Nutrition supplements and the eye

NICHOLAS A. PHELPS BROWN, ANTHONY J. BRON, JOHN J. HARDING, HELEN M. DEWAR

Abstract

Purpose **A review of the role of vitamins, minerals, carotenoids and essential fatty acids in relation to eye health. The mode of action may be directly on the eye or by promoting bodily health on which the eye depends.**
Results **The lens and retina suffer oxidative damage and the anti-oxidant vitamins A, C and E are implicated as protective. Studies in man give indifferent support to the role of nutrition in the development of cataract. In the elderly, vitamin intake may be inadequate, so that a vitamin supplement may be reasonable. Zinc has a role in retinal metabolism and may be beneficial in macular degeneration. Selenium has an anti-oxidant role. Other minerals including copper have a less defined role. Carotenoids are concentrated at the macula and have an anti-oxidant role. A reduced risk of macular degeneration is found in relation to a high serum level. The essential fatty acid, gamma-linolenic acid (GLA), is useful in Sjögren's syndrome and may help in other dry eye conditions. Omega-3 fatty acids are important in retinal development and have a role in preventing cardiovascular disease.**
Conclusion **All persons should be encouraged to maintain healthy nutrition. Middle-aged and elderly patients may benefit from a supplement. An intake in excess of the recommended daily intake may be beneficial, but this is not proven. Further clinical trials are indicated to define the advisability of vitamin, mineral and other supplements. Dosages for recommended intake and for supplements are given.**

Key words Nutrition, Vitamins, Minerals, Carotenoids, Essential fatty acids, Cataract, Retinal degeneration

The health of the eye is dependent on the health of the body. There are about 50 known essential nutrients for the human body, which include the vitamins and about 20 minerals. Nutrition and the eye continues to be a field of very active research and the information available can be used as a guide for advising proper dietary habits and for considering vitamin and mineral supplements, rather than as firm recommendations. Some nutrients are known to be toxic if taken in excess and so there is an upper limit for consumption that should not be exceeded.

The role of vitamins in eye health

Vitamins are today often referred to as micronutrients. Vitamin A is essential in the formation of the retinal photoreceptor pigments and vitamin A deficiency leads to defective night vision. Vitamin A is also important in maintaining the health of the ocular surface and keratomalacia occurs when the diet is grossly deficient in vitamin A. In common with vitamins C and E, vitamin A has anti-oxidant properties. Vitamin C is secreted into the aqueous humour where it is more concentrated than in other body fluids, suggesting its particular importance to the lens. The level of vitamin C in the aqueous increases with increased dietary intake, which suggests that the lens will feel the effects of increased vitamin C intake.[1]

The role of vitamins has been considered in maintaining the health of the retina and lens. Both are considered to be under threat of damage by oxidation due to free radicals that are generated in part by normal metabolic processes and in part by exposure to radiation in sunlight. Cigarette smoke is also a source of free radicals.

The development of cataract has been associated with a number of systemic diseases, including cardiovascular,[2,3] diabetic, renal and gastrointestinal (diarrhoea),[4] and with increased mortality.[5] Similarly hypertension is a risk factor for age-related retinal macular degeneration (ARMD). It is possible that vitamins and other nutrients may have a direct action in protecting the lens and retina, or separately in promoting the health of the body to benefit the eye indirectly. An extensive literature exists concerning the role of the anti-oxidant vitamins in the prevention of vascular disease.[6]

Vitamins and the lens

The lens is under threat by oxidation.[7] Biochemical evidence demonstrates that proteins and lipids undergo oxidative damage by free radicals.[8] The proteins are important as

N.A. Phelps Brown
A.J. Bron
J.J. Harding
Clinical Cataract Research Unit
Nuffield Laboratory of Ophthalmology
Oxford, UK

H.M. Dewar
Nutrition and Dietetics Department
John Radcliffe Hospital
Oxford, UK

N.A. Phelps Brown ✉
69 Harley Street
London W1N 1DE, UK

the constituents of the cytoplasm within the fibre cells and lipoproteins are important in the cell membranes of the lens cells. The lipids are also important in the photoreceptor elements in the retina. The free radicals are neutralised by the body's anti-oxidant enzymes and by the anti-oxidant vitamins. Thus it is rational to consider enhancing the anti-oxidant status of the eye by nutritional means to promote eye health and to prevent cataract.

