

Antioxidant Supplements In The Prevention And Management Of Cataracts And Macular Degeneration Of The Eye

Convincing Proof That Antioxidant Supplementation Prevents Macular Degeneration

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There has been much debate in recent years as to the ability of antioxidant supplements to prevent or forestall the development of cataracts and macular degeneration of the eye and to their efficacy as natural agents to slow or halt the further progression of these conditions in patients with these afflictions. This debate has now been resolved to a large degree, according to the much-anticipated results of the Age-Related Eye Disease Study, a multi-center, intervention trial involving 4,757 patients between the ages of 55 and 80 years old. In this study, conducted by the National Eye Institute (NEI), patients who were at high risk of developing more advanced stages of age-related macular degeneration (AMD), reduced their risk by approximately 25% when treated with a high-dose combination of Vitamin C, Vitamin E, Beta-carotene, and zinc. According to the NEI this is the first effective treatment that has been shown to successfully slow the progression of AMD. Participants in this double-blind, placebo-controlled clinical study, who suffered from varying degrees of AMD, were given one of four treatments: zinc alone; antioxidants alone; a combination of antioxidants and zinc; or a placebo. After 6.3 years of treatment the results showed that taking zinc alone (80 mg per day, plus 2mg of copper) or antioxidants alone (Vitamin C--500mg, Vitamin E--400 IU, Beta-carotene--25,000 IU per day) were effective interventions, but the best results occurred in those taking both antioxidant and zinc supplements at the above described doses.

Although all the details as to the underlying causes of AMD are not fully understood, it has been shown that free radical damage from ultra-violet light (sunlight) reaching the macula is likely a significant contributing factor. Based upon the findings of the Age-Related Eye Disease Study, the researchers conclude that all persons older than 55 years should have dilated eye examinations to determine their risk of developing advanced AMD. Those with extensive intermediate size drusen (fatty or fibrous deposits under the retina), at least 1 large drusen, non-central geographic atrophy in one or both eyes, or advanced age-related macular degeneration or vision loss due to AMD in one eye, and without contraindications to the use of antioxidant or zinc supplementation, should consider taking a supplement of antioxidants plus zinc at the same or similar doses used in this study. Age-related macular degeneration is the leading cause of blindness in people over the age of 55 in the U.S., Canada and in most developed countries around the world.⁽¹⁾ As such, any safe and effective low-cost intervention that can prevent the development of AMD or significantly slow its progression would save the health care system enormous sums of money and improve the quality of life for many thousands of members of our aging society.

It is estimated that 150,000 Americans are legally blind from AMD, with 20,000 new cases occurring per year. In addition to the effects of ultra-violet light, other risk factors for AMD include smoking, advancing age, atherosclerosis and high blood pressure.⁽²⁾

Previous Studies Demonstrating Antioxidant Protection In AMD

Earlier studies have provided evidence that more optimal status of antioxidant vitamins and minerals could reduce the risk of AMD. In one study, higher blood levels of antioxidants were shown to be related to a lower risk of developing AMD.⁽³⁾ Another investigation revealed that individuals in the top 20% blood levels of selenium, Vitamin C and Vitamin E had a 70% lower risk of developing AMD than did those with blood levels in the lowest 20%.⁽⁴⁾ In the Physicians' Health Study male doctors taking Vitamin E supplements had a 13% reduced risk of AMD. Risk was reduced by 10% in those taking a multiple vitamin and mineral, after controlling for other confounding variables.⁽⁵⁾

Two previous intervention trials, using a commercially available broad-based antioxidant formula in patients with established AMD, demonstrated that supplementation halted or significantly slowed the further progression of the disease and, in some cases, vision actually improved. These studies were only 6 months and 18 months in duration, thus the research and medical community demanded a longer term, multi-center, double-blind, placebo-controlled study to confirm these findings. This was the impetus for the design and implementation of the Age-Related Eye Disease Study reviewed above. In these previous intervention trials the supplement formula contained Beta-carotene, Vitamin C, Vitamin E, zinc, copper, manganese, selenium and riboflavin.⁽⁶⁾

