

Invited commentary

Time to stop giving indiscriminate massive doses of synthetic vitamin A to Indian children

The purpose of this invited commentary is to indicate why the mass administration of massive doses of synthetic vitamin A to Indian children is outdated, may have lasting adverse effects especially on young children, and is a distraction from sustainable solutions to undernutrition and poverty in India. Current policies and practices are clearly wrong.

Vitamin A deficiency is now uncommon

Vitamin A deficiency was a major public health problem in India in the 1950s and 1960s. Clinically evident deficiency is common only in some districts. Severe deficiency, causing corneal xerophthalmia or keratomalacia and eventual blindness in children, is now uncommon^(1,2).

Clinical signs of mild xerophthalmia such as Bitot's spots and night blindness, still seen in children from deprived communities, are declining. The first repeat survey of the Indian National Nutrition Monitoring Bureau carried out in the same villages showed that prevalence of Bitot's spots had declined in 1988–90 compared with 1975–9, from 1.8% to 0.7%⁽²⁾. A survey of the Indian Council of Medical Research in 1988, covering sixteen districts mostly in northern and eastern regions, showed that prevalence of Bitot's spots ranged from 0 to 4.7% and that of night blindness from 0.4 to 4.8%⁽³⁾. Prevalence rates vary widely between and also within states.

The context is general improvement of child health in India. Prevalence of severe protein–energy malnutrition dropped from 15% in 1975 to less than 2% in 2000. Immunisation coverage for measles and other vaccine-preventable diseases has improved from 5–7% in the early 1970s to the current 80–90%. The national government of India has addressed the issue of food insecurity diligently, one result being significant improvement in intake of foods rich in vitamin A.

Problems with current policy

Current national government policy in the form of the Integrated Child Development Programme, which covers 90% of rural India, is to provide nutritional supplements in physiological doses to children less than 6 years of age, nutrition education to mothers, and also mega-doses of vitamin A. A total of nine massive doses of synthetic vitamin A are given to children between the ages of 9 and 60 months. The programme undoubtedly continues to treat and prevent clinical deficiency with its

consequences. The problems, some ethical, are to do with its scope and prominence.

Indiscriminate mega-dosing

Universal supplementation of vitamin A to Indian children is being undertaken irrespective of their family background and nutritional status. But as stated, deficiency is now limited to isolated geographical pockets in India. Also, there is no good evidence of benefit of supplementation of children without clinical signs of deficiency.

Vitamin A is toxic in high doses. The mega-dose of vitamin A (200 000 IU) given to children is 500 times higher than the daily recommended dose (400 IU). Children hospitalised for acute infectious diseases with low vitamin A status on admission tend to benefit from high-dose supplements, but no benefits and even adverse effects are observed among those with adequate pre-admission vitamin A status⁽⁴⁾. It is therefore bad practice to administer a pharmacological dose of vitamin A to a child whose vitamin A status is adequate.

Possible adverse effects

After administration of mega-doses of vitamin A to young children, signs of intra-cranial tension showing as bulging of the anterior fontanels are evident in up to 16% of all cases^(5,6). The first twelve months of life are crucial for brain development. This is the time when billions of brain cells are multiplying and establishing thousands of inter-neuronal synaptic connections.

Adverse effects of high doses of vitamin A on bone resorption and bone formation have been demonstrated in animals. Studies have not yet been undertaken on young undernourished children subsisting on low Ca intakes. Meanwhile the best policy is prudence.

Unjustified claims of benefit

Massive administration of massive doses of vitamin A is advocated on the grounds that this could bring about a 23% reduction in mortality. However, benefits on this scale have been found only in areas with rudimentary health-care facilities where clinical deficiency is common, and the biological mechanisms suggested as explanations are conjectural.

Reports claiming that blindness due to vitamin A deficiency in India is a public health emergency needing

immediate drastic solutions have never been properly substantiated. The claim of massive benefit of supplementation is largely the result of investigations carried out by scientists from one centre, the John Hopkins School of Hygiene and Public Health. However, investigations carried out from the Harvard School of Public Health, and from the Indian National Institute of Nutrition, have not substantiated this claim. It has been suggested that the reduction in mortality is actually caused by the Hawthorne Effect, whereby a period of attention and special care, and not medicine, improves health^(7,8).

