Intervention Programs to Control Vitamin A Deficiency in Asia : A Review

Sri Raharjo

Food and Nutrition Development and Research Center
Gadjah Mada University, Jln. Teknika Utara, Yogyakarta 55281, Indonesia

ABSTRACT

Existing prevalence data suggest that vitamin A deficiency among children still represents a major problem in developing Asian countries including Indonesia, Bangladesh, India, Philippines, and Thailand. Plasma retinol is the most common assessment method for determining vitamin A status. The severity stages of xerophthalmia, along with their characteristics, are used frequently to follow clinical signs of vitamin A deficiency. Massive dosings of 200,000 IU of vitamin A (60 mg ratinol equivalent) every six months interval or fortification of vitamin A on food items have been done for the period of 12 to 24 months. The results were decreased in the risk of night blindness, incidence of keratomalacia and Bitot's spots, and lower mortality rate.

INTRODUCTION

Vitamin A deficiency is a major nutritional problem in developing countries, second only in incidence and prevalence to protein-energy malnutrition. The problem is of particular concern in tropical countries. Xerophthalmia, a clinical term for the disease entity involving the eye as a result of vitamin A deficiency, occurs in most developing countries especially in infants and young children (Oomen, 1974).

Xerophthalmia occurs against the background of poverty, ignorance, and defective dietary practices. Dietary deficiency of vitamin A is one, but not the only one, of the factors responsible for xerophthalmia. Infectious diseases also play an important role on the incidence of xerophthalmia (Solon et al., 1979). The objective of this review is to discuss the prevalence of xerophthalmia due to vitamin A deficiency and its intervention programs in five Asian countries including Indonesia, Philippines, Thailand, Bangladesh and India. It is well recognized that these five countries have a significant number of xerophthalmic children.

PREVALENCE OF VITAMIN A DEFICIENCY

Oomen and Doesschate (1973) reported that during the period of 1961 – 1965, 2,443 cases of xerophthalmia were found in children under 12 years in Bangalore, India. They also indicated that the periodicity of xerophthalmia was confirmed with the annual fluctuations in serum retinol levels of the children. A report from the United Nation in 1987 indicated that approximately 20 to 40 million children worldwide are estimated to have at least mild vitamin A deficiency, and approximately half of them are found in India (Rahmathullah et al., 1990).

It was reported that one out of every 662 children in Cebu, Philippines, ages 1 – 6 years was blinded by factors associated with xerophthalmia (Solon et al., 1979). Study in Bangladesh showed that the prevalence of blindness among children of ages less than 6 years in rural area was 6.4 per 10,000, while the prevalence for children in urban slums was 10.0 per 10,000 (Cohen et al., 1987). Vitamin A deficiency is also a major public health problem in Thailand, especially in the rural areas of Sakorn Nakhon province. It was reported that 12.6% of the preschool children had deficient serum retinol levels (less than 0.35 μmol/l) and 1.3% were night blind (Bloem et al., 1990).

Data from a national xerophthalmia survey in Indonesia in 1980 indicated that the mean prevalence of Bitot's spots among preschool children especially in rural areas was approximately 1.0%, while the prevalence of corneal disease related to vitamin A deficiency was 6.4 per 10,000 children (Ministry of Health, 1980; Muhilal et al., 1991). It was estimated that every year approximately 50,000 children were in danger of becoming blind (Sommer, 1982). Unfortunately, vitamin A deficient children are at increased risk of respiratory disease, diarrhea and mortality (Sommer et al., 1983; 1984).

Existing prevalence data suggest corneal xerophthalmia is at least as common in areas of India, Bangladesh, Thailand and the Philippines, as it is in Indonesia. In 1981 it was estimated that roughly 500,000 preschool children in Asia developed xerophthalmia (Sommer et al., 1981; Sommer 1989).

ASSESSMENT OF VITAMIN A DEFICIENCY

Determining factors of vitamin A status include intake, storage, mobilization, utilization and excretion. Vitamin A deficiency occurs whenever there is imbalance among these processes, mainly as a result of liver store depletion of vitamin A (Tomkins and Hussey, 1989). Currently available techniques for vitamin A status assessment include clinical, retinal function, conjunctival integrity, biochemical, and dietary assessment.

