Vitamin A: Nutritional Value and Role in Public Health

* Sofia Ahmed, Muhammad Ali Sheraz and Iqbal Ahmad

ABSTRACT:

For the past nine decades, research on different aspects on vitamin A (retinol) including nutrition, biochemistry, molecular and cell biology, physiology, toxicology, medical therapy and public health is being conducted all over the world. Vitamin A is an essential micronutrient for all vertebrates. It is required for normal vision, reproduction, embryonic development, cell and tissue differentiation, and immune function in animals and humans. Many aspects of the transport and metabolism of vitamin A, as well as its functions, are well conserved among species. On the other hand, deficiency of vitamin A is also known to be associated with different specific disease conditions such as xerophthalmia, which is manifested as night blindness and corneal abnormalities, softening of the cornea (keratomalacia) and ulceration leading to irreversible blindness along with increased susceptibility to infections and abnormalities in reproduction. Research evidence suggests that diet supplemented with butter, fish, oils, milk and meat could be used as a better source to overcome vitamin A deficiency leading to a healthy life.

Keywords: Vitamin A, nutrition, public health.

INTRODUCTION

Vitamin A is a generic term that refers to compounds with the biological activity of retinol. Dietary vitamin A is ingested in two main forms, preformed vitamin A (retinyl esters and retinol) and provitamin A carotenoids (B-carotene, a-carotene, B-cryptoxanthin), although the proportion of vitamin A obtained from each of these forms varies considerably among animal species and individual human diets¹⁻³. These precursors serve as substrates for the biosynthesis of two essential metabolites of vitamin A: 11-cis-retinal, required for vision, and all-trans-retinoic acid, required for cell differentiation and the regulation of gene transcription in nearly all tissues. They are provided in the diet by green and yellow or orange vegetables and some fruits and preformed vitamin A, namely retinyl esters and retinol itself: present in foods of animal origin, mainly in organ meats such as liver, other meats, eggs, and dairy products. All-trans-retinoic acid, is the most bioactive form of vitamin A, when given to vitamin

A-deficient animals, retinoic acid restores growth and tissue differentiation and prevents mortality, indicating that this form alone, or metabolites made from it, is able to support nearly all of the functions associated to vitamin A. It is also evident that different forms of vitamin A differ in their biological activity per unit of mass and therefore the bioactivity of vitamin A in the diet is expressed in equivalents with respect to alltrans-retinol rather than in mass units¹⁻⁷.

LIERATURE REVIEW

Nutritional Aspects Vitamin A

Vitamin A was discovered in the early 1900s by McCollum and colleagues at the University of Wisconsin and independently by Osborne and Mendel at Yale University. Both groups were studying the effects of diets made from purified protein and carbohydrate sources, such as casein and rice flour, on the growth and survival of young rats. They observed that growth ceased and the animals died unless the diet was supplemented with butter, fish oils, or a quantitatively minor ether-soluble fraction extracted from these substances, milk, or from meats. The unknown substance was then called "fat-soluble A". After that, it was recognized that the yellow carotenes present in plant extracts had similar nutritional properties, and it was postulated that this carotenoid fraction could give rise through metabolism to the bioactive form of fat-soluble A, now called vitamin A, in animal tissues. Although the discoveries made in the early 1900s may now seem long ago, it is interesting to note, that physicians in ancient Egypt, around 1500 BC, were already using the liver of ox, a very rich source of vitamin A, to cure what is now referred to as night blindness⁸.

Recommended Dietary Allowance (RDA) and Upper Intake Level (UL)

The recommended dietary allowance (RDA) is defined as "The average daily intake level that is sufficient to meet the nutritional requirement of nearly all (97-98%) apparently healthy individuals in a particular life stage and gender group". Similarly the upper intake level (UL) is the "highest level of daily nutrient intake that is likely to pose no risk of adverse health effects in almost all apparently healthy individuals in the specified life stage group. As intake increases above the UL, the potential risk of adverse effects increases"9. The Recommended Dietary allowances (RDA) and Upper Intake Level (UL) values for vitamin A by life stage group are indicated in Table-1. It is important to note that the UL applies only to chronic intakes of preformed vitamin A (not carotenoids, which do not cause adverse effects). For several life stage groups, the UL values are less than three times higher than the RDA¹⁰. However, the contents of vitamin A and carotenoids in foods can vary substantially with crop variety or cultivar, the environment in which it is grown, and with processing and storage conditions^{11,12}.