Vitamin penetration of the lens

Vitamins are only likely to benefit the lens directly if vitamin supplementation can raise the vitamin level within the lens. The evidence from animal experimentation for vitamin E is not encouraging: the lens contains low levels of vitamin E and there is little change in the vitamin E concentration in relation to the dietary intake.[9,10] Congenital malabsorption of vitamin E is not associated with cataract.[11]

In the case of vitamin C, the concentration of this vitamin in the lens does increase with dietary intake in the experimental animal (rat).[12] A high vitamin C intake in man produced an increase in the total ascorbate in the lens, but only 50% of the ascorbate was in the reduced form.[1]

Cataract and nutrition studies in animals

Vitamin C has been shown to be protective in a number of experiments. Malik *et al.*[13] showed an increased susceptibility to UV-induced cataract in the vitamin C deprived guinea pig. A vitamin C supplement was shown to reduce the development of cataract in diabetic rats.[12] Vitamin C protected against heat-induced lens changes in the guinea pig, an animal which resembles the human in its inability to synthesise vitamin C.[14]

Cataract and nutrition studies in humans

Epidemiological studies give inconsistent support to the suggestion that nutrition plays a role in the development of cataract in man. In different areas of the world, cataract is more common in those of low socio-economic status, low stature and low educational achievement.[15,16] The anti-oxidant status of persons with cataract has been shown to be reduced compared with persons without cataract.[17–19] A case-control study showed that persons who take regular supplements of vitamins E and C have a reduced risk of cataract.[20] In the study by Leske *et al.*[19] the use of multivitamins reduced the risk of all cataract types. Intake of riboflavin, vitamin C, vitamin E and beta-carotene (provitamin A) reduced the risk of cortical, nuclear and mixed cataract types. In a further study by Leske *et al.*[21] a high serum vitamin E level was found to reduce the risk of cataract to less than half and a protective role of riboflavin (vitamin B_2) was also found. The study by Hankinson *et al.*[22] in US nurses showed a reduced incidence of cataract in association with a high intake of spinach. A further study[23] has shown a reduced risk of nuclear cataract in association with higher levels of plasma vitamin E and a reduced risk of cortical cataract with medium levels of plasma vitamin E, but this study did not show a relationship between cataract prevalence and anti-oxidant status. A recent study in US physicians shows a reduced incidence of cataract (risk factor 0.7) in those taking a multivitamin supplement, compared with the incidence in physicians taking no vitamin supplement, but the benefit appears to have been only for smokers.[24] This study did not show any effect in those who took only vitamin C and/or E supplements, but the numbers of subjects in this group were small. The Beaver Dam study in Wisconsin[25] showed that the use of a multivitamin supplement was associated with a reduced rate of nuclear cataract, but only in smokers.

Other studies have not shown an association between vitamin status and cataract. A study in Finland[26] showed no difference between cataract subjects and controls for vitamin E, beta-carotene and selenium. Studies in Italy[27,28] have shown no association between plasma vitamin C and E levels and cataract. The Beaver Dam study in the USA[29] has not shown a protective effect of higher serum levels of vitamin E or carotenoids. In India, where an association between vitamin status and cataract might seem more likely, a study[30] showed no association between vitamin E, pyridoxine and thiamine (vitamin B_1) levels with cataract. An increased risk of nuclear with posterior subcapsular cataract was associated with high levels of ascorbate (vitamin C).

The recent review by Gerster[31] on the subject of nutrition and cataract presents the view that controlled clinical trials are now desirable. One such placebo-controlled trial has recently been completed in China, the Linxian Cataract Study, in which subjects were given multiple vitamin and mineral supplements. A significant reduction in the incidence of nuclear cataract was found in the treatment group.[32]

In the studies supporting the concept that persons who take additional vitamins are less likely to develop cataract, the benefit has been shown for those taking a multivitamin supplement.[33] However, it seems most likely that the important vitamins are the anti-oxidant vitamins: beta-carotene (provitamin A), ascorbic acid (vitamin C) and alpha-tocopherol (vitamin E). The molecule of beta-carotene is converted to two molecules of vitamin A on absorption in the intestine. The anti-oxidant vitamins are of plant origin, particularly in green leaves, where they serve to protect the plant from the oxidative stress that results from the UV in sunlight and also from the plant's own generation of oxygen by photosynthesis. Animals must have reaped the benefit of eating these plant vitamins from the earliest days of evolution.

It is likely that vitamin supplements given to populations with poor nutrition would have a significant impact in preventing the development of cataract and that vitamin supplements given to persons with good nutrition[33] would have a minor impact in preventing the development of cataract. It is also likely that vitamins would have a significant impact on those with good nutrition but at increased risk of cataract because of smoking. What is at present less certain is the effect of giving vitamin supplements to those persons already affected by cataract.

