Supplement & Eye Disease

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Introduction

The global longer life expectancy over the past decades has numerous impacts on health care system. There are eye conditions that are associated with aging population such as Age-related Macular Degeneration and cataract and there is also plenty of researches finding the way to stop those diseases. The treatments can be in the form of surgery, medication, supplement or life style change. Normally, patients will receive surgeries or medications when their treatment criteria is met but the questions about what to do to cease the disease before the treatment is initiated still prevail and inquiries about vitamin & supplements to promote or improve eye conditions have been frequently asked. Some of these products are claimed to be beneficial for eyes and vision. This review article on major clinical trials relating to supplements and eye disease is anticipated to yield advice on patient recommendations.

Age-related Macular Degeneration

Age-related macular degeneration (AMD) is the disease of macula and the leading cause of visual impairment and blindness among people 65 years or older worldwide. AMD is divided into dry AMD (non-neovascular) or wet AMD (neovascular) and may be caused by aging process, genetics, smoking and race. Dry AMD is the early stage of AMD and is diagnosed when drusen or pigmentary changes are found at the macula. Through a period of times dry AMD can progress to late-stage geographic atrophy (GA) or wet AMD, which can cause an irreversible severe vision loss. Clinical trials have evaluated the impact of diet and supplements on the development and progression of AMD. The Age-Related Eye Disease Study (AREDS) and the Age-Related Eye Disease Study 2 (AREDS2) are two of the largest clinical trials supported by the United States National Institutes of Health (NIH) that have assessed the effects of supplements included by Vitamin C 500 mg, Vitamin E 400 IU, Beta-Carotene 15 mg, Zinc 80 mg, Copper 2 mg on the progression of dry AMD to wet AMD.[1]

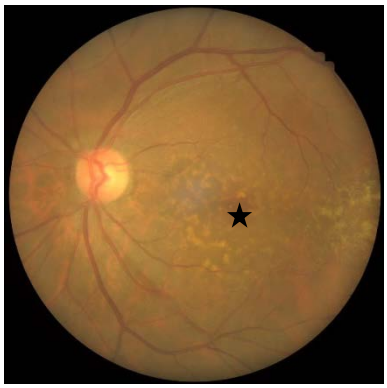

Figure 1 Dry AMD with drusen (asterisk) at macula

AREDS was first published in October 2001, over 3,500 patients with dry AMD took this supplement for a minimum of 5 years, the study found that patients with AMD category 1 (few or no drusen) or AMD category 2 (small or a few intermediate-sized drusen) would be at low risk of progression to advanced AMD thus treatment targeting progression to advanced AMD is not warranted, participants of AMD category 3 (extensive intermediate-sized drusen or large drusen or noncentral GA in at least 1 eye and who did not have advanced AMD in either eye) and AMD category 4 (advanced AMD [macular scar or wet AMD] or vision loss due to AMD in 1 eye only) at 10 years of follow-up demonstrated a significant reduction in the risk of progressing to advanced AMD or wet AMD (odds ratio [OR] 0.66; 95% confidence interval [CI], 0.53-0.83 , and OR 0.60; 95% CI, 0.47-0.78, respectively).[2]No adverse effects were associated with the AREDS formulation supplement with possible contraindications for smokers to avoid beta-carotene due to the risk of developing lung cancer.[3]

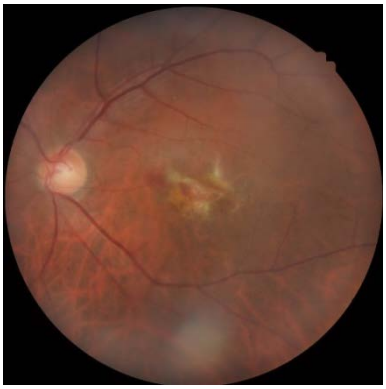

Figure 2 Wet AMD with subretinal hemorrhage

Then the AREDS2 was released in 2013 and they adjusted the formula by replacing Beta-Carotenoids with Lutein (10 mg) + Zeaxanthin (2 mg) as a result of the association between high doses of Beta-Carotene and an increased risk of lung cancer in current or former smokers, Zinc was also reduced from 80 mg to 25 mg for the link to digestive problems, and Omega-3 long-chain polyunsaturated fatty acids (350 mg Docosahexaenoic acid [DHA] + 650 mg Eicosapentaenoic acid [EPA]), was added to the presumption of additional benefit on AMD progression risk reduction. However, they found that the AREDS2 formulation did not further reduce the risk of progression to advanced AMD but because of potential increased incidence of lung cancer in former smokers, Lutein + Zeaxanthin could be an appropriate carotenoid substitute.[4]