Anthropometric and dietary assessments for vitamin A deficient children are less important than the biochemical and clinical assessments, because anthropometric measurement is not specific. The dietary recall methods are subject to under-reporting and the method used to assess vitamin A distribution in the diet is also subject to error (Martinez et al., 1986). There were found, however, that xerophthalmic children are usually underweight (Oomen, 1974).

Biochemical Assessment

One of the biochemical assessments for vitamin A status in the body is liver store of vitamin A. A concentration of 20 μg vitamin A, as retinol, per gram liver can maintain the steady state plasma retinol levels for approximately four months in adults (Olson, 1987). Liver biopsy procedure, however, is rarely used in large-scale human studies. The only practical biochemical measurement available is serum or plasma retinol. Although retinol levels are useful for long-term intake evaluation, they do not tell anything about liver stores (Pi-Sunyer and Woo, 1984).

A relative-dose-response (RDR) test has been successfully used in determining vitamin A status in human studies (Campos et al., 1987; Tanumihardjo et al., 1990a; 1990b). The RDR test is based on the fact that when liver stores of retinol are high, plasma retinol is not significantly affected by an oral or intravenous dose of vitamin A (Loerch et al., 1979). When the liver stores are depleted or low, the plasma retinol level increases and reaches a peak at 5 h after vitamin A supplementation. The RDR test, however, requires two blood sample within an interval of 5 h. Tanumihardjo et al. (1990b), however, has modified RDR test so that only one blood sample required for the analysis.

In children, serum vitamin A level of 0 to 9 $\mu g/dl$ considered as deficient, 10 to 19 $\mu g/dl$ is low and 20 μ/dl or higher is adequate (Sommer et al., 1980). World Health Organization (WHO), however, categorizes plasma retinol levels into four groups: deficient (less than 10 $\mu g/dl$), low (10 to 20 $\mu g/dl$,), normal (20 to 50 $\mu g/dl$), and high (higher than 50 $\mu g/dl$) (WHO, 1976).

Plasma carotenoids have wide range fluctuation, 24 to 216 $\mu g/dl$, and it reflects directly the consumption of carotenoids. Therefore, plasma carotenoids cannot be used as a good indicator (Olson, 1981). The association of low serum albumin and of low serum vitamin A level in protein-energy malnutrition is accompanied by low level of retinol binding protein. It has also been reported that subsequent feeding with protein diet only resulted in an increase of serum retinol (Smith and Goodman, 1976).

In the case of vitamin E deficiency, the liver stores of vitamin A are depleted more rapidly (Napoli et al., 1984). Further study also suggested that vitamin E inadequacy, which impairs vitamin A absorption and storage, could contribute to the high incidence of clinical vitamin A deficiency (Bergen et al., 1988).

Clinical Assessment

Bitot's spots with conjunctival xerosis are the most prevalent and acceptable clinical criterion. But this criterion is considered to be a late manifestation of the disease and requires experienced observers to recognize it (Sommer et al., 1980). Night blindness is considered the earliest symptom of clinical xerophthalmia, but objective assessment of scotopic vision is difficult in young children, while asking parents whether their children are night blind is considered too subjective.

The stages of xerophthalmia need to be well recognized by the observers in the field to get an accurate diagnosis. The WHO proposed a classification of xerophthalmia which includes night blindness, conjunctival xerosis, Bitot's spot, corneal xerosis, corneal ulceration-keratomalacia, corneal scar, and xerophthalmic fundus (WHO, 1976). A population is pronounced to be at risk of having a major problem of vitamin A deficiency if more than 2% of them suffers Bitot's spot, 0.01% of them suffers corneal ulceration, and 0.1% of them have corneal scar (WHO, 1976).

