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Vitamin A Deficiency – Overkill

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The achievement of optimal nutritional status calls for an adequate intake of nutrients (macronutrients, micronutrients and phytonutrients), all of which can be derived from a balanced diet based on a judicious combination of available, traditional foods. Nutrition scientists from the time of McCollum and McCarrison had recognised the importance of such balanced diets and had promoted their intake as the sure way of achieving optimal nutrition.

In recent years, however, with the advent of modern technologies for manufacture of synthetic nutrients in bulk, there have been attempts to promote some individual nutrients perceived as being of special importance. Following the “protein fiasco” and the subsequent welcome dissolution of the Protein Advisory Group (PAG), the nutrient that has been occupying centre stage in the international nutrition scene, for over three decades, has been vitamin A.

Vitamin A is undoubtedly an important essential nutrient, involved in quite a wide range of metabolic functions. Ensuring optimal vitamin A nutrition is, therefore, important. Vitamin A is, however, one of several scores of nutrients that also perform important functions with respect to health promotion and disease prevention. The near-exclusive emphasis on vitamin A should not obscure the need for a sensible food-based approach towards ensuring the well being of populations. There is considerable information today on the inter-relationships among micronutrients. Exclusively pushing

the intake of a single micronutrient in a population suffering from multiple micronutrient deficiencies could lead to undesirable results.

Keratomalacia, arising from vitamin A deficiency, aggravated by respiratory infections (often consequent to an attack of measles) and protein-calorie malnutrition (PCM) was a major public health problem in India till the late 1960s. Keratomalacia was a clinical emergency and the use of synthetic vitamin A in the treatment of this acute and fulminant form of vitamin A deficiency was justified. Keratomalacia, like kwashiorkor, ceased to be a major public health problem from the late 1970s. What is now being seen is a mild form of chronic vitamin A deficiency (Bitot's spots) among the populations in some highly malnourished pockets of the country. Data from National Nutrition Monitoring Bureau (NNMB)^{1,2} and Indian Council of Medical Research (ICMR)³ micronutrient surveys indicate that over decades there has been a reduction in the prevalence of Bitot's spots.

Pro-vitamin A carotenes and carotenoids such as alpha carotene, beta carotene and cryptoxanthins that are present in fruits and vegetables are good sources of vitamin A. Earlier claim⁴ that pro-vitamin A carotenoids are not bioavailable, have been effectively contradicted in a series of subsequent studies^{5,6,7,8}. A comprehensive and elegant study by Tanumihardjo⁹ has shown that not only are pro-vitamin A carotenoids bioavailable, but because of bio-regulation of conversion of carotenoid to vitamin A depending on

vitamin A levels in the liver, their intake does not result in vitamin A toxicity, unlike when pre-formed vitamin A is administered. Thus, the food-based approach has been clearly shown to be a safe, sure and sensible way of preventing vitamin A deficiency.

Massive-dose Vitamin A Prophylaxis

Long after the disappearance of keratomalacia and serious forms of vitamin A deficiency, a programme of massive-dose vitamin A prophylaxis was promoted following the claims from a study by Sommer et al.^{10,11} that this approach would reduce child mortality. In a series of articles^{12,13,14,15}, I had adduced arguments to show that this claim is unsustainable and unacceptable. The claim regarding the benefits of massive-dose vitamin A rests mostly on findings from studies conducted by one school and its collaborators. Other important institutions like Harvard¹⁶ and the National Institute of Nutrition (NIN)¹⁷ in India have reported negative findings in respect of the impact of massive-dose on mortality. In these studies, contrary to the claims of studies carried out by Sommer et al and collaborators, massive-dose vitamin A administration did not bring about any reduction in child mortality.

One of the largest studies exploring whether massive dose of vitamin

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A administration is associated with a reduction in childhood mortality was taken up in 72 blocks in Uttar Pradesh in India between 1999-2004. In this study, children from different areas were given six-monthly massive dose of vitamin A, six-monthly deworming, or both or neither. About 1 million children were followed and mortality rates in 1-6 years were recorded. There was **no** significant difference in the death rates between children who received the massive dose of vitamin A and those who did not¹⁸.

