Review Article

Vitamin E and supplements offer eye neuroprotection – Myth or reality?

ABSTRACT

Background: Several studies suggested that nutrition might affect~~have an effect on~~ eye health. Although exposure to nutrients is ubiquitous, on the other hand without it, we generally cannot survive, and ~~an~~ exposure to too high or too low causes health problems. Vitamins are a good example and the ubiquitous exposure to vitamins has led to many epidemiological studies for many diseases, including glaucoma.

The main~~Main~~ body of the abstract: Leading causes of vision loss include several eye conditions such as cataracts~~cataract~~ and glaucoma. The role of nutritionalsupplementationin preventing~~to prevent~~ the progression of ocular disease is of greatinteresttohealthcare~~health care~~professionalsIt is recognized that the crystalline lens and retina suffer oxidative damage and the most protective agents are anti-oxidant vitamins A, C, and E. The Age-Related Eye Disease Study (AREDS), found that supplementation with vitamins C and E, reduced the risk of developing various ocular diseases. The RDA for vitamin E is 15 mg/day α-tocopherol for both women and men. Vitamin E exists naturally in nuts and seeds, in addition to dark leafy vegetables. A~~In a~~ recent study reported lower plasma levels of vitamin E in POAG subjects.

Conclusion: In conclusion, exposure to nutrients ~~although~~ is ubiquitous, without it, in general, we cannot survive. Conflicting evidence is presented for vitamins A and E in the prevention of ocular disease.Several~~A number of~~epidemiologicalstudiesshowed an increased risk of nuclearorcorticalcataracts~~cataract~~ in peoplewith low blood levels of vitamin E.Furthermore, several~~a number of~~studiessuggestedthatnutritionmightaffect~~have an effect onthe~~ intraocularpressure (IOP) or glaucoma, arbitrated by oxidative stress.

Keywords: *glaucoma; vitamin E; antioxidant supplements; crystalline lens; oxidative stress; cataract*

Introduction

A recent advance in eye health is the suggestion that vitamins and supplements may be affecting directly the eye or supporting bodily health, on which the eye depends. Vitamins are today often referred to as micronutrients [1]. It is well known that the crystalline lens and retina suffer oxidative damage and the antioxidant~~anti-oxidant~~ vitamins A, C, and E are protective agents. On the other hand, more or less ~~of~~ 250 million people worldwide suffer from varying degrees of vision loss [2]. Leading causes include several eye conditions such as cataracts~~cataract~~, AMD, glaucoma, and diabetic retinopathy. Once~~All at once~~, recent studies gave controversial reinforcement of~~to~~ the role of nutrition in cataract development [3]

Furthermore, epidemiological studies give contradictory support to the suggestion that nutrition plays a role in the development of cataracts~~cataract~~ in humans~~man~~. In different areas of the world, cataract is more common in people of low socio-economic status, low health care, and low educational level [4, 5]. The role of nutritional supplementation in preventing~~to prevent~~ the progression of ocular disease is of interest to healthcare~~health care~~ professionals and patients.

Those highlighted for possible inclusion were vitamins A, B, C, and E. Conflicting evidence is presented for vitamins A and E in the prevention of ocular disease; these vitamins have significant involvement in the production of rhodopsin and prevention of lipid peroxidation respectively. Improvements in visual function in patients with age-related macular disease have been noted with lutein and zeaxanthin supplementation [6].

The Age-Related Eye Disease Study (AREDS), sponsored by the National Eye Institute in the US, found that supplementation with vitamins C and E, β-carotene, zinc, and copper (Table 1) at levels well above the recommended daily allowances reduced the risk of developing advanced AMD by about 25% [7].

Table 1

Nutrient	Daily dosage	% daily value
Vitamin C (ascorbic acid)	452 mg	754
Vitamin E (DL-α-tocopheryl acetate)	400 IU	1334
Zinc (zinc oxide)	69.6 mg	464
Copper (cupric oxide)	1.6 mg	80
Vitamin A (β-carotene)	28,640 IU (17 mg)	572

Table 1. Nutrition content of the Age-Related Eye Disease Study (AREDS) formulation (after Rasmussen and Johnson, 2013)

Vitamin E

Vitamin E exists naturally as eight distinct fat-soluble compounds of tocopherols and tocotrienols, each subgroup having α, β, γ, and δ subtypes. Nuts and seeds such as sunflower seeds, almonds, and hazelnuts are rich sources of vitamin E, in addition to dark leafy vegetables like spinach and collard greens.