The Blue Mountains Eye study was conducted in Australian population to assess the relationship between baseline dietary and supplement intakes of antioxidants and the long-term risk of incident AMD. In contrast to the ARED2, this study shown that higher dietary Lutein and Zeaxanthin intake reduced the risk of long-term incident AMD (risk ratio [RR] 0.35; 95% CI, 0.13–0.92), the discrepancy between 2 studies may be explained by the population differences, a high intake of vegetables also was protective for any AMD and the Blue Mountains Eye study confirmed the AREDS finding of protective influences from zinc against AMD when compared the top Zinc intake with the remaining population, the RR for the top decile intake was 0.56 (95% CI, 0.32–0.97) for any AMD and 0.54 (95% CI, 0.30–0.97) for early AMD.[5]

Besides supplement, diet may play a role on AMD risk reduction. The EYE-RISK Consortium has 2 European population-based prospective cohorts investigating the associations of adherence to the Mediterranean diet (MeDi), which is food rich in fruits, vegetables, legumes and fish, with incidence of advanced age-related macular degeneration. They found that the higher adherence to the MeDi was associated with a 41% reduced risk of incident advanced AMD (P = 0.046).[6]

Regular exercise has been shown to increase antioxidant enzyme activity and increase resistance to oxidative stress[7]. Oxidative stress has long been theorized to contribute to be one of the key components in the pathogenesis of AMD[8]. An oxidative stress is one of several possible pathways influenced by physical activity, the increase in oxidative resistance conferred by regular physical activity may lead to prevention of AMD or a delay of its progression. The systematic review and meta-analysis from Mcguinness et al supported this theory by showing the protective association between physical activity and early AMD (8 studies, n = 38 112, OR 0.92, 95% CI 0.86-0.98) late AMD (7 studies, n = 28 854, OR 0.59, 95% CI 0.49-0.72).[9]

To summarize, patients with intermediate or advanced AMD should be recommended to take the AREDS or AREDS2 formulated supplements for former or current smokers. Smoking is a risk factor for the development of AMD and should be discontinued. Diet consisting of fish, fruits, leafy greens, and nuts has been shown to be beneficial in some studies. Physical activity should be encouraged, as it has been demonstrated to have a modest protective effect.[10]

Cataract

A cataract is a clouding of the lens in the eye that affects vision. The lens is made of mostly water and protein which is arranged in a precise way that keeps the lens clear. Most cataracts are related to aging, as we age, some of the protein inside the lens may clump together and start to cloud a small area resulted in a cataract. Over time, the cataract may grow larger and cloud more of the lens, making it harder to see. Currently surgery is the only effective treatment of cataract by removing the cloudy lens and replacing it with an artificial lens.[11]

Several studies have been conducted to investigate the effectiveness of supplements against cataract. The result from AREDS study found that individuals with highest dietary intake of riboflavin had a 22% and 38% lower likelihood of mild and moderate nuclear cataracts at baseline, respectively, compared with participants reporting the lowest dietary intake (OR 0.78; 95% CI, 0.63-0.97; P = 0.02; and OR, 0.62; 95% CI, 0.43-0.90; P = 0.01). A similar reduction in likelihood of having mild and moderate nuclear cataracts was seen for individuals reporting the highest intake of vitamin B12 (OR, 0.78; 95% CI, 0.63-0.96; P = 0.02, and OR, 0.62; 95% CI, 0.43-0.88; P = 0.01, respectively).[12] But no statistically significant effect of the antioxidant formulation (vitamin C, 500 mg; vitamin E, 400 IU; and beta carotene, 15 mg) was seen on the development or progression of age-related cataract (OD = 0.97, P =.55).[13]

The Blue Mountain Eye Study investigated the relationships between a wide range of nutrients and cataract in older people. The result was suggesting that higher intakes of protein, vitamin A, niacin, thiamin, and riboflavin were associated with reduced prevalence of nuclear cataract. The odds ratios for those in the highest intake groups compared to those in the lowest intake were 0.5 (95% CI, 0.3-0.8) for protein, 0.5 (95% CI, 0.3-0.9) for vitamin A, 0.6 (95% CI, 0.4-0.9) for niacin, 0.6 (95% CI, 0.4-0.9) for thiamin, and 0.5 (95% CI, 0.3-0.9) for riboflavin.[14]

