A Vitamin Formula for AMD

Oral supplementation with antioxidants and certain vitamins may be important in the prevention of AMD.

BY MITCHELL S. FINEMAN, MD

The first randomized placebo-controlled clinical trial evaluating vitamin supplementation for age-related macular degeneration (AMD) was the Age-Related Eye Disease Study (AREDS), which enrolled patients between 1992 and 1998. The study's results were published in 2001 and suggested that oral supplementation with high-dose antioxidants (vitamins C and E and beta-carotene), as well as zinc, reduced the risk of vision loss in patients with AMD. Specifically, AREDS demonstrated that treatment with zinc in combination with these antioxidants reduced the risk of progression to advanced AMD in susceptible individuals by 25%. In addition, among those most at risk of developing advanced AMD, there was almost a 20% reduction in their risk of vision loss.[1]

AREDS AND SMOKING

Midway through AREDS, patients were notified of the results of two unrelated studies linking beta-carotene supplementation with an increased risk of lung cancer in smokers.[2,3] Obviously, these data had negative implications regarding the smokers randomized to the groups taking antioxidants in AREDS, and affected participants were given the option of removing beta-carotene from the supplement to avoid any potential risk.[1]

When AREDS concluded and its supplements were made commercially available, many questions regarding their use by smokers remained unanswered. For example, how many years does a patient have to be free of tobacco before he or she is considered a nonsmoker? What about exposure to second-hand smoke in the home or workplace? In response, the manufacturers of the supplements modified the AREDS formula by replacing the beta-carotene with lutein and identifying the product as "AREDS based." Because lutein was not studied in the trial, it is not known whether this modified formula is superior or inferior to the original AREDS formula containing beta-carotene.

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LUTEIN AND ZEAXANTHIN

Although not proven to slow the rate of vision loss in AMD, there are significant reasons to believe that oral supplementation with lutein and zeaxanthin (dietary carotenoids that do not have vitamin A activity) may be superior to the use of beta-carotene for the prevention of AMD. Most significantly, lutein and zeaxanthin are the only major dietary carotenoids, including beta-carotene, found in the retina.[4] The concentration of these xanthophylls within the retina varies with the amount in an individual's diet and, therefore, is modifiable with supplementation.[5] Furthermore, an inverse relationship exists between the intake of dietary lutein and zeaxanthin and AMD, according to numerous studies.[6-8]

OILY FISH

A vast body of scientific evidence has demonstrated an inverse relationship between the dietary intake of omega-3, long-chain, polyunsaturated fatty acids, and AMD. The richest sources of omega-3 are oily fish and fish oil supplements. High-quality fish oil supplements provide consistent dosing while minimizing the potential risks associated with the consumption of fish such as mercury, polychlorinated biphenyl, and dioxin contamination. Furthermore, highly refined fish oil supplements provided in the triglyceride form are more bioavailable than less-refined supplements of the ethyl-ester type. Because the triglyceride form more

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closely resembles fish oil in its natural state, it allows for easier and better absorption.[9,10]

AREDS2 was initiated in 2006 to answer the question of whether supplemental dietary xanthophylls (lutein and zeaxanthin) and omega-3, long-chain, polyunsaturated fatty acids, particularly the docosahexaenoic acid and eicosapentaenoic acid subtypes, influence the development of AMD. In addition, this study will secondarily examine the effects of eliminating beta-carotene and reducing the amount of zinc from the original AREDS formulation—important questions for reasons previously mentioned. The study was fully enrolled as of 2008, and patients will be followed through December 2012, after which clinical results are expected.

OTHER VITAMINS AND AMD

In 2009, a randomized study published in the *Archives of Internal Medicine* indicated that supplementation with B-complex vitamins reduces the risk of developing AMD.[11] Researchers analyzed the results of a study primarily examining supplementation with B vitamins and cardiovascular disease in women. A secondary data set collected was the development of AMD by patient self-report. The results indicated that women taking B-complex supplements had a 34% reduction in their risk of developing AMD and a 41% reduction in their risk of visually significant AMD. The main limitation of this study was that the diagnosis of AMD was neither determined nor confirmed by an independent ocular examination. However, the findings certainly indicate that more research is necessary, and they strongly suggest that daily supplementation with B-complex vitamins may reduce individuals' (at least women's) risk of developing AMD.

Epidemiologic evidence suggests that serum levels of vitamin D are inversely associated with early AMD. According to results from the National Health and Nutrition Examination Survey published in 2007, vitamin D intake via supplementation, especially among individuals who do not consume milk, may protect against the development of early AMD.[12] The National Academy of Sciences Institute of Medicine has established guidelines on the minimal intake of vitamin D.[13] Not only do the recommendations suggest a higher daily total dose of 1,000 IU of vitamin D for at-risk groups, including the elderly, but they also suggest that the supplementation be in the of the form of vitamin D3, the natural form of vitamin D, and not vitamin D2.

In conclusion, dry AMD remains a leading cause of vision loss in the elderly. Prevention remains the most current treatment and continues to evolve as scientific studies suggest which supplements are the most safe and efficacious. ■

Mitchell S. Fineman, MD, is a partner with Mid Atlantic Retina and associate professor of ophthalmology, Retina Service of Wills Eye Institute, Thomas Jefferson University, Philadelphia. Dr. Fineman may be reached at (856) 755-1278; mfineman@midatlanticretina.com.

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