Vitamin E is a fat-soluble antioxidant that prevents the oxidation of fatty acids by reactive oxygen species. The retina is a lipid-rich environment and is bombarded by ultraviolet radiation. In cell culture, vitamin E has been found to enhance the antioxidant ability of lutein to protect retinal pigment epithelial cells from acrolein-induced oxidation [8]. If a molecule of α-tocopherol neutralizes a free radical, then its antioxidant capacity is ~~totally~~ lost. Nevertheless, other antioxidants, like vitamin C, are capable of regenerating the antioxidant ability of α-tocopherol [9].

Vitamin E portrays a family of eight fat-soluble antioxidants: four tocopherols (α-, β-, γ-, and δ-) and four tocotrienols (α-, β-, γ-, and δ-). α-Tocopherol is the form of vitamin E that is actively maintained in the human body and also the major form in blood and tissues [1]. Furthermore, it is the chemical form that assembles~~assemble~~ the RDA for vitamin E.

The α-tocopherol shows an antioxidant main function. In contrast, fats are susceptible to destruction by free radicals, through ~~the~~ oxidation. α-Tocopherol attacks free radicals one by one to prevent lipid oxidation. Since the retina contains a high concentration of fatty acids, this seems to be of great~~grate~~ importance [10].

The recommended intake of vitamin E is 22.4 IU, [11,12] whereas the dose used in AREDS2 was 400 IU daily. One ounce of sunflower seeds satisfies the daily RDI, yet 18 times that is needed to reach the doses used in AREDS2.

Other functions of α-tocopherol that would be of benefit to ocular health include effects on the expression and activities of molecules and enzymes in immune and inflammatory cells. Furthermore, α-tocopherol has been shown to inhibit platelet aggregation and to improve vasodilation [13].

The RDA for vitamin E is 15 mg/day α-tocopherol for both women and men (≥19 yrs) [13]. The average intake of vitamin E from foods in the US for men and women over 50 years of age is 8.6 and 7.3 mg/day, respectively. Only men and women in the 95th percentile of vitamin E intake or greater have intakes of vitamin E from a diet that meets~~meet~~ the RDA. Vitamin E-rich foods and some suggested serving sizes are shown in Table 2 [11].

Table 2

Food	Serving	Milligrams (α-tocopherol equivalents)
Almonds, slivered	1/4 cup (27 g)	7
Corn oil	1 tb (14 g)	2
Peanuts	1/4 cup (37 g)	3
Peanut butter, smooth	2 tb (32 g)	3
Sunflower seeds	1/4 cup (35 g)	12
Safflower oil	1 tb (14 g)	5
Soybean oil	1 tb (14 g)	1
Wheat-germ oil	1 tb (14 g)	20

Note:

*Edible portion.

Abbreviation: tb, tablespoon.

Table 2. Vitamin E content of foods (after Rasmussen and Johnson, 2013)

Vitamins and glaucoma

Several studies suggested that nutrition might affect~~have an effect on~~ eye health. Although exposure to nutrients is ubiquitous, on the other hand without it, we generally cannot survive, and ~~an~~ exposure to too high or too low causes health problems. Vitamins are a good example and the ubiquitous exposure to vitamins has led to many epidemiological studies for many diseases, including glaucoma [22].

Glaucoma is a group of optic neuropathies that involve progressive death of retinal ganglion cells, degeneration of the optic nerve, and ultimately typical alterations, like defects in the visual field [14, 15].
Primary open-angle~~open angle~~ glaucoma (POAG) is the most common type and it differs from normal tension glaucoma (NTG) given that in the former, IOP is often elevated [14, 16]. If glaucoma remains uncontrolled, then it forms irreversibly devastating visual consequences [17,18,19]. Current treatment typically involves topical ocular hypotensives as first-line~~first line~~ therapy [17].

Age and high intraocular pressure (IOP) have been identified as risk factors for glaucoma development~~developing~~. The need to study glaucoma about~~in relation to~~ vitamins comes from the observation that glaucoma is the leading cause of irreversible blindness, that almost half of the glaucoma cases are undiagnosed, and that the prevalence is increasing over time [20, 21].

Elevated intraocular pressure (IOP) is considered to be the main risk factor. Despite~~In spite of~~ useful therapies by lowering IOP, the disease progress is important for a grade number of patients.Oxidative stress occurs when more reactive oxygen groups are formed than~~then~~ the anti-oxidative capacity of the cell can handle. This leads to damage of the aqueous humor~~humour~~ outflow system of the eye, and the trabecular meshwork, resulting in an increase in IOP and eventually death of retinal ganglion cells [23, 24].

As a result, alternative strategies aiming mainly to delay RGC degeneration are~~is~~ the existing therapeutic scheme for glaucoma [25]. Even so, reducing IOP by hypotonizing drugs or other surgical procedures remains the only available therapy, at present~~at the present time~~ [26].