In the eye, zinc plays a vital role. It is required by two important enzymes in the retina that are, in part, responsible for vision.⁽⁷⁾ Zinc also is required as the prosthetic group for an important antioxidant enzyme known as superoxide dimutase. In the absence of the prosthetic group superoxide is unable to function as an antioxidant. Selenium participates in a similar way with respect to the antioxidant enzyme known as glutathione peroxidase.⁽⁸⁾ In a double-blind trial supplementation with 45 mg of zinc alone significantly reduced the rate of visual loss in people with AMD over a one to two year period.⁽⁷⁾ However, a second study failed to show a protective effect when zinc supplementation was tested in 112 patients with AMD.⁽⁹⁾

Other studies indicate that certain carotenoids are also important antioxidants in regards to the prevention and management of AMD. The macula, especially the central portion (the fovea) owes its yellow color to its high concentration of lutein and zeaxanthin. These yellow carotenes function as macular pigments that absorb photon energy from ultra-violet light, which may otherwise cause free radical damage to the retina. Dietary intake of lutein and zeaxanthin (mostly dark green vegetables) and supplementation with these two carotenoids has been shown to significantly increase the amount of macular pigment.^(10, 11,12 13) One study showed that adults with the highest intake of lutein had a 57% reduced risk of developing AMD than did those with low levels of this carotenoid.⁽¹⁴⁾ In an intervention trial with 16 participants (13 with retinitis pigmentosa and 3 with other retinal degeneration problems), vision improved significantly after 26 weeks of supplementation with lutein (40 mg for 6 weeks, followed by 20 mg for 20 weeks). These researchers have shown similar results in small trials involving patients with AMD as well.⁽¹⁵⁾ Harvard researchers reported that adults consuming an average 5.8 mg per day of lutein-zeaxanthin had a 57% decreased risk of developing AMD compared with subjects ingesting less than this amount.⁽¹⁶⁾ Other investigations have demonstrated a strong correlation between higher intake levels of lutein-zeaxanthin and a lower risk of AMD.⁽¹⁷⁾

The evidence linking free radical damage to the development of AMD is strong and consistent. Sunlight triggers oxidative damage to the eye, which in turn leads to macular degeneration.⁽¹⁸⁾ Animals given antioxidants have been shown to lower risk of visual problems in experimental studies.⁽¹⁹⁾

Flavonoids And AMD

There are also some specific flavonoid compounds that are known to concentrate in the macula, in a similar fashion as do certain carotenoids. These flavonoid compounds not only enhance the macular pigment and exert antioxidant effects, but they have been shown to improve blood flow and help stabilize fragile blood vessels, as often occurs in cases of diabetic retinopathy. Clinical studies in humans have demonstrated that all three of the following flavonoid-based supplements are capable of aiding in the treatment of AMD.^(20,21,22,23) The standardized grade of bilberry (std to 25% anthocyanidin content) concentrates as part of the visual purple of the retina, helping to reduce free radical damage. Bilberry flavonoids (anthocyanidins) also reduce capillary fragility by improving collagen integrity and reduced capillary permeability. This is most important in cases where diabetic retinopathy is present and in the

prevention of diabetic retinopathy, as indicated by its use in certain parts of Europe. The therapeutic dose of bilberry in these cases requires 40-80 mg, up to three times per day.⁽²⁵⁾

A double-blind study indicated that Ginkgo Biloba Extract improved long-distance visual acuity in cases of both macular degeneration and diabetic retinopathy. The therapeutic dose for this purpose is 40-80 mg two to three times per day, using a standardized grade of 24% ginkgo-flavone glycosides and 6% terpene content.⁽²⁶⁾

Grape Seed Extract may also be useful in the prevention and management of AMD and diabetic retinopathy. The flavonoids in grape seed extract are known to strengthen the wall of blood vessels and provide antioxidant protection. Like lutein-zeaxanthin, bilberry flavonoids and certain other antioxidants, flavonoids from grape seed extract have been shown to concentrate in the area of the macula (as well as in other tissues). Preliminary studies have implicated its role as an intervention, which can help preserve retinal function in diabetics and myopic patients. The therapeutic dose for this application is 150-300 mg per day, using a standardized grade of 95% proanthocyanidolic compounds.^(27,28) Thus, it may be prudent to include some or all of these interventions in patients at high risk for these retinal conditions, in addition to the doses and nutrients used in the Age-Related Eye Disease Study.

