discharge from the hospital, respectively. Anthropometric measurements were obtained at baseline and at monthly visits to the study clinics during 12 months after the initial hospitalization. Surveillance on the incidence and severity of diarrhea and respiratory infections was conducted during biweekly visits, alternately at a study clinic and the child's home, using a pictorial diary that the mothers were trained to use. A blood specimen was drawn at baseline for determination of HIV status, malaria infection, and hemoglobin levels. We used mixed effects models to compare estimated total weight and height increases after 1 year of follow-up between treatment arms, overall and within levels of HIV status, malaria, and other possible baseline effect modifiers. We also assessed the potential modulating effect of vitamin A on the risk of stunting (height-for-age <-2 standard deviations of the gender-specific National Center for Health Statistics median reference) attributable to diarrheal and respiratory infections during

follow-up, in the subset of children who were not stunted at baseline. A similar approach was followed for wasting (weight-for-height <-2 standard deviations of the reference median). Cox regression models were used to estimate relative risks and 95% confidence intervals (CI), treating episodes of infection as time-dependent covariates.

Results. A total of 554 children had at least 2 follow-up measurements of height or weight and constituted the study base. Baseline characteristics did not differ significantly by treatment arm. Seventy-three percent of the children were <2 years of age, and 37% were <12 months; 31% were stunted at baseline and 9% were wasted. Malaria (*Plasmodium falciparum*) and HIV infection were found in 24% and 9% of the children, respectively. Median duration of follow-up was 351 days, with 10 measurements/child, on average, irrespectively of treatment assignment. Supplementation with vitamin A among children who had HIV infection and were <18 months of age resulted in a significant length increase. Four months after the first dose, infants who were HIV positive in the vitamin A arm had gained, on average, 2.8 cm (95% CI: 1.0–4.6) more than children who received placebo, whereas no effect was observed among infants who were HIV negative (difference at 4 months: -0.2 cm; 95% CI: -0.8 – 0.5). Children who were <12 months of age and had malaria at enrollment experienced a 747-g (95% CI: 71–1423) higher yearly weight gain attributable to vitamin A; among children without malaria, however, the supplements did not have a significant effect (-57 g; 95% CI: -461 – 348). These results remained unchanged after controlling for indicators of the socioeconomic and nutritional status at baseline. Linear growth was also improved by vitamin A among children from households with poor water supply (0.8 cm/year; 95% CI: 0–1.5) but not in children with tap water in the house or compound (-1.0 cm/year; 95% CI: -1.9 – 0). Weight gain was greater among children with mid-upper arm circumference below the 25th percentile of the age-specific distribution at baseline (458 g/year; 95% CI: 1–905), but no benefit was evident among children with higher mid-upper arm circumference. The risk of stunting associated with episodes of persistent diarrhea (lasting 14 or more days) during follow-up was virtually eliminated by vitamin A supplements. Among children in the placebo group, the average risk of stunting associated with 1 or more episodes of persistent diarrhea between 2 consecutive visits was 5.2 times higher (95% CI: 2.4–11.2) than that of children without diarrhea or with acute episodes. In contrast, among children who received vitamin A, there was virtually no risk of stunting associated with persistent diarrhea (relative risk: 1.0; 95% CI: 0.3–1.3). This effect was slightly attenuated after controlling for the number of household possessions, gender, baseline low arm circumference, HIV infection, and presence of malaria parasites in blood. Vitamin A supplements did not modify the associations between respiratory infections and the risk of stunting or wasting.

Conclusions. Vitamin A supplementation improves linear and ponderal growth in infants who are infected with HIV and malaria, respectively, and decreases the risk of stunting associated with persistent diarrhea. Supplementation could constitute a low-cost, effective intervention to decrease the burden of growth retardation in settings where infectious diseases are highly prevalent.

Topics:

cachexia, diarrhea, malaria, vitamin a, hiv infections, hiv