

The Role of Diet and Nutritional Supplements in Preventing Cataracts

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Each installment of the "Peer Review" column examines an important issue in ophthalmology through key studies from the peer-reviewed literature selected by Section Editor Mitchell C. Shultz, MD.

OVERVIEW

Cataract is an age-related condition characterized by progressive opacification of the crystalline lens. The exact mechanism underlying this pathological process is unknown, but researchers have hypothesized that oxidative stress impairs the lens' ability to neutralize antioxidants produced by normal ocular metabolic activities.¹ Compared with the young eye, the aging eye contains more free radicals and also has a lower concentration of the proteins that maintain the lens' clarity (ie, α -crystalline and glutathione reductase). The resulting imbalance leads to agglutination and crosslinking of the lens' proteins and the development of cataracts.¹

The oxidative stress model of cataract formation has led many researchers to investigate the link between nutrition and the opacification of the crystalline lens. Fernandez and Afshari¹ presented a general review of physiologic and dietary factors that may contribute to oxidative stress and discussed how antioxidants such as vitamins C and E, lutein, and zeaxanthin could prevent or delay the formation of cataracts. Although many of the observational and in vitro studies described by Fernandez and Afshari appeared to support the benefits of a healthy diet and multivitamins for preventing

cataracts, the researchers warned that "nutritional supplementation is clearly not a quick fix."¹ They cited a lack of interventional studies supporting the use of multivitamins and concluded that supplementary "antioxidants, lutein, and zeaxanthin may only reduce the risks of cataracts for individuals exposed to oxidative stress (smoking or poor nutrition)."¹

As noted by Fernandez and Afshari, studies investigating the link between nutrition and cataract often produce contradictory results. Nevertheless, investigators continue to examine various nutritional and supplementary strategies.

DIET AND CATARACTS

General Nutrition

An analysis of food frequency questionnaires completed by 479 women for the Nutrition and Vision Project showed a lower incidence of nuclear cataracts among participants who adhered most closely to the *Dietary Guidelines for Americans*.^{2,3} The investigators found that the 316 women who did not have cataracts consumed more fruit and whole grains (as measured by the Healthy Eating Index) than the 163 participants who had lenticular opacities. Additional analyses of the participants' Healthy Eating Index scores, however, did not find an association between the intake of vitamin C or the "consumption of [a] large number of USDA-recommended food items, without reference to food group or quantity" and the prevalence of cataracts among the study population.²

Intake of Carbohydrates

Investigators have long suspected that chronic hyperglycemia contributes to the development of cataracts

in diabetic patients. According to Tan et al, "prolonged exposure of the lens proteins to elevated glucose [causes the] accumulation of polyol and glycation, which may then produce oxidation, crosslinking, aggregation, and precipitation of lens proteins."⁴ This relationship was supported by data from the Blue Mountains Eye Study, which showed that patients in the highest quartile for intake of carbohydrates (mean, 280 g/day) and dietary glycemic index (mean, 62.3 ± 2.9) were significantly more likely to develop cortical cataracts than those in the lowest quartile for the same parameters (mean carbohydrate intake, 182 g/day; mean glycemic index, 51.1 ± 2.4). Tan et al did not find a similarly predictive relationship between a high dietary glycemic index and the incidence of nuclear or posterior subcapsular cataracts in the same population.⁴

A cross-sectional analysis of data from the Age-Related Eye Disease Study (AREDS) also showed a positive relationship between the intake of carbohydrates and risk of cataracts. The results of this study differ from those reported by Tan et al,⁴ however, because the incidence of cortical opacities in the AREDS was linked to total carbohydrate intake versus dietary glycemic index. Higher dietary glycemic indices were associated with the occurrence of nuclear cataracts in the AREDS.⁵

DIETARY SUPPLEMENTS

Multivitamins

The reported efficacy of multivitamins and their individual components for preventing age-related cataracts varies widely in the published literature. For example, Seddon's analysis of the AREDS found that supplements containing vitamins C and E, β-carotene, and zinc with cupric oxide were more likely to slow the progression of age-related macular degeneration than to prevent the formation of cataracts.⁶

In contrast, investigators from the Clinical Trial of Nutritional Supplements and Age-Related Cataract (CTNS) found that, compared with placebo, one tablet of the multivitamin Centrum (Wyeth Consumer Healthcare, Richmond, VA) taken every day reduced the incidence of nuclear cataracts (hazard ratio [HR], 0.66; confidence interval [CI], 0.50 to 0.88; $P=0.004$) and, to a lesser extent, cortical cataracts (HR, 0.78; CI, 0.60 to 1.02; $P=0.07$).⁷ Centrum's label states that the supplement contains the recommended daily allowance of vitamins C and E, β-carotene, and other minerals with antioxidative characteristics.