Anti-oxidant vitamins and the retina

The information concerning vitamins and retinal health is limited to a relatively small number of laboratory experiments, some epidemiological studies and a few clinical trials in humans.

A significant role for vitamin C in the retina has been indicated in the experimental animal. In one laboratory experiment the amount of ascorbic acid in the retina fell under conditions of continuous light exposure, indicating that the ascorbic acid was being used up and may be depleted in protecting the retina from the effects of light.[34] In another study[35] ascorbic acid was found to protect the retina from light damage. In the monkey, retinal degeneration may be induced by anti-oxidant vitamin deprivation.[36]

Epidemiological studies in man have shown inconsistent results. Studies[18,24,37,38] have indicated the protective role of anti-oxidant vitamins for the retina, particularly against the development of age-related retinal macular degeneration (ARMD). The study of West *et al.*[38] showed that vitamin E was significantly associated with a protective effect for ARMD. However, the case-control study of Sanders *et al.*[39] showed no differences in serum anti-oxidant vitamin levels between ARMD cases and controls. The study of Mares-Perlman *et al.*[40] also failed to confirm a definite relationship between anti-oxidants and ARMD. The Eye Disease Case Control Study Group,[41] who studied neovascular ARMD, showed a significant protective role for carotenoids, but no significant effect of vitamin C, vitamin E, selenium and zinc.

Other vitamins and the eye

Other known vitamins have a role to play in eye health.[42] Nicotinic acid (vitamin B_3) and the other B vitamins (B_1, B_2, B_6 and B_{12} are essential to the maintenance of optic nerve function. The effects of deficiency are not generally seen in Western populations, except in those taking excess alcohol or smoking excessively. The recommended daily allowance for adults is 1.4 mg of vitamin B_1 (thiamine) and 1.6 mg of vitamin B_2 (riboflavin).

Sources of vitamins

The anti-oxidant vitamins A, C and E are present in green leaf foods, fruits, nuts and root vegetables. Provitamin A (beta-carotene) is present in dairy products, green plants and in yellow or orange fruits. Parsley and spinach are particularly rich sources and the best root vegetable for vitamin A is the carrot. Vitamin A is present in fruits, but fruits have a lower concentration than leaves.

A vitamin supplement may be considered for persons over the age of 50 years and this should logically be a multivitamin preparation, particularly with an adequate content of beta-carotene, vitamin C and vitamin E. There is no recognised upper limit for the amount of vitamins C and E that can be taken, but vitamin A is toxic in excess and a teratogenic role has been implicated in pregnancy.[43] A reasonable upper dietary limit is: beta-carotene 10 mg, vitamin C 1000 mg and vitamin E 600 mg per day. A vitamin E supplement of 800 mg a day has been shown to have no adverse effect in the short term in the elderly.[44] However, the evidence of long-term safety of anti-oxidant vitamin supplements is still lacking.[45]

Conclusions concerning vitamins

Young persons in Western countries may have an adequate vitamin intake since their appetites are usually large, although their diet may not be well chosen. But in young persons with severe self-induced nutritional deprivation, anorexia nervosa, a cataract occurs occasionally which matures rapidly. In the elderly in Western countries who eat less, the vitamin intake may be inadequate, so that a vitamin supplement may be reasonable. The protective role that this may have in cataract appears to be slight, if any, except in those who have an increased risk of cataract from smoking. It is possible that vitamins may have some indirect beneficial action on the lens by promoting vascular health. Further clinical trials should help define the role of vitamin supplements.

Essential minerals for the eye

About 20 different minerals are required for human health. Many of these are essential cofactors in enzymes catalysing biochemical reactions providing the energy and synthetic capabilities upon which all life forms depend. These enzymes include those with anti-oxidant properties: glutathione peroxidase, superoxide dismutase and catalase. Only a sufficient intake of a mineral is required to satisfy all the available sites on the enzymes that need it, and it is unlikely that taking extra amounts of the mineral would have any further benefit.

Zinc

Zinc is thought to play an important role in the metabolism of the retina and the lens of the eye.[46] Zinc is an essential constituent of many enzymes and so is necessary for the regulation of much of the body's metabolism. Zinc ions are present in the enzyme superoxide dismutase, which plays an important role in scavenging superoxide radicals. The zinc concentration in the retina and choroid is normally one of the highest levels in the body,[47] which further suggests the special importance of zinc to the eye. Zinc is considered to have an interaction with vitamin A in the generation of the visual pigments of the retina; night blindness occurs with zinc deficiency even in the presence of adequate vitamin

A.[48] Like the anti-oxidant vitamins, zinc has an anti-oxidant role and, as with the vitamins, it is the elderly whose diet is most likely to be inadequate in zinc.