Vitamin A and Public Health

Vitamin A is considered as one of the most important fat-soluble vitamins due to its uncountable advantages for humans and animals and for this purpose its daily requirements should be fulfilled very carefully. Several research workers have proved that insufficient quantity of vitamin A (retinol) in the body may lead to serious disease conditions either temporarily or sometimes permanantly¹³⁻³³. Some important cases of vitamin A deficiency are discussed below:

1. Prevention of Xerophthalmia

Retinoic acid plays an important role during embryonic eye development. It promotes normal development of the ventral retina and optic nerve through its activities in the neural crest cellderived periocular mesenchyme³⁴. Its deficiency may cause a variety of retinal diseases³⁵. Vitamin A is the primary cause of xerophthalmia which is manifested as night blindness and corneal abnormalities, softening of the cornea (keratomalacia). and ulceration leading to irreversible blindness. In the early 1990s, it was estimated by WHO that approximately 3 million children, most living in India, parts of Southeast Asia, and sub-Saharan Africa, had some form of xerophthalmia annually, and, on the basis of blood retinol levels, another 250 million were subclinically deficient¹³. The use of vitamin A to prevent or treat xerophthalmia represents an important break through in the field of nutritional sciences¹⁴.

2. Morbidity and Mortality

It was reported in the early 1980s by Sommer and colleagues, from the studies conducted in Indonesia, that young children suffering from night blindness were found to have died at a higher rate than children with normal eyes¹⁵. Some other investigators also reported that pre-school aged children in poor regions of Southeast Asia, India and Africa showed reduced rate of mortality by preventing A deficiency¹⁶. On this basis, it was estimated that the administration of 200.000 IU dose of vitamin A every six month would likely reduce total mortality rate by 35% in pre-school children¹⁷, and the amounts of vitamin A similar to RDA would be helpful in 23% reduction in mortality in children less than 6 years¹⁸, in newborns¹⁹ and in pregnant women^{20,21}. On the other hand Gogia and Sachdev¹⁶ have suggested for not initiating such supplementation as a public health intervention in developing countries for reducing infant mortality and morbidity. There study showed no convicing evidence of a reduced risk of mortality and possibly morbidity after neonatal supplementation with vitamin A.

3. Subclinical Deficiency

The subclinical forms of vitamin A deficiency have been a topic of debate for a long period of time and was proved to be associated to an increased risk of developing respiratory and diarrheal infections, decrease growth rate, slow bone development, and decreased likelihood of survival from serious illness²².

36

Vitamin A is also helpful to reduce measles-related morbidity and mortality²³ and therefore it is recommended by WHO to integrate vitamin A supplementation into the expanded program of immunization (EPI), at the time of measles and diphtheria, pertussis, tetanus vaccinations to deliver vitamin A to infants and children in countries where vitamin A deficiency is $prevalent^{24,25}$.

3. Immune System Changes

It is widely thought that the ability of vitamin A to reduce mortality is due to the effects on the immune system of animals which increases the rate of suvival and reduces the severity of disease^{26,37-39}. A number of animal models have been used to understand the effects of vitamin A deficiency, and repletion, on the immune system²⁷ and it was concluded that vitamin A deficiency results in multiple abnormalities in natural and adaptive immunity involving cell differentiation, hematopoiesis and blood and lymphoid organ cell populations. The abnormalities are mostly or completely reversible by treatment with vitamin A or retinoic acid by stimulating natural and adaptive immune responses²⁸⁻³¹.

DISCUSSION

The literature review presented above has supported the fact that vitamin A has secured maximum attention of nutritionists and physicians to overcome many servere disease conditions which may occur due to its deficiency in daily routine diet. As it is considered an essential micronutrient for all vertabrates, its deficiency is also associated with several indications of reversible body disorders. A diet containing recommended amounts of vitamin A according to different life stage groups may therefore accounts for a better source to face the challenges of treating various deficiency related diseases. The contents of vitamin A and carotenoids in foods can vary substantially with crop variety or cultivar, the environment in which it is grown, and with processing and storage conditions^{11,12}. Foods with the highest concentrations of preformed vitamin A are liver (4-20 mg retinol~100g) and fortified foods such as powdered breakfast dinks (3-6mg ~ 100g), ready-to-eat cereals (0.7-1.5mg \sim 100g), and margarines $(0.8 \text{mg} \sim 100 \text{g})^{10}$. The highest levels of provitamin A carotenoids are found in carrots, cantaloupes, sweet potatoes, pumpkin, kale, spinach, collards, and squash (roughly 5-10mg RAE 1~00g)^{10,40}. These data are compiled for both genders and for all

age groups. It is also reported by the Institute of Medicine's Micronutrients that an adequate intake of vitamin A can be obtained even if a vegetarian diet containing only provitamin A carotenoids is consumed⁴¹.

CONCLUSION

In the light of above mentioned facts, it seems quiet clear that vitamin A is one of the most useful components for body functions and that it should be included in daily diet according to the recommended amounts (RDA) for all age groups to achieve a better life style. It protects the body from many life threatening diseases by strengthening the immune system efficiency and the organism's ability to respond to pathogens, antigens, and mitogens, effectively. Due to its requirement from infants to pregnant women for normal body functioning and high immune response, its use would surely be helpful in reducing subclinical deficiency symptoms.