The NIN had carried out studies on the massive-dose approach in the early 1970s (long before Sommer), when keratomalacia was a major public health problem, and found it ineffective as a public health programme. Periera and Begum¹⁹ from the Christian Medical College Vellore had also reported the ineffectiveness of this approach.

A powerful partnership of pharmaceutical agencies and some international organisations has strenuously tried to promote the massive-dose approach. Many of our national decision-makers and health agencies seem to have been successfully co-opted to endorse this approach. As a result, it is distressing that, in India, this approach has been permitted as a “universalised” public health policy. Between the ninth and 36th months of life, a child receives massive doses totalling 9,00,000 I.U. This is a ‘universal’ programme, involving all children. There is now a proposal to raise this further to 17,00, 000 I.U. to cover all children up to six years of age!

It is well-known that massive doses of vitamin A can lead to acute toxicity symptoms in a certain proportion of cases. These toxic symptoms consist of signs of increased intracranial tension. De Francisco et al.²⁰ had observed that even with relatively lower doses of vitamin A (25,000 I.U. or 50,000 I.U. as against 200,000 I.U. which is now given in the massive-dose prophylaxis), a considerable number of children develop fontanelle bulging, indicating increased intracranial tension. Administration of a massive dose of 200,000 I.U. vitamin A after fontanelle closure can be expected to lead to significant increase in intracranial tension lasting for the next few days. Subjecting children to repeated increase in intracranial tension could retard brain development that takes place in the postnatal period. There have also been several instances of

fatalities in children following the inappropriate use of massive-dose vitamin A in field programmes. For instance, an unfortunate episode in Assam in which several children died as a result of massive-dose vitamin A attracted severe censure and condemnation from the judiciary. Apart from such acute toxic effects, repeated administration of massive doses could also result in chronic toxicity.

Vitamin A & Vitamin D Antagonism

DeLuca and colleagues^{21,22} have demonstrated that vitamin A antagonises the action of vitamin D. Massive doses of vitamin A have been shown to intensify the severity of bone demineralisation and to inhibit the ability of vitamin D to prevent such demineralisation. Increasing amounts of retinyl acetate were shown to produce progressive and significant decreases in total bone ash and increases in epiphyseal plate width. Increasing the levels of retinyl acetate abrogated the ability of vitamin D to elevate the level of serum calcium.

Comments of Dr. Hector F. DeLuca

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“I have read Dr. Gopalan’s paper on the practical problem of combating vitamin A deficiency in Indian children with great interest. I entirely share his view of the danger of using massive vitamin A to combat this practical problem. We are not at all clear what large amounts of vitamin A will do, and we certainly do not know what large amounts of vitamin A will do to the metabolism of other nutrients. Clearly vitamin D activity is suppressed with large amounts of vitamin A. The antagonism is small but nevertheless significant. With low doses of vitamin D, it is very clear that large doses of vitamin A can induce rickets in the rat. Presumably, this also occurs in people. I read with great interest the fact that many Indian children might be borderline vitamin D deficient because of insufficient exposure to sunlight. Their vitamin D deficiency would certainly be greatly aggravated by the provision of large amounts of retinol. I am pleased that this basic science study of vitamin D/vitamin A antagonism really finds some practical use in considering how to treat the deficient children in India.”

Currently, 38 percent of Indian children are stunted, with linear growth levels below-2 SDs of the international standard. The prevalence of stunting in India is higher than that in Sub Saharan Africa. These findings are widely accepted and published by all international agencies. Yet there has been no significant dent in the problem of stunting in Indian children during the last several years.

Detailed studies have shown that, in children of poor communities, the downward deviation from normal growth sets in during the third and fourth months of infancy and progresses till the fifth year of age. It is precisely during this critical phase of growth, when stunting sets in, in the poor socio-economic groups, that the massive dose of vitamin A prophylaxis is also delivered to the children!

In poor families, there is a high prevalence of deliveries of low-birth-weight infants because of maternal malnutrition. Vitamin D content in breast milk is low. These very young children get hardly any exposure to sunlight in their dingy houses. Their calcium intake is also low. There are no public health programmes designed to address these deficiencies. Apart from vitamin D deficiency, there is also the possibility that zinc deficiency, which is already present in these children, could be aggravated by massive doses of vitamin A. Under these circumstances, the administration of massive doses of vitamin A to children who are deficient in a multiplicity of vitamins including vitamin D, and also deficient in zinc, could have the effect of aggravating growth retardation.