Although fewer patients in the CTNS who were randomized to treatment with Centrum (227 of 510 or 44.5%) developed nuclear or cortical cataracts compared with patients in the placebo group (255 of 510 or 50.0%),

the multivitamin was associated with a significantly higher risk of posterior subcapsular cataracts in the treatment versus placebo group (HR, 2.00; CI, 1.35 to 2.98; $P<0.001$). Because the multivitamin had a quantitatively different effect on nuclear and posterior subcapsular cataracts and the CTNS did not provide sufficient information about the supplement's effect on visual acuity and patients' need for cataract surgery, however, the investigators declined to make "recommendations about the use of the once-daily multivitamin for preventing cataracts."⁷

In a recent editorial, Chong and Wong agreed with the investigators from the CTNS that the currently available literature does not support "definitive recommendations on the use of a multivitamin supplement in preventing age-related cataract."⁸ Chong and Wong noted that randomized clinical studies (including the CTNS) fail to answer important questions such as the following:

- (1) What is the optimum dosage of antioxidants needed to prevent cataracts?
- (2) Which vitamins or minerals provide the best protection against oxidative stress?
- (3) When should people start taking multivitamins to protect themselves from cataracts?
- (4) How effectively do multivitamins prevent the progression of preexisting cataracts?

Christen et al⁹ partially answered the second question posed by Chong and Wong by showing that vitamin E did not prevent the development of cataracts in middle-aged and older women who participated in the Women's Health Study. After 9.7 years of follow-up, the investigator observed a similar number of cataracts among women randomized to use 600 IU of vitamin E or a placebo every other day (1,159 vs 1,217, respectively; relative risk [RR], 0.96; CI, 0.88 to 1.04).

Carotenoids

Several studies suggest that an increased dietary intake of the carotenoids lutein and zeaxanthin significantly reduces the risk of age-related cataracts. A multivariate analysis of nutritional data from the Women's Health Study by Christen et al also showed that participants who ingested approximately 6,716 μg of lutein/zeaxanthin per day had an 18% lower risk of developing cataracts than subjects with a median intake of 1,177 μg (RR, 0.82; CI, 0.71 to 0.95; $P=0.04$).¹⁰ Of all the nutrients evaluated by the study, only β-carotene also showed a possible inverse relationship with cataract (RR, 0.87; CI, 0.75 to 1.00; $P=0.11$). Nonetheless, "the test for trend across quintiles was not significant in the multivariate model or after adjustment for intake of other nutrients."¹⁰

Moeller et al found that women (n = 883) with high dietary levels of lutein and zeaxanthin (mean intake,

2,889 mg/day; age-adjusted odds ratio, 0.77; CI, 0.62 to 0.96) were 23% less likely to have nuclear cataracts than those with a low intake of dietary lutein/zeaxanthin (n = 919; mean intake, 791 mg/day).¹¹ The investigators also observed that “women in the highest quintile category of diet or serum levels of lutein and zeaxanthin were 32% less likely to have nuclear cataract than those in the lowest quintile category (multivariate-adjusted odds ratio, 0.68 [$P=.04$] vs 0.68 [$P=.01$], respectively).¹¹

Vu et al also observed an inverse association between a high dietary intake of lutein/zeaxanthin and the prevalence of nuclear cataract in the Melbourne Visual Impairment Project. An analysis of approximately 2,322 completed food frequency questionnaires showed that the multivariate odds ratios for nuclear cataract were “0.67 (CI, 0.46 to 0.96) and 0.60 (CI, 0.40 to 0.90) for every 1-mg increase in crude and energy-adjusted daily intake of [lutein/zeaxanthin], respectively.”¹² The investigators did not observe a similar relationship between high dietary levels of lutein/zeaxanthin and the incidence of cortical or posterior subcapsular cataracts.

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TOPICAL TREATMENT OPTION

Several years ago, researchers in Russia developed an eye drop that reportedly increased the levels of a specific anti-oxidative dipeptide in the aqueous and thus reversed lenticular opacity caused by nuclear cataracts. In a randomized, placebo-controlled study, 90% of eyes (n = 41) treated with topical N-acetylcarnosine (Can-C; Innovative Vision Products, New Castle, DE) b.i.d. for 6 months showed improvement in BCVA from baseline. The same patients demonstrated an 88.9% improvement in sensitivity to glare during the same time period. In comparison, the visual acuity and severity of glare increased among the eyes in the control group (21 received a placebo, and 14 did not use any drops) during the 6-month trial.¹³

Although these data are promising, they are limited by a lack of independent investigation. To date, only one researcher has evaluated the cataract-reducing effects of N-acetylcarnosine. In addition to inventing Can-C, Mark A. Babizhayev, MA, PhD, founded the company that manufactures and sells the over-the-counter eye drop. ■

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