The study by Newsome in the USA,[49] in which a zinc supplement has been given to elderly people with the early stages of retinal macular degeneration, has shown better maintenance of visual acuity in those receiving zinc than in those receiving placebo. Also, photographs taken of the retinas showed less deterioration in the treated group. This study may indicate a specific role for zinc in maintaining retinal health, or it may be that zinc is having the non-specific effect of enhancing the anti-oxidant status of the eye. Newsome's study[49] was relatively limited; further studies are required before conclusions can be drawn about the advisability of giving zinc supplements to affected patients.

Zinc may also be important in maintaining the health of the lens of the eye. A low level of zinc and copper in persons developing cataract was reported in one study[50] and cataract was not found to be related to low levels of other minerals. Zinc deficiency causes cataract in salmon.[51]

Zinc is naturally present in meats, eggs and in seafood, whole cereals, eggs and pulses. There is some in milk, but whole-grain products contain inadequate levels and people whose diet is mainly whole-grain foods are at risk of deficient intake. Unfortunately the intake of large amounts of dietary fibre, which is health-promoting, impedes zinc absorption. Zinc absorption is similarly impeded in chronic diarrhoeal conditions. Zinc is non-cumulative in the body and is only toxic if taken in large excess. A reasonable supplement to take is 20 mg a day. Taking a zinc supplement may depress copper levels and so copper should also be taken.

Selenium

It was established in 1957 that selenium has anti-oxidant properties, making it apparently comparable with vitamin E, although chemically quite different. It was later discovered that selenium is the metal element in the enzyme glutathione peroxidase – an enzyme that destroys lipid peroxides and so reverses the oxidation of lipids. There may be other, as yet unidentified roles for selenium since other selenium enzymes are found in micro-organisms.

Selenium is possibly harmful if taken to excess and the healthy range of selenium intake, as advocated by the Food and Nutrition Board of the National Academy of Sciences of the USA, is 50–200 μg per day for adults. A range is given, rather than a fixed level, since there is no consensus on the ideal requirement. In the UK the recommended intake of selenium and other nutrients is designated as the Reference Nutrient Intake (RNI).[52] The RNI for selenium is 60–75 μg per day.

Natural sources of selenium include seafoods, meats, cereals, dairy products, fruits and vegetables in descending order of importance. A reasonable supplement to take is 23 μg a day, but the need for a selenium supplement is yet to be defined.

Other minerals

Other essential minerals for the body include copper, chromium, iodine, magnesium, manganese, molybdenum and potassium. Copper and manganese, together with zinc, are present in the enzyme superoxide dismutase. But generally the role of such minerals in eye health is not well understood. An increased zinc intake can antagonise the utilisation of copper by the body, so that some available zinc supplements also contain copper.

Other essential nutrients for the eye

Carotenoids

In addition to the vitamins, which humans and other species derive from vegetables, the carotenoids are vegetable products that are also essential to the health of the eye.[53] Carotenoids are yellow pigments that are found particularly in coloured fruits and vegetables.

The carotenoids from the diet are concentrated in the retina at the macula lutea and are responsible for the yellow colour that gives the macula its name. Of about ten carotenoids that are carried in the blood stream two are concentrated in the macula. These are zeaxanthin, the major carotenoid of maize, and lutein, the carotenoid of melon and spinach.[53] The function of these pigments is probably, in part, to improve the visual image by the absorption of blue light. But they are considered also to have an important role in the biochemical protection of the macula against the effects of free radicals, like the anti-oxidant vitamins.

Carotenoids are likely to be important in protecting the eye against ARMD. A reduced risk of macular degeneration is found in people with a good serum level of carotenoids, particularly lutein and zeaxanthin,[33] and in animals the formation of drusen in the retina has been shown to occur faster in animals deprived of carotenoids. Low carotenoid levels have also been associated with cataract,[54] but the numbers in this study were small. Eating spinach, which is a good source of both vitamin E and of lutein, has been shown in one study to protect against cataract,[22] but in the same study this effect was not shown for carrot.