INTERVENTION PROGRAMS

The first idea of providing 60 mg of retinol, or equivalent with 200,000 IU of vitamin A, to 1 to 4 years old children at risk was proposed by McLaren (1964). This amount of retinol can maintain serum retinol 20 μg/dl or higher for 3 to 6 months. That is why most of the intervention programs keep using vitamin A at that level within 6 months intervals (West et al., 1988). In other studies 40 IU of vitamin E is also provided together with the vitamin A, because there are evidences that vitamin E will improve the storage of retinol in the liver and it may reduce vitamin A toxicity symptoms (Kusin et al., 1974; Jagadeeson and Reddy, 1978; Bergen et al., 1988).

Nutrition education and public health campaign are the other type of interventions. The emphasis of these two interventions is on increasing the available carotene content or other sources of provitamin A in the diet (Oomen, 1974). Also improving the environmental sanitation can minimize the wide spread of infectious diseases (Solon et al., 1979).

Fortification of specific food items with vitamin A is another alternative. The main considerations on choosing which food ingredients is suitable to be fortified are: (1) the food ingredient should be widely consumed, (2) passes through manufacturing process in a limited numbers of factories where fortification is feasible, (3) limited variation in per capita consumption, (4) organoleptically suitable and stable when added into food stuff, and (5) the price of the fortified products is not greatly affected (Muhilal et al., 1988a).

Indonesia

In 1984, there was a study on morbidity among vitamin A deficient children. Children with mild xerophthalmia developed respiratory disease and diarrhea two and three times higher, respectively, than children with normal eyes after 18 months period (Sommer et al., 1984).

The mortality rate among children with mild xerophthalmia (night blindness and/or Bitot's spots) was on average four times the rate among children without xerophthalmia (Sommer et al., 1983). In addition, the mortality rate increased almost linearly with the severity of mild xerophthalmia.

A study conducted by Sommer et al. (1986) showed that vitamin A supplementation to vitamin A deficient children decreases mortality by as much as 34%. Subsequent study, conducted by the same group, in rural areas of Sumatra, showed that after the first distribution of vitamin A (200,000 IU), mortality rates among non-recipients were at least 13 times that of capsule recipients. Mortality rates in control villages were at least six times those of capsule recipients but half or less of non-recipients (Tarwotjo et al., 1987).

A randomized community trial was conducted West et al. (1988) in Aceh, Indonesia, to assess the impact of semiannual vitamin A (60 mg retinol equivalent or 200,00 IU) supplementation on growth of preschool children. The findings suggest that vitamin A supplementation program may not only reduced xerophthalmia incidence but also improve growth among preschool children (West et al., 1988).

Bergen et al. (1988) found that serum retinol of approximately 34% of children in West Java province was less than 0.35 μmol/l or 10 μg/dl. Ten days after oral administration of 24.4 μmol vitamin A, mean serum retinol level increased from 0.42 μmol/l to 0.70 μmol/l. Children treated with 244 or 314 μmol vitamin A maintained a serum retinol level of 0.56 μmol/l for 165 days. Bergen et al. (1988) also suggested that vitamin E inadequacy may well contribute to the high incidence of clinical vitamin A deficiency in those children.

The ministry of Health of Republic of Indonesia has decided that fortification of a commonly consumed food material with vitamin A can be used as means of controlling vitamin A deficiency. Four food items including cane sugar, flour, monosodium glutamate (MSG), and salt are widely consumed across the nation. Among these four potential food items, MSG is considered as the most suitable carrier for vitamin A (Ministry of Health, 1980).

Muhilal et al. (1988a) conducted a controlled trial to determine the effectiveness of MSG fortified with 810 μg retinol equivalent vitamin A per gram MSG as a mean to provide adequate amount of vitamin A in the area of endemic vitamin A deficiency. The MSG retained 84% of its initial level of vitamin A after four months of distribution, and after 11 months only 54% of the vitamin A was retained by the MSG. They reported that serum vitamin A levels increased from 0.67 μmol/l (base line level) to 0.92 μmol/l after 11 months of fortification, while serum vitamin A levels in control group did not change. The prevalence of Bitot's spots among children in program villages decreased progressively from 1.2% at base line to 0.2% after 11 months of introduction of the vitamin A fortified MSG (Muhilal et al., 1988b). They also found that mortality rate of preschool children in control group was 1.8 times higher than the rate of vitamin A treated group.