REFERENCES

- 1. McDowell, L.R. Vitamins in Animal and Human Nutrition, 2nd ed., lowa State University Press, 2000; Chap.2.
- 2. Albalat, R. The retinoic acid machinery in invertebrates: ancestral elements and vertebrate innovations. Mol. Cell Endocrinol., 2009; 313: 23-35.
- 3. Nagao, A. Absroption and function of dietary carotenoids. Forum Nutr. 2009; 61: 55-63.
- 4. Ball, G.F.M. Vitamins in Foods Analysis, Bioavailability and Stability, CRC Press. Boca Raton, FL., 2006; Chap.3.
- 5. Litwack, G. (Ed.) Vitamin A, Vitamins and Hormones Advances in Research and Applications, In: Vitamins and Hormones, Vol. 75, 2007; Elsevier Inc. Amsterdam.
- Ross, A.C. Harrison, E.H. Vitamin A: Nutritional Aspects of Retinoids and Carotenoids, In: Zempleni, J., Rucker, R.B., McCormick, D.B., Suttie, J.W. (Eds.), Handbook of Vitamins, 4th ed., CRD Press, Boca Raton, FL, 2007; Chap.1.

- Eitenmiller, R.R., Ye, L., Landen, W.O. Jr. Vitamin Analysis for the Health and Food Sciences, 2nd ed., CRC Press, Boca Raton, FL., 2008; Chap.1.
- 8. Wolf, G. A history of vitamin A and retinoids. FASEB J., 1996; 10: 1102-1107.
- Food and Nutrition Board, Institute of Medicine, Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulphate. Washington, DC: National Academics Press, 2004.
- 10. USDA, USDA Nutrient Database for Standard Reference Laboratory, Agricultural Research Service, 2004, http://www.nal.usda.gov.
- Surles, R.L. Weng, N., Simon, P.W., Tanumihardjo, S.A. Carotenoid profiles and consumer sensory evaluation of specially carrots (Daucus carola, L.) of various colors. J. Agric. Food Chem., 2004; 52: 3417-3421.
- 12. Rodriguez-Amaya, D.B. Food carotenoids: analysis, composition and alterations during storage and processing of foods. Forum Nutr. 2003; 56: 35-37.
- Food and Agriculture Organization of the United Nations / World Health Organization, Human Vitamin and Mineral Requirements, In: Report of a joint FAO/WHO Expert Consultantion,, Bangkok, 2002, (Chapter 7). http://www.fao.org/DOCREP/004/Y2809E/ Y2809E00.HTM.
- Buyckx, M. The FAO program for the prevention and control of vitamin A deficiency. Food Nutr. Agric., 1991; 1: 16-24.
- Sommer, A., Tarwotjo, I., Hussaini, G., Susanto, D. Increased mortality in children with mild vitamin A deficiency. Lancet, 1983; 322: 585-588.
- 16. Sommer, A. Vitamin A deficiency and the global response. Forum Nutr. 2003; 56: 33-35.
- Sommer, A. Vitamin A, infectious disease, and childhood mortality. J. Infect. Dis., 1993; 167: 1003-1007.

- Beaton, G. H., Martorell, R., Aronson, K.A., Edmonston, B., McCabe, G.A., Ross, C., Harvey, B. Vitamin A supplementation and child morbidity and mortality in developing countries. Food Nutr. Bull., 1994; 15: 282-286.
- Rahmathullah, L., Tielseh, J.M., Thulasiraj. R.D., Katz, J., Coles, C. Devi, S., John, R., Prakash, K., Sadanand, A.V., Edwin, N., Kamaraj, C. Impact of supplementing newborn infants with vitamin A on early infant mortality: community based randomised trial in southern India. Br. Med. J., 2003; 327: 254.
- West, K.P. Jr., Katz, J., Khatry, S.K., LeClerq, S.C., Pradhan, E.K., Shrestha, S.R., Connor, P.B., Dali, S.M., Christian, P., Pokherl, R.P., Sommer, A. Double blind, cluster randomised trial of low dose supplementation with vitamin A or B carotene on mortality related to pregnancy in Nepal. Br. Med. J., 1999; 318: 570-575.
- Radhika, M.S., Bhaskaram, P., Balakrishna, N., Rantalakshmi, B.A., Devi, S., Kumar B.S. Effects of vitamin A deficiency during pregnancy on maternal and child health, BJOG, 2002; 109: 689-693.
- 22. Office of Dietary Supplements, N.I.H., Dietary Supplement Fact Sheet: Vitamin A and carotenoids, NIH: Washington, 2006; http://ods.od.nih.gov/factsheets/vitamina.asp.
- D'Souza, R.M., D'Souza, R. Vitamin A for the treatment of children with measles-a systematic review. J. Trop. Pediatr., 2002; 48: 323-327.
- Committee on Infectious Diseases. Vitamin A treatment of measles. Pediatrics, 1993; 91: 1041-1015.
- 25. WHO/UNICEF. Integration of vitamin A supplementation with immunization: policy and programme implication, in: Report of a meeting, 12-13 January 1998, UNICEF, New York, 1998; pp. 1-20, WHO/EPI/GEN/98.07, http://202.54.104.236/intranet/eip/immunizat ionmanager/pdf/IntegrationVitASupplWHO_ EPI_GEN_98_07.pdf.