The possible role of the ongoing programme of massive-dose vitamin A prophylaxis in the aggravation and persistence of stunting in our poor children requires serious consideration. Unlike India, South Asian countries have avoided the massive-dose approach to vitamin A deficiency prophylaxis, and in the children of those countries stunting is not a major problem.

The comments of Dr. DeLuca, internationally well known for his work on vitamin D, on this aspect are given in the box.

Distorted Priorities

According to available survey reports of the NNMB^{1,2} Bitot’s spots, the mild form of vitamin A deficiency, is seen

in just 0.7 percent of children under five years of age in India. This figure of 0.7 percent is an average, and does not necessarily indicate that 0.7 percent of children of all regions of the country and in all seasons show Bitot's spots. Moreover, the NNMB survey covers only part of the country. In fact, a survey by the ICMR³ had shown that Bitot's spots are present to a significant extent only in isolated pockets of the country.

As against the reported 0.7 percent prevalence of Bitot's spots, there are reports to show that 90 percent of children suffer from anaemia²³; it may be safely asserted that children suffering from Bitot's spots, if properly investigated, will show deficiency of several other micronutrients. Nothing much is being done to combat these deficiencies. Under the circumstances, the near-exclusive emphasis on vitamin A deficiency reveals the distorted priorities of health agencies arising from the pressure of commercial sources. In effect, what we are seeing is **commercial exploitation of poverty and undernutrition.**

Ethical Issues

There is also an ethical issue. Though the programme is labelled as "universal", in actual practice, it is the children of the poor who are being subjected to this procedure and not the children of the affluent and the policy makers. In short, this programme, which carries the risk of acute toxicity, is not for "our children" but for "their children" – the children of the poor. This raises serious ethical and moral issues.

Commercial Exploitation of Poverty and Undernutrition

Apart from the massive dose of vitamin A prophylaxis in children, *vanaspati* (hydrogenated fat), the main source of edible fat for poor populations, is also fortified with vitamin A. Now there is strong political pressure for vitamin A fortification of milk.

A Mid Day Meal Programme for school children had been initiated by the Government of India. There was recently a move on the part of commercial agencies to hijack this Programme. In place of the fresh hot cooked meal which had been proposed to be given to the school children, some political and commercial interests had sought to substitute biscuits containing some synthetic micronutrients. Fortunately,

due to the alertness and timely intervention of public-spirited citizens, this ill-conceived move was stopped. There are also ongoing attempts at capturing supplementation programmes of Intergrated Child Development Scheme (ICDS); "sprinklers" containing some arbitrary cocktail of micronutrients are being sought to be introduced in some the supplementation programmes.

Concluding Comments

- Public-spirited citizens must ensure the scrapping of the massive-dose vitamin A prophylaxis approach. This will not only avoid the considerable unnecessary expenditure which the Government is incurring on the programme but, more importantly, will save our children from undesirable side-effects.

- Vegetables and fruits are a good source not only vitamin A but also of several other micronutrients. A balanced diet that includes adequate amounts of a variety of vegetables would be the surest way of preventing micronutrient deficiencies. An intensive, well-structured programme to promote the consumption of locally available inexpensive fruits and vegetables should be mounted as a major National Programme and given high priority. The services of the chain of Home Science colleges throughout the country should be enlisted for a sustained programme of Nutrition Education targeted to the rural households and aimed at increasing the intake of locally available vegetables and fruits as part of household diets. The ongoing wastage of vegetable and fruits due to poor processing and storage facilities in the countryside must be prevented by promoting village-based technologies for processing and storage of fruits and vegetables.

- As part of our Rural Health Mission and ICDS programmes, children who exhibit Bitot's spots or who have just recovered from an attack of measles could receive synthetic vitamin A in recommended daily doses (not massive doses) for a fortnight, while simultaneously promoting adequate daily intake of vegetables and fruits.

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