Philippines

Solon et al. (1979) conducted three types of intervention programs to control vitamin A deficiency problem in Cebu, Philippines. These programs include public health campaign and horticulture, massive dosing of vitamin A (200,000 IU), and fortification MSG with vitamin A (15,000 IU of vitamin A per 2.2 g of MSG). The results indicated that the MSG fortification was the only intervention that significantly reduced clinical signs of xerophthalmia and significantly increased serum vitamin A levels. The massive dosing of vitamin A, however, does not maintain adequate serum vitamin A levels for as long as six months in subjects whose initial levels are deficient or low.

Thailand

Bloem et al. (1990) studied a group of 134 school children aged three to nine years with signs of conjunctival xerosis in the rural area of the Sakorn Nakhon province in northeast Thailand. Two weeks after a single oral dose of 110 mg vitamin A, they found a significant increase of serum retinol (from 0.60 μmol/l to 0.75 μmol/l). They suggested that vitamin A supplementation can improve the iron status within two week in areas where mild vitamin A deficiency and anemia are endemic.

Bangladesh

A six-monthly massive dosings of preschool-age children with oral vitamin A (200,000 IU) and vitamin E (40 IU) was conducted in rural areas and urban slums in Bangladesh (Cohen et al., 1987). The results indicated that the risk of night blindness was reduced by 50% for children given vitamin A. However, there was no significant reduction in the prevalence of Bitot's spots. Risk of corneal ulcers (keratomalacia) was 2.7 times higher in children not given vitamin A. In addition, Cohen et al. (1987) suggested that for maximum impact on eye lesions, massive dosing with vitamin A has to be at ideally less than six months intervals. The main problem with this study is low coverage. The overall coverage was less than 50%, while for favorable impact in mild xerophthalmia the coverage should be 65% or higher. The low coverage was due to failure of capsule supply, absence of health worker, and lack of supervision in the field.

India

Fifty thousands children were given 200,000 IU of vitamin A once every six months. During the period of study, the incidence of keratomalacia in areas covered by the program decreased by about 80%, while in control areas a reduction of only 20% was observed (Vijayaraghavan et al., 1984). It also clearly indicated that keratomalacia was more prevalent in children not receiving supplements.

Vijayaraghavan and Rao (1982) conducted massive dosing of vitamin A (200,000 IU) within six months intervals to children aged one to five years. The result indicated that there was evidence of reduction in the prevalence of Bitot's spots. Poor coverage, poor records maintenance, and inadequately prepared community for utilizing the program were found as major problems in this study. Another intervention program, including administration of 200,000 IU of vitamin A every four months on children, completely eliminated night blindness and prevented the development of new cases of Bitot's spots in a number of children (Sinha and Bang, 1976).

Rahmathullah et al. (1990) conducted a randomized, placebo-controlled, masked clinical trial among 15,419 preschool children using a small, weekly dose of vitamin A (8.7 μmol or 8333 IU) for one year given directly to the children by community health volunteers. The dose of vitamin A was meant to stimulate the amount that could be obtained from food (approximately 1 to 1.4 μmol vitamin A). The result showed that weekly provision of vitamin A significantly reduces mortality rate by 54%.

SUMMARY

The prevalence of vitamin A deficiency among preschool children in Asia is simply because less vitamin A available to them. Lack of nutritinal knowledge of mothers in rural areas, in preparing foods, is part of the current problem. The other factors which result in protein-energy malnutrition may aggravate the severity of vitamin A deficiency. For short-term intervention, massive dosing with vitamin A 200,000 IU seems to be successful in decreasing the development of clinical symptoms due to deficiency in vitamin A. Fortification, which has been done using MSG or other food items, may give longterm effect in maintaining serum retinol and in preventing the clinical signs of xerophthalmia. Some of those intervention programs showed relatively low in coverage, poor records maintenance and lack of participation from the community at risk. To deal with these problems, a better approach to create stronger motivation among population at risk is required. Since most of untreated vitamin A deficient children in the developing Asian countries end up with vision impairments, blindness, higher risk for other infectious diseases or even death, therefore the problem should be addressed immediately by the local governments.

