Infections and Vitamin A

Vitamin A deficiency is widely prevalent among children of poor communities in many developing countries and is often associated with other nutritional defects. Although an inadequate diet is the main cause of the poor nutritional status, the unhygienic environment that these children live in results in a high incidence of infections which accentuate the nutritional deficiencies. Thus, malnutrition and infection have a synergistic interaction with mutually adverse effects. Vitamin A is believed to be important in such interactions.

The mechanisms involved are complex and include a decreased intake particularly of carotene-rich foods. Malabsorption associated with infection aggravates the situation. Sheehy et al. found that Puerto Rican army recruits with severe hookworm disease suffered from steatorrhoea and showed a decreased absorption of vitamin A and xylose. Reddy and Sivakumar, using 11,12-3H retinyl acetate and retinyl palmitate, demonstrated absorptive defects in children suffering from bronchopneumonia, diarrhoea and ascariasis. However, the decrease in vitamin A absorption was not associated with fat malabsorption.

In 1892, Spicer first observed that clinical signs of xerophthalmia often followed an episode of acute or chronic illness and in 1917 McCollum described the association between vitamin A deficiency and infection in an animal model. A decade later Green and Mellanby referred to it as the anti-infective vitamin and in 1985 the induction of solitary vitamin A deficiency in experimental animals was shown to lead to immunosuppression and an increased susceptibility to infection. Children suffering from febrile illnesses and acute infections have been reported to have low levels of circulating carotenoids and retinol and recently, Bhaskaram et al. have shown lower levels of serum retinol in children suffering from acute infections such as measles, bronchopneumonia and gastroenteritis. In a prospective study of children living in urban slums, the same investigators found a fall in serum retinol and retinol binding protein levels during an acute attack of measles. Interestingly, the fall was greater in children whose pre-measles nutritional status was poor.

Several epidemiological and clinical studies have demonstrated an increased mortality and morbidity among children with severe vitamin A deficiency. However, vitamin A deficiency is usually associated with severe protein energy malnutrition in children and these studies failed to define the effect of vitamin A deficiency alone.

Like other nutritional deficiencies vitamin A deficiency is only an indication of the much wider problems of malnutrition. Most apparently normal pre-school children in India suffer from mild vitamin A deficiency and have serum retinol levels of less than 20 µg/dl with or without clinical signs of xerophthalmia. Sommer et al. were the first to report the adverse effects of mild vitamin A deficiency on childhood morbidity and mortality. The results of such studies have important policy implications and the United Nations Subcommittee on Nutrition has called for more controlled studies from different parts of the world to
elucidate the relationship between vitamin A infection and childhood mortality.

Several studies have revealed that a certain association exists between mild vitamin A deficiency and infections, though the pattern of infections was not uniform. While reports from Indonesia indicated an association with respiratory and gastrointestinal infections, Bloem et al. from Thailand found a greater risk of respiratory infections. These observations were similar to the results reported by Milton et al. from a retrospective study in India of urban slum children who had clinical vitamin A deficiency as well as a later prospective community study by Vijayaraghavan et al.

The Indonesian workers found an association between mild vitamin A deficiency and higher childhood mortality rates and reversal of both morbidity and mortality following periodic administration of large doses of vitamin A. However, the strong claims made by the Indonesian workers about the relation between vitamin A, morbidity and mortality have been subjected to severe criticism and the conclusions should be accepted with caution. The major controversies relate to:

- the disregard of other confounding variables;
- the lack of a placebo group in the supplementation study;
- the effect of the ‘contact factor’ with the health worker in the experimental group;
- how representative the study area was, given the differences in mortality rates of the control area and the national figures;
- the lack of information on the exact age and cause of death.

Subsequent studies from Nepal, India, Bangladesh and Sudan have shown conflicting results. The Nepalese workers support the observations made by the Indonesian group. Daulaire demonstrated that periodic administration of large doses of vitamin A (ranging from 50,000 IU to 200,000 IU depending on age) reduced deaths due to diarrhoea, pneumonia and measles in a population of children with high underlying mortality rates and xerophthalmia.

In the two Indian studies, Vijayaraghavan et al. from Hyderabad found that 200,000 IU of vitamin A given once in 6 months to rural pre-school children produced no significant effect while the community study reported from Madurai demonstrated a 50% reduction in mortality rates in a double blind controlled study where the experimental group of children received 800 IU vitamin A weekly while the control group received a placebo. These two studies are not strictly comparable because of major differences in the dose and mode of administration of vitamin A and a higher rapport between the health worker and the test population in the latter study. However, both failed to account for other associated factors which might lead to childhood mortality.

In Bangladesh, Bardhan et al. examined the effect of administering a single dose of vitamin A to the mother and/or infant at birth on the morbidity of breast fed babies. Morbidity was determined by the number of episodes of diarrhoea or respiratory infections and this did not differ between the supplemented and unsupplemented infants.

Herrera et al. from Sudan found no significant effect on mortality or morbidity when 200,000 IU of vitamin A was given every 6 months to asymptomatic children who did not have clinical signs of xerophthalmia.

These investigations have all been carried out on poor children in whom the increased morbidity could have been attributed to a number of other poverty related nutritional and non-nutritional factors. However, it is fairly well established that vitamin A has an effect on the integrity of epithelial tissue and adjuvant effects on the immune system, so its deficiency might increase susceptibility to infections.

The prevalence of vitamin A deficiency and the mortality rates in a given community appear to be important factors determining the beneficial effects, if any, of vitamin A administration on morbidity and mortality. The available information fails to provide unequivocal support for the spin-off benefits of a massive vitamin A prophylactic programme in communities where malnutrition and infectious illnesses are widely prevalent. Giving all children regular and massive doses
of vitamin A to improve their survival may not be cost-effective and the possible adverse metabolic and immunological effects of repeated administration of large doses cannot be ignored. It may therefore be prudent to limit the administration of large vitamin A supplements to children at risk.

REFERENCES


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