

## **Potential Toxicity of Vitamin A Supplementation in Infancy**

*[Baqi AH, Francisco A de, Arifeen SE, Siddique AK, Sack RB. Bulging Fontanelle after supplementation with 25,000 IU of Vitamin A in infancy, using immunization contacts. Ada Pediatr 1995, 84: 863-866].*

In an attempt to improve child survival, regular vitamin A supplementation has been recommended in childhood. However there is a paucity of data on the safety and efficacy of administering vitamin A in infants younger than 6 months. To evaluate its safety, vitamin A in a dose of 25,000 IU was supplemented in a double blind placebo controlled trial along with DPT/OPV immunization. The trial was conducted at the International Centre for Diarrheal Disease Research Hospital, Bangladesh. One hundred and sixty seven infants completed all 3 doses at 6.5 ( $\pm 0.9$ ), 11.8 ( $\pm 1.2$ ) and 17.0 ( $\pm 1.3$ ) weeks of age. Eighty six infants received vitamin A and the remaining 81 received placebo. The treatment and-placebo groups were comparable differing only in terms of vitamin A supplementation. Nine infants (10.5%) supplemented with vitamin A had episodes of bulging of anterior fontanelle compared with 2 infants (2.5%) in the placebo group ( $p < 0.05$ ). In total, there were 14 episodes of bulging of fontanelle of which 12 occurred in vitamin A supplemented group. Of the 12 episodes, none occurred in association with the first dose, 3 with the second and 9 with the third dose suggesting a cumulative effect. Bulging of the fontanelle following vitamin A supplementation was positively associated with anorexia, drowsiness and vomiting. This randomized double blind placebo controlled trial suggests a significantly higher incidence of bulging of

fontanelle in infants supplemented with 25,000 IU of vitamin A simultaneous to DPT/OPV vaccination.

### **Comments**

The role of vitamin A supplementation in reducing morbidity and mortality among children has generated considerable controversy in recent years(1-3). Nevertheless, routine vitamin A supplementation is being extensively promoted as a cost effective intervention to improve child survival in developing countries. In order to improve coverage, WHO recommends distribution of vitamin A to young children through immunization contacts(4). The World Health Organization/United Nations Children Fund/International Vitamin A Consultative Group (WHO/ UNICEF/IVACG) Task Force recommends universal distribution of 200,000 IU of vitamin A every 3-6 months prophylactically to children over 1 year and under 6 years of age. It also recommends 100,000 IU of vitamin A to infants aged 6-12 months along with measles vaccination and 50,000 IU of vitamin A orally to infants less than 6 months of age(4,5).

In view of the controversy surrounding the utility of Universal Vitamin A supplementation, it is crucial to evaluate the safety of this intervention, particularly in infancy, before embarking on large scale national programmes. Routine vitamin A supplementation even in doses as low as 25,000 IU may not be safe as suggested by the present study. Similarly acute vitamin A toxicity was reported from Bangladesh when three doses of 50,000 IU of vitamin A were administered to infants along with DPT/OPV vaccination(6). Bulging of fontanelle was noticed in 11.5% of infants in the vitamin A supplemented group. Moreover, there was a tendency towards a cumulative effect of toxicity with as many as 50% of bulging episodes occurring after the third dose of DPT/OPV vaccination.

Membrane stability gets lost in hypervitaminosis A thus enhancing permeability leading to acute toxicity. Vitamin A also has a long biological half-life and it bioaccumulates after repeated doses(7). DPT/OPV vaccination has also been known to cause bulging of fontanelle(8). Administration of vitamin A along with DPT/OPV vaccination may be producing a combined effect.

The wisdom of administering vitamin A along with measles vaccine has also been questioned by the findings of decreased immune response to immunization. In a study from Indonesia, the efficacy of measles vaccine was found to be lower in infants who were simultaneously administered 100,000 IU of vitamin A(9). There is some evidence that even titres of polio antibodies are lower in the supplemented group (Agarwal KN, personal communication).

In India, the surveys of National Nutrition Monitoring Bureau indicated a decline in the prevalence of Bitot's spots in preschool children from about 2% in 1975-79 to about 0.7% in 1988-90(10). Similarly, recent national surveys had indicated that vitamin A deficiency contributes to only 0.04% of total blindness as compared to 2% about 2 decades ago(11).

Considering the reduction of prevalence of vitamin A deficiency in the country, doubtful efficacy of the intervention and the genuine concern regarding the potential toxicity of vitamin A supplementation in infancy, the recommendations of Child Survival and Safe Motherhood (CSSM) Programme of administering 100,000 IU of vitamin A in infancy(12) needs an immediate review.

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