REFERENCES

Bergen, H.R., Natadisastra, G., Muhilal, Dedi, A., Karyadi, D. and Olson, J.A. 1988. American Journal of Clinical Nutrition. 48: 279-285.

Bloem, M.W., Wedel, M., van Agtmaal, E.J. and Speek, A.J. 1990. American Journal of Clinical Nutrition. 51: 76-79.

Campos, F.A.C.S., Flores, H. and Underwood, B.A. 1987. Effect of an infection on vitamin A status of children as measured by the relative dose response. American Journal of Clinical Nutrition. 46: 91-94.

Cohen, N., Rahman, H., Mitra, M., Sprague, J., Islam, S., Leemhuis de Regt, E. and Jalil, M.A. 1987. Impact of massive doses of vitamin A on nutritional blindness in Bangladesh. American Journal of Clinical Nutrition. 45: 970-976.

Jagadeeson, V. and Reddy, V. Interrelationship between vitamin E and A: a clinical study. Clinical et Chimaca Acta. 90: 71-74.

Kusin, J.A., Reddy, V. and Sivakumar, B. 1974. Vitamin E supplements and the absorption of a massive dose of vitamin A. American Journal of Clinical Nutrition. 27: 774-776.

Loerch, J.D., Underwood, B.A. and Lewis, K.C. 1979. Response of plasma levels of vitamin A to a dose of vitamin A as an indicator of hepatic vitamin A reserve in rats. Journal of Nutrition. 109: 778-786.

Martinez, H., Shekar, M. and Latham, M. 1986. (Letter). Lancet. II: 451-452.

McLaren, D.S. 1964. Xerophthalmia: A neglected problem. Nutrition Review. 22: 289-291.

Ministry of Health of Republic of Indonesia. 1980. Nutritional blindness prevention project. Characterization of vitamin A deficiency and xerophthalmia and the design of effective intervention program. Ministry of Health, Jakarta, Indonesia.

Muhilal, Murdiana, A., Azis, I., Saidin, S., Jahari, A.B. and Karyadi, D. 1988a. Vitamin A-fortified monosodium glutamate and vitamin A status: a controlled field trial. American Journal of Clinical Nutrition. 48: 1265-1270.

Muhilal, Permaisih, D., Idjradinata, Y.R., Muherdiyantiningsih and Karyadi, D. 1988b. Vitamin A-fortified monosodium glutamate and health, growth, and survival of children: a controlled field trial. American Journal of Clinical Nutrition. 48: 1271-1276.

Muhilal, Husaini, M.A. and Karyadi, D. 1991. Nutritional problems in Indonesia. Indonesian Food Journal. 2: 23-36.

Napoli, J.L., McCormick, A.M., O'Meara, B. and Dratz, E.A. 1984. Vitamin A metabolism: α-tocopherol modulates tissue retinol levels in vivo retinyl palmitate hydrolysis in vitro. Archives of Biochemistry and Biophysic. 230: 194-202.

Olson, J.A. 1981. (Letter). American Journal of Clinical Nutrition. 34: 435-436.

Olson, J.A. 1987. Recommended dietary intakes (RDI) of vitamin A in humans. American Journal of Clinical Nutrition. 45: 704-716.

Oomen, H.A.P.C. 1974. Vitamin A deficiency, xerophthalmia and blindness. Nutrition Review. 32: 161-166.

Oomen, H.A.P.C. and Doesschate, J.T. 1973. The periodicity of xerophthalmia in south and east Asia. Ecology of Food and Nutrition. 2: 207-217.

Pi-Sunyer, F.X. and Woo, R. 1984. Laboratory assessment of nutritional status. In "Nutrition assessment".

ed. M.D. Simko, C. Cowell and J.A. Gilbride, pp. 139-174. Aspen System Corporation, Rockville.