Cataracts And Antioxidants

Cataracts are white, opaque lesions that form on the normally transparent lens of the eye. They occur as a result of damage to the protein structure of the lens. In recent years it has been identified that oxidative stress (free radicals) is a major contributing factor to the development of age-related (senile) cataracts and that the normal antioxidant protective mechanisms in the lens have been found to be significantly compromised in cases where senile cataracts occur. Strong evidence indicates that oxidative stress from ultra-violet light (sunlight) and radiation exposure induces free radical damage to the lens that contributes to senile cataracts development. The lens of the eye has been shown to be devoid of the antioxidant enzymes, superoxide dismutase (SOD), catalase and glutathione peroxidase, and is thus, completely dependent upon nutritional antioxidants including Vitamin E, Vitamin C, selenium and carotenes for its antioxidant defenses. It should be noted that cigarette smoking, which also increases oxidative stress to the body, is also a known risk factor for the development of cataracts.^(29,30)

Cataracts are the leading cause of blindness and impaired vision in the United States. Forty thousand Americans are blind due to cataracts, and cataract surgery is the most prevalent major surgery among Medicare recipients in the U.S.⁽²⁹⁾ In Canada, estimates suggest that there were about 884,000 prevalent cases of senile cataracts in 1988, and a further 330,000 new cases, plus 1.2 million cases of senile lens changes were expected by the end of 1993. In Canada, each cataract surgery cost \$3,000 on average in 1991. The Canadian Study by J. Robertson et al suggested that if all individuals over 55 years of age took a supplement of Vitamin C and Vitamin E each day, at appropriate doses, it would reduce cataract incidence by at least 50% and cut related health care costs in half.⁽³¹⁾ A number of intervention trials have demonstrated that 1000mg of Vitamin C per day (or more) can reduce cataract development and/or halt or slow the further progression of cataracts, in the early stages.^(32,33,34) Other case-control and prospective studies have suggested that higher blood levels and/or intake levels of Vitamin C are associated with a significant reduction in risk of cataracts. For instance, in the study by P Jacques, plasma Vitamin C at 40 umol/L was associated with an 11.3 times greater risk of cataract development than occurred in subjects with a plasma level of 90 umol/L or higher.^(29,35)

Vitamin E supplementation has also been shown to be protective in regards to cataract prevention. However, a dosage of 400 IU was shown to be effective in this regard, whereas a dosage of only 50 IU failed to provide protection against cataract development in a double-blind trial.^(36,37,38,39)

As well, the intake of lutein-zeaxanthin-rich vegetables, such as spinach, kale and broccoli, is also linked to a reduction in cataract risk, which may be as sizeable as a 20-22% reduction. This data stems from large prospective studies, including the Beaver Dam Eye Study (n=1,354), the Nurses' Health Study (n=50,461) and the Health Professionals Follow-up Study (n=36,644).^(40,41,42,43) Curiously, the antioxidant carotenoids, lutein and zeaxanthin are known to be present in the lens of the eye, whereas beta-carotene is not.⁽⁴²⁾ Animal studies have demonstrated that melatonin, which possesses antioxidant properties blocks the formation of cataracts under experimental conditions and a Chinese formula known as Hachimijiogan (Baweiwan), has been used successfully in the treatment of cataracts. This formulation contains a variety of antioxidant-rich herbs.^(29, 44)

Finally, diabetics are at increased risk for cataract development, primarily due to the build up of sorbitol in the lens of the eye that occurs under uncontrolled hyperglycemic conditions. The lens lacks the ability to break down sorbitol, which leads to morphological changes associated with cataract development. The flavonoid quercetin, when supplemented (500 mg, one to three times per day), is an effective aldose reductase inhibitor, which blocks the conversion of glucose to sorbitol and thus, may be considered as an additional supplementation intervention in diabetic patients to help further reduce the risk of cataracts.⁽⁴⁵⁾

Summary and Conclusion

The results of the Age-Related Eye Disease Study have confirmed that antioxidant supplementation is an effective means by which an individual can prevent and/or slow the underlying metabolic activities that lead to advanced and clinically important age-related macular degeneration. The body of evidence also suggests that antioxidant supplementation may prevent early stage development of both cataracts and age-related macular degeneration and, thus has the potential to markedly reduce financial costs to the health care system and improve the quality of life for millions of individuals. Consuming more fruits and vegetables, dark green leafy vegetables, not smoking and implementing lifestyle behaviors to prevent or better manage diabetes should be emphasized as preventive measures. However, the use of antioxidant supplements at levels beyond which an individual can customarily consume from food alone, has emerged as an extremely important practice through which these eye conditions may be prevented and/or treated.

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