The death of RGCs is the result of several mechanisms including trophic factor deprivation [27], inflammation [28], oxidative stress [29], mitochondrial dysfunction [30], excitotoxicity [31], autophagy dysregulation [32], protein misfolding [33], ischemia, and hypoxia [34]. Each of these methods may support the etiology and progression of the disease, and it is a prospective aim for new neuroprotective, but IOP-independent, management. Significantly, sustained oxidative stress actions should be considered as a key factor [28, 29, 35].

The retina is mainly vulnerable to oxidative stress due to its high consumption of oxygen and proportion of polyunsaturated fatty acids, and its direct exposure to light [36]. This weakness increases with aging, due to the physiological decrease of antioxidant defense mechanisms [36]. High levels of oxidative stress markers have been found in the aqueous humor of patients with primary open-angle~~open angle~~ glaucoma (POAG) and primary-angle~~primary angle~~ closed glaucoma (PACG) [37, 38].

In a recent study, Zanon-Moreno and colleagues (2013) reported lower plasma levels of vitamin E in POAG subjects [39]. Contrariwise, some studies showed an increase in vitamin E serum levels in glaucoma patients [40]. Two studies on NTG patients showed no difference in vitamin E plasma levels between patients with glaucoma and controls [41, 42] and vice versa, Lopez-Riquelme and colleagues (2015) reported lower vitamin E plasma levels in NTG patients [43].

Nutrition and Cataract

Age-related cataract stands as the major cause of blindness in the world. The prevalence and effects of age-related cataracts~~cataract~~ are increasing dramatically as the proportion of elderly in our population continues to rise. Diabetic cataracts are caused by an elevation of polyols within the lens of the eye catalyzed by the enzyme aldose reductase. It is estimated that more than 68% of people aged 79 and older have some degree of lens opacification or cataract [44].

Mechanisms~~Mechanism~~ of cataract formation include poor glutathione level add to a not working antioxidant defense system within the eye crystalline lens. Nutrients that may boost glutathione levels~~level~~ and activity include lipoic acid, vitamins E and C, and selenium [45]. With age, the highly organized crystalline fibers of the transparent crystalline lens are believed to become dehydrated and photo-oxidized, leading to crosslinking and aggregation. Because oxidative damage is supposed to be fundamental in cataract development, many studies have been requiredto investigate any protective effect of oral antioxidant supplementation [46].

The results of observational studies suggest that a healthy lifestyle with a diet containing foods rich in antioxidants, particularly lutein and zeaxanthin, as well as n−3 fatty acids, appears possibly beneficial for cataracts~~cataract~~. Concerning the relation between cataracts~~cataract~~ and supplements, a few randomized trials were initially designed to evaluate cataracts~~cataract~~ (2 of these were in China) [47, 48, 49], and 2 other studies evaluated cataracts~~cataract~~ later in the clinical trials designed for other diseases [50, 51]. A multivitamin-multimineral supplement with a combination of vitamin C, vitamin E, beta-carotene, and zinc (with cupric oxide) may be recommended for AMD but not for cataracts~~cataract~~ [52].

The cataract analysis of the AREDS trial showed no difference between the intervention groups and placebo on the development or progression of age-related cataracts~~cataract~~ or loss of visual acuity [47[. Quite the opposite to the Linxian study, the participants in AREDS were predominantly white (96%) and well nourished. The primary outcomes of the study were originally the~~that~~ progression of lens opacity or cataract surgery and additionally, loss of visual acuity, measured by loss of 15 or more letters in one eye over time. The likelihood of a lens-related event was calculated to be 30% over 5 years in all persons despite the consequences of the intervention [47].

Although the pathogenesis of cortical and age-related~~age related~~ nuclear cataracts~~cataract~~ are different, oxidative damage has been implicated as an underlying cause of the distinctly different damage phenotypes [53, 54, 55, 56, 57]. Because of this relationship between oxidative stress and cataract formation, it has been proposed that topical application and dietary interventions with antioxidants can be used as therapies to delay or prevent cataract progression. Other nutrients and botanicals, that~~which~~ may prevent or help prevent cataracts, include pantethine, folic acid, melatonin, and bilberry.

Several~~A number of~~ epidemiological studies showed an increased risk of nuclear or cortical cataracts~~cataract~~ in people with low blood levels of vitamin E [58, 59]. The deficit of vitamin E may lead to the formation of toxic peroxides and malondialdehydes due to a generally speeding up of tissue oxidation resulting in lens opacification. Regrettably, an unsophisticated view of supplementing the lens with antioxidants has proven to be ineffective, and in some cases harmful, in delaying cataract progression [53].