- Villamor, E., Fawzi, W.W. Effects of vitamin A supplementation on immune responses and correlation with clinical outcomes. Clin. Microbiol. Rev., 2005; 18: 446-464.
- Stephensen, C.B. Vitamin A, infection, and immune function. Annu. Rev. Nutr. 2001; 21: 167-192.
- Iwata, M., Eshima Y., and Kagechika, H. Retinoic acids exert direct effects on T cells to suppress Th1 development and enhance Th2 development via retinoic acid receptors. Int. Immunol., 2003; 15: 1017-1025.
- Iwata, M., Hirakiyama, A., Eshima, Y., Kagechika, H., Kato, C., Song, S.Y. Retinoic acid imprints gut-homing specificity on T cells. Int. Immunol., 2004; 21: 527-538.
- Ma, Y., Chen, Q., Ross, A.C. Retinoic acid and polyriboinosinic: polyribocytidylic acid stimulate robust anti-tetanus antibody production while differentially regulating type 1/type 2 cytokines and lymphocyte populations. J. Immunol., 2005; 174: 7961-7969.
- 31. Ma, Y., Ross, A.C. The anti-tetanus immune response of neonatal mice is augmented by retinoic acid combined with polyriboinosinic: polyribocytidylic acid. Proc. Natl. Acad. Sci. USA, 2005; 102: 13556-13561.
- 32. Caminha Mde, F., Batista Filho, M., Fernandes, T.F., Arruda, I.K., Diniz Ada, S. Vitamin A supplementation during puerperium: systematic review. Rev. Saude Publica, 2009; 43: 699-706.
- 33. Borooah, S., Collins, C., Wright, A., Dhillon, B. Late-onset retinal macular degeneration: clinical insights into an inherited retinal degeneration.

Postgrad. Med. J., 2009; 85: 495-500.

- Cvekl, A., Wang, W.L. Retinoic acid signaling in mammalian eye development. Exp. Eye Res., 2009; 89: 280-291.
- Maeda, T., Maeda, A., Ohguro, H. Retinal degeneration diseases and the retinoid cycle. Nippon Ganka Gakkai Zasshi, 2009; 113: 83-94.
- 36. Gogia, S., Sachdev, H.S. Neonatal vitamin A supplementation for prevention of mortality and morbidity in infancy: sytematic review of randomised controlled trials. BMJ, 2009; 338: b919.
- Ruhl, R. Retinoids, vitamin A and pro-vitamin A carotenoids. Regulation of the immune system and allergies. Pharm. Unserer Zeit, 2009; 38: 126-131.
- 38. Moro, J.R., Iwata, M., von Andriano, U.H. Vitamin Effects on the immune system: vitamins A and D take centre stage. Nat. Rev. Immunol., 2008; 8: 685-698.
- Pino-Lagos, K., Benson, M.J., Noelle, R.J. Retinoic acid in the immune system. Ann. N.Y. Acad. Sci., 2008; 1143: 170-187.
- 40. United States Department of Agriculture. What We Eat in America, Nhanes, 2009; http://www.ars.usda.gov/Services/docs.htm?d ocid=15044.
- Food and Nutrition Board, Institute of Medicine. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc, National Academy Press: Washington, 2001; pp.8-9.

39

Life Stage Group	RDA (µg / day)ª	UL (µg / day) ^b
Infants		
0-12 months	400	600
Children		
1-3 years	300	600
4-8 years	400	900
Adolescent and adults males		
9-13 years	600	1700
14-18 years	900	2800
19 to > 70 years	900	3000
Adolescent and adults females		
9-13 years	600	1700
14-18 years	700	2800 ,
19 to > 70 years	700	3000
Pregnancy		
< 18 years	750	2800
19-50 years	770	3000
Lactation		
< 18 years	1200	2800
19-50 years	1300	3000

Table 1:Recommended dietary allowances (RDA) and upper level (UL) values for
Vitamin A by life stage group.

^a As retinol activity equivalents (RAEs).

^b As µg preformed vitamin A (retinols).

^c Adequate intake (RAEs).