Essential fatty acids

The essential fatty acids are so called because the body can not synthesise them, so the fatty acid, or its precursor is needed in the diet. Recently the nutritional value of evening primrose oil has come to notice. Evening primrose is a good source of the essential fatty acid gamma-linolenic acid (GLA). This is required to form prostaglandins, which are important regulators of many functions in the body. Evening primrose oil is a good source of GLA but it is not the only source, and *cis*-linoleic acid from the diet can also be converted by the body into GLA. Star flower oil is another good source of GLA.

Table 1. *Recommended daily intake for vitamins and minerals essential to eye health*

	Recommended daily allowance (RDA)	Reference nutrient intake (RNI)	Reasonable daily supplement	Reasonable upper limit
Vitamins				
A (beta-carotene)	800 μg	Male 700 μg Female 600 μg	1000 μg (none in pregnancy)	10 mg
B_1 (thiamine)	1.4 mg	0.4 mg/1000 kcal	1.4 mg	
B_2 (riboflavin)	1.6 mg	Male 1.3 mg Female 1.1 mg	1.6 mg	
C (ascorbate)	60 mg	40 mg	500–1000 mg	1000 mg+
E (alpha-tocopherol)	10 mg	3–4 mg	300 mg	600 mg
Minerals				
Copper	1.5–3 mg	1.2 mg	2 mg	
Selenium	70 μg	Male 75 μg Female 60 μg	70 μg	200 μg
Zinc	15 mg	Male 9.5 mg Female 7.0 mg	20 mg	40 mg

The Recommended Daily Allowance (RDA) is an international standard for the basic daily need for an adult.[63] The Reference Nutrient Intake (RNI) is the UK standard.[52] The 'reasonable daily supplement' and the 'reasonable upper limit' are the authors' estimates.

The eye's requirement of GLA has not been defined, but there are reports of the beneficial effects of dietary evening primrose oil on conjunctivitis sicca, which might be useful to persons with a tendency to dry eyes. In the instance of Sjögren's syndrome there is theoretical and practical evidence of a therapeutic effect.[55] Patients with Sjögren's syndrome have high levels of circulating prostaglandins coupled with depletion of prostaglandin precursors dihomogammalinolenic acid and arachidonic acid. Supplementation of essential fatty acids might therefore be beneficial in Sjögren's syndrome and a placebo-controlled trial has confirmed this.[55] An uncontrolled trial of evening primrose oil plus a zinc supplement has suggested a beneficial effect in contact-lens-using patients with dry eyes (G. Wilson, personal communication).

The omega-3 long-chain polyunsaturated essential fatty acids such as docosahexaenoic acid (DHA) are components of cell lipids and are present in oils of animal origin and especially in those from oily fish, such as the mackerel and herring. Omega-3 fatty acids are absent from some plant oils, such as corn oil. The omega-3 fatty acids are essential for the normal development of the eye and brain in the infant[56] and are provided by breast milk, which is rich in essential fatty acids. Breast-fed infants have been shown to have better visual performance than those on substitute feeding.[57] Omega-3 fatty acids are essential to retinal function at all ages and are found in the receptor outer segments.[58] The retinal pigment epithelium is considered to have a role in recycling the omega-3 from digested receptor outer segments.[59] Omega-3 fatty acids are metabolised to prostaglandin 13,[60] which indicates a further importance of these essential fatty acids. Consumption of omega-3 fatty acids has been shown to reduce the incidence of cardiovascular disease,[1,2] so that they can be considered to have a role of promoting general health with an indirect benefit to the eye.

Conclusion

The information available provides an indication that nutrition is a significant factor in eye disease and that nutritional supplements may have a role in the prevention of eye disease. For the clinician it is clear that further randomised clinical trials are needed. The information is not so clear in indicating whether individual patients should be advised to take a supplement.

Patients of all ages should be encouraged to maintain healthy nutrition, including the consumption of fresh fruit and vegetables, especially green vegetables, and vegetable and fish oils in place of animal fats. They should also be encouraged to avoid the adverse effects of smoking on nutrition. Middle-aged and elderly patients may benefit from a dietary supplement that ensures they receive an adequate daily intake of the various vitamins and minerals. The recommendation for an adequate daily intake has been known as the Recommended Daily Allowance (RDA).[63] In the UK the RDA has been replaced since 1991 by the Reference Nutrient Intake (RNI).[52] In the case of the anti-oxidants, a daily intake in excess of the RDA or RNI may be beneficial, but this is yet to be proven. For patients already affected by cataract, it is uncertain that a supplement taken at this stage will have any effect. For those with ARMD affecting the vision in one eye there is a possible case that a vitamin and/or mineral supplement may help protect the unaffected eye. Further clinical trials are indicated to define the advisability of vitamin, mineral and other supplements.

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