The dietary amount of vitamin E supplementation ~~clearly~~ affects~~effects~~ the alteration of protein structure accompanied by the change of glutathione level in the lens. This elevation might effectively protect the lens membrane from lipid peroxidation, which in turn probably reduces the risk of protein oxidation. Accordingly, sufficient antioxidant supplements such as vitamin E mayprotect lens proteins from oxidative abuse. On the other hand, an excess of vitamin E intake may reduce its inherent advantage of antioxidation.

In summary, there appears to be a general compromise that a diet high in fruit and vegetables containing Vitamins~~Vitamin~~ C, E, and A (Table 3) and multivitamin-mineral supplements may be protective against cataracts~~cataract~~. Data on supplemental antioxidants provided as low-dose~~low dose~~multivitamins~~multivitamin~~ appear generally positive, while results obtained using single nutrient antioxidants ranged from moderately effective to possibly harmful. Based on current data, a healthy diet, and a multivitamin supplement may offer protection against cataracts. If this is the case, it is important to consider how these nutrients can~~are able to~~ reach the lens in sufficient quantities to be effective in protecting the lens from oxidative damage.

Table 3

Vitamins	Sources
Vitamin C (L-ascorbic acid)	Citrus fruit, potatoes, broccoli, bell peppers, spinach, strawberries, tomatoes, Brussels sprouts
Vitamin D (cholecalciferol)	Fortified milk and cereals, fatty fish
Vitamin E (tocoferol)	Vegetable~~Vegetables~~ oils, leafy green vegetables, whole grains, nuts

Table 3. Main sources of vitamins (After Harvard Health Publishing, Harvard Medical School, 2021)

Discussion

Many studies support that vitamin E is an essential antioxidant. Six studies reported a possible association between~~of~~ vitamin E blood levels and glaucoma. One of these studies reported lower plasma levels of vitamin E in the POAG group [43]. One study reported no association [60], and two other studies found increased serum vitamin E levels in glaucoma patients.

For normal tense glaucoma (NTG), one study exhibited lower plasma levels of vitamin E in NTG patients [60], while other studies found no difference in plasma levels of vitamin E between patients with NTG and control groups [60, 61, 62]. Concerning aqueous humor~~humour~~, lower levels of vitamin E have been reported in patients with POAG and PACG [63]. On the other hand, studies on the dietary intake of vitamin E and its association with OAG announced no significant relation [60].

In conclusion, exposure to nutrients although is ubiquitous, without it, in general, we cannot survive and ~~an~~ exposure to~~on~~ too high or too low amounts causes health problems. Vitamins are a good example and the ubiquitous experience of~~to~~vitamin~~vitamins~~ action has led to many epidemiological studies for many diseases and glaucoma as well [22]. Furthermore, several~~a number of~~ studies suggested that nutrition might affect~~have an effect onthe~~ intraocular pressure (IOP) or glaucoma, arbitrated by oxidative stress.

Conclusions and Future Strategies

The underlying principle of using nutritional supplementation in glaucoma is persistent by a considerable amount of literature demonstrating that natural compounds~~compound~~ enriched with antioxidant, anti-inflammatory, and anti-apoptotic activities are quite successful in preventing~~to prevent~~ RGC death in models of retinal degeneration. On the other hand, the clinical significance of these data is so far to be proven. Indeed, in a considerable quantity of clinical studies, the small number of included patients, the heterogeneity of the study design, and the short follow-up period make it hard to produce the clinical benefit of the treatment. In addition, further vigilance is required in interpreting the results. Nevertheless, although further investigations are desirable to establish their efficacy and safety, nutritional supplementation may stand as~~for~~ an auxiliary in the therapeutic management of glaucoma

The worldwideWorldwide population is aging, and as a consequenceage-relatedage related cataracts have grown to an epidemic extent, placing harsh pressures on global and local health systems. Given that the launch of lens cataractscataract is strongly linked with oxidative damage, the use of exogenous antioxidant interventions has been promoted as a technique to keep the progression of lens cataractscataract slow. nevertheless, the majority of these studies are unsuccessful in slowingto slow down cataract progression.

None of the described medical prevention studies demonstrated a convincing success. The mainstream of the results suggestssuggest that the protective effect of antioxidant vitamins recognized in earlier case-control and epidemiological studies may have been perplexed by other lifestyle factors [64]. Individuals who are regular users of multivitamin preparations are more likely to be health conscious. Further randomized clinical trials and meta-analysesmeta-analysis of data from previous randomized trials will be required to determine whether cataractscataract could be prevented or delayed by using vitamin supplements of any type. Although oxidation and inflammation are highlyhigh associated withto the etiology of these age-related eye diseases, a recent survey among middle-agedmiddle age patients showed that well over half of those surveyed were not aware of the important nutrients that play a key role in eye health.

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