The validity of meta-analyses whose results evidently support the claim has also been questioned^(9,10). Data for these analyses are from studies of different designs of varying quality from different regions. In the studies analysed, estimation of vitamin A levels was either not done in the recipient children or else only a few children were subjected to investigation. By contrast, a recent meta-analysis of all the Indian studies shows that the findings from vitamin A trials are inconsistent⁽¹¹⁾.

The most recent findings are from the largest ever randomised controlled De-worming and Enhanced Vitamin A (DEVTA) trial, in which one million rural children in the state of Uttar Pradesh in north India were included. Half the children were given vitamin A supplements and half were not. There was no significant difference in the death rates between children who received the massive dose of vitamin A and those who did not⁽¹²⁾.

The wrong way and the right way

There is no good evidence of substantive benefit of universal vitamin A supplementation of Indian children. The era of gross and rampant vitamin A deficiency leading to blindness is over. It is time to resist the soft option of mega-doses of synthetic vitamin A. This evades responsibility to improve the diets of young children, with all this implies.

Children in impoverished communities need adequate healthy food, rather than pills, tablets or sprays. Mass use of mega-doses of synthetic vitamin A creates a culture of perpetual dependency and does not teach communities to improve their diets.

The sustainable way to prevent vitamin A deficiency is well-known. The solution is to increase local production and consumption of green leafy vegetables and other plant foods that are rich or good sources of carotenoids. This will do more than protect against xerophthalmia. Green leafy vegetables, and many fruits and other plant foods, are also good sources of folate, vitamin C, Fe, Ca and many other micronutrients and bioactive compounds. They contribute to improvement of the overall nutritional status of children and protection against infectious and other diseases.

In India micronutrient deficiencies are often the result not of poor-quality food, but lack of food. A child with signs of subclinical vitamin A deficiency may really be suffering from overall undernutrition. Often when children have adequate amounts of their typical local diets, signs of specific micronutrient deficiencies disappear. With the exception of communities where acute clinical deficiency of vitamin A is common, the food-based approach is the economical, effective and sustainable way.

We must look to our farmers, not to pharmaceutical companies, to protect the health of our children. The main solution to vitamin A deficiency should not be drug-based, but food-based.

Umesh Kapil

Professor, Department of Human Nutrition
All India Institute of Medical Sciences
Ansari Nagar, New Delhi, India
Email: umeshkapil@yahoo.com

References

1. Bhattacharya AK & Chatopadhyaya PS (1986) Xerophthalmia in West Bengal, India. *Bull Calcutta Sch Trop Med* **34**, 444-7.
2. National Nutrition Monitoring Bureau (1991) *Report of Repeat Survey (1989-1990)*. Hyderabad: National Institute of Nutrition.
3. Toteja GS, Singh P, Dhillon BS & Saxena BN (2002) Vitamin A deficiency disorders in 16 districts of India. *Indian J Pediatr* **69**, 603-605.
4. Solomons NW & Schumann K (2004) Update on vitamin A-related deaths in Assam, India. *Am J Clin Nutr* **80**, 1083-1084.
5. de Francisco A, Chakraborty J, Chowdhury HR, Yunus M, Baqui AH, Siddique AK & Sack RB (1993) Acute toxicity of vitamin A given with vaccines in infancy. *Lancet* **342**, 526-527.
6. Gopalan C & Tamber B (2003) Food-based approaches to prevent and control micronutrient malnutrition: scientific evidence and policy implications. *World Rev Nutr Diet* **91**, 76-131.
7. Gopalan C (1986) Reviews and comments: Control of vitamin A deficiency – priorities for future research in India. *NFI Bull*, p 8.
8. Vijayraghavan K, Radhaiah G, Praksam BS, Sarma KVR & Reddy V (1990) Effect of massive dose vitamin A on morbidity and mortality in Indian children. *Lancet* **336**, 1342-1345.
9. Gopalan C (1993) Efficacy of mega dose of vitamin A: the Sudan-Harvard study. *NFI Bull*, pp 4-5.
10. Humphrey JH & Rice AL (2000) Vitamin A supplementation of young infants. *Lancet* **356**, 422-424.
11. Gupta P & Indrayan A (2002) Effect of vitamin A supplementation on childhood morbidity and mortality: critical review of Indian studies. *Indian Pediatr* **39**, 1099-1118.
12. Awasthi S, Peto R, Read S & Bundy D (2007) Six-monthly vitamin A from 1 to 6 years of age. DEVTA: cluster-randomised trial in 1 million children in North India. <http://www.otsu.ox.ac.uk/projects/devta/resolveuid/081055e104b96b5203fc2c8da5091096> (accessed May 2008).