Rahmathullah, L., Underwood, B.A., Thulasiraj, R.D., Milton, R.C., Ramaswamy, K., Rahmathullah, R. and Babu, G. 1990. Reduced mortality among children in southern India receiving a small weekly dose of vitamin A. The New England Journal of Medicine. 323: 929-935.

Sinha, D.P. and Bang, F.B. 1976. The effect of massive doses of vitamin A on the signs of vitamin A deficiency in preschool children. American Journal of Clinical Nutrition. 29: 110-115.

Smith, F.R. and Goodman, D.S. 1976. Vitamin A transport in human vitamin A toxicity. The New England Journal of Medicine. 294: 805-808.

Solon, F., Fernandez, T.L., Latham, M.C. and Popkin, B.M. 1979. An evaluation of strategies to control vitamin A deficiency in the Philippines. American Journal of Clinical Nutrition. 32: 1445-1453.

Sommer, A. 1982. Nutritional blindness: Xerophthalmia and keratomalacia. Oxford University Press, New York.

Sommer, A. 1989. New imperatives for an old vitamin A. Jurnal of Nutrition. 119: 96-100.

Sommer, A. and West, K.P. 1986. Vitamin A supplementation and childhood mortality (reply). Lancet. II: 451-452.

Sommer, A., Hussaini, G., Muhilal, Tarwotjo, I., Susanto, D. and Saroso, J.S. 1980. History of night blindness: A simple tool for xerophthalmia screening. American Journal of Clinical Nutrition. 33: 887-891.

Sommer, A., Tarwotjo, I. and Hussaini, G. 1981. Incidence, prevalence, and scale of blinding malnutrition. Lancet. I: 1407-1408.

Sommer, A., Tarwotjo, I., Hussaini, G. and Susanto, D. 1983. Increased mortality in mild vitamin A deficiency. Lancet II: 585-588.

Sommer, A., Katz, J. and Tarwotjo, I. 1984. Increased risk of respiratory disease and diarrhea in children with preexisting mild vitamin A deficiency. American Journal of Clinical Nutrition. 40: 1090-1095.

Sommer, A, Tarwotjo, I., Djunaedi, E., West, K.P., Loedin, A.A., Tilden, R. and Mele, L. 1986. Impact of vitamin A supplementation on childhood mortality: A randomized controlled community trial. Lancet I: 1169-1173.

Tarwotjo, I., Sommer, A., West, K.P., Djunaedi, E., Loedin, A.A., Mele, L. and Hawkins, B. 1987. Influence of participation on mortality in a randomized trial of vitamin A prophylaxis. American Journal of Clinical Nutrition. 45: 1466-1471.

Tanumihardjo, S.A., Muhilal, Yuniar, Y., Permaesih, D., Sulaiman, Z. Karyadi, D. and Olson, J.A. 1990a. Vitamin A status in preschool-age Indonesian children as assessed by the modified relative-dose-response assay. American Journal of Clinical Nutrition. 52: 1068-1072.

Tanumihardjo, S.A., Koellner, P.G, and Olson, J.A. 1990b. The modified relative-dose-response assay as an indicator of vitamin A status in a population of well-nourished American children. American Journal of Clinical Nutrition. 52: 1064-1067.

Tomkins, A. and Hussey, G. 1989. Vitamin A, Immunity and Infection. Nutrition Research Reviews. 2: 17-28.

Vijayaraghavan, K., Sarma, K.V.R., Rao, N.P. and reddy, V. 1984. Impact of massive doses of vitamin A on incidence of nutritional blindness. Lancet. II: 149-151.

Vijayaraghavan, K. and Rao, N.P. 1982. An evaluation of the national prophylaxis programme against blindness due to vitamin A deficiency. Nutrition Report International. 25: 431-441.

West, K.P., Djunaedi, E., Pandji, A., Kusdiono, Tarwotjo, I., Sommer, A. and the Aceh Study Group. 1988. Vitamin A supplementation and growth: a randomized community trial. American Journal of Clinical Nutrition. 48: 1257-1264.

World Health Organization (WHO). 1976. Vitamin A deficiency and Xerophthalmia. WHO Technical Report Series no. 590. Geneva.