On the contrary, researchers from an international research group called the Cochrane Collaboration examined the benefits of vitamin supplements for cataracts. They looked for randomized controlled trials that compared these products either with one another or with placebo. The researchers analyzed nine studies involving a total of almost 120,000 people between the ages of 35 and 85. The participants used products with vitamin C, vitamin E and/or beta-carotene for up to twelve years. The results of the studies clearly showed that vitamin supplements are not effective against cataracts. People who had taken these products developed cataracts just as often as people who had been taking a placebo. These supplements also did not slow down the progression of the cataracts and did not have any effect on eyesight thus there is no reason to take dietary supplements to try to prevent or slow down cataracts.[15]

Sunlight exposure may play a role in occurrence of cataract. There are studies supporting a link between sun exposure and nuclear cataract and the risk was highest among those with high sun exposure at younger ages.[16,17] As well, NIH is recommending people to wear sunglasses and a hat with a brim to block ultraviolet sunlight in order to help delaying cataract.[15]

Dry eye

Dry eye disease is a common chronic, inflammatory, age-related condition that causes ocular discomfort, fatigue, and visual disturbances that interfere with reading, computer use, driving, and other aspects of quality of life[18-20], and also one of the most common reasons for seeking eye care[20]. Patients with dry eye disease use a variety of approaches for symptom relief, including artificial tears, lid scrubs, punctal plugs, and prescription anti-inflammatory eye drops. Many clinicians recommend and many patients take dietary supplements of n−3 fatty acids (omega-3 fatty acids), because they have anti-inflammatory activity and are not associated with substantial side effects.[21,22]

The Dry Eye Assessment and Management Study Research Group (DREAM) shown that among patients with dry eye disease, those who were randomly assigned to receive supplements containing 3000 mg of fish-derived n-3 eicosapentaenoic and docosahexaenoic acids (omega-3 fatty acids) for 12 months did not have significantly better outcomes than those who were assigned to receive olive oil placebo.[22]

Oxygen is the primary oxidant that is utilized during mitochondrial oxidative metabolism of various organic molecules in metabolic reactions providing cellular energy. Reactive oxygen species (ROS) that might be potentially damaging to tissues are generated

as by-products during oxidative metabolism.[23] Recently literature suggests that oxidative stress may have a direct and/or indirect effect on ocular surface health and plays an important role in the pathogenesis of several forms of dry eye.[24] An antioxidant defense system in the ocular surface is essential for the protection against oxidative damage.[25] Thus, therapeutic modalities employing topical/systemic use of antioxidants may have a promising future in the treatment of dry eye disease.[24]

Glaucoma

Glaucoma is a chronic, irreversible optic neuropathy. There has been a longstanding interest in the potential impact of lifestyle factors such as diet on glaucoma development and progression.[26]

Coffee is a source of caffeine, a biologically active compound that exerts physiological effects on the human body.[27] A transient elevation in IOP has been noted following caffeine ingestion in patients with glaucoma.[28] But no significant association was found between the consumption of coffee and glaucoma risk.[27-29]

It is speculated that Ginkgo biloba extract (GBE) can decrease the risk of developing glaucoma and the evidence is still inconclusive. No effect of ginkgo biloba extract on visual field defect in normal tension glaucoma (NTG) patients from a study by Guo et al[30], which differ from other reports suggesting that GBE may be helpful in improving visual function in some individuals with NTG.[31,32] However the patient demographics and treatment period were different among the studies and that can affect the results.

There is a consideration that fruits and vegetables can decrease the risk of developing glaucoma.[27] A study from Coleman et al found a higher intake of certain fruits and vegetables such as green collards, kale, carrots and peaches may be associated with a decreased risk of glaucoma.[33]

A firm dietary advice to glaucoma patients would be to avoid excessive coffee consumption and increase the intake of fruits and vegetables. However, patients should be advised that nutritional management may complement, but would not substitute conventional glaucoma treatment.[27]

Conclusion

There is evidence suggesting that a combination of vitamins E and C, beta-carotene, and zinc (AREDS formulation) may reduce the risk of developing advanced AMD

with beta-carotene abstention in current or former smokers due to the risk of developing lung cancer. Diet rich in fruits, vegetables, legumes, fish and regular exercise may also help lower the chance of AMD. Current data do not support the use of supplement as treatment for dry eye, cataract or glaucoma.

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