Can high-dose supplementation with vitamins C and E, beta carotene, and zinc slow the progression of macular degeneration?


- **BACKGROUND** Age-related macular degeneration (ARMD) is the leading cause of blindness in the United States among people aged 65 years or older. Observational and experimental data suggest that antioxidant or zinc supplements may delay progression of ARMD and visual loss.
- **POPULATION STUDIED** Eleven retinal specialty clinics enrolled participants aged 55 to 80 years in 4 ARMD categories determined by the size and extent of drusen and retinal pigment epithelial abnormalities in each eye, the presence of advanced ARMD (each determined by evaluation of color photographs at a reading center), and visual acuity. Persons in category 1 had no ARMD; those in category 2 had mild or borderline ARMD; those in category 3 had moderate ARMD; and those in category 4 had advanced ARMD. At least 1 eye had a best corrected visual acuity of 20/32 or better (the study eye). Among participants, 56% were women, 96% were white, and the median age was 69 years. Potential participants were excluded for illness or disorders (history of cancer with a poor 7-year prognosis, major cardiovascular or cerebrovascular event within the previous year, or hemochromatosis) that would have made long-term follow-up or compliance with the study protocol unlikely or difficult.
- **STUDY DESIGN AND VALIDITY** This was a randomized, double-masked, placebo-controlled trial (concealed allocation assignment). Participants were assigned to 1 of 4 treatment groups: (1) antioxidants (500 mg vitamin C, 400 IU vitamin E, 15 mg beta carotene); (2) 80 mg zinc as zinc oxide and copper, 2 mg as cupric oxide; (3) antioxidants plus zinc; or (4) placebo. The groups did not differ in their baseline characteristics. Average follow-up was 6.3 years, with 2.4% lost to follow-up. Analysis was by intention to treat. The judicial assessors of outcomes were masked to treatment group assignment.
- **OUTCOMES MEASURED** Two primary outcomes were defined for study eyes in the ARMD trial: (1) progression to advanced ARMD and (2) at least a 15-letter decrease in visual acuity score.
- **RESULTS** Patients with no ARMD (category 1) and mild or borderline ARMD (category 2) did not benefit from antioxidant and/or zinc supplementation. However, participants in the moderate and advanced ARMD groups (categories 3 and 4) had a lower risk of progression to advanced ARMD and visual acuity loss in the good eye if they took both zinc and antioxidants compared with placebo for 7 years (35.7% vs 26.7%, respectively; P < .001; number needed to treat = 11).

**RECOMMENDATIONS FOR CLINICAL PRACTICE**

Patients with moderate to advanced ARMD should consider taking an antioxidant/zinc supplement. Treatment of 11 such patients with high-dose supplementation of vitamin C, vitamin E, beta carotene, and zinc for 7 years will prevent progression of ARMD in one of them. Although some may argue that the results of this study justify routine screening for this condition, we need further evidence on both the number needed to screen for a benefit and the overall cost-to-benefit ratio of the intervention. In addition, we should remember that beta carotene has been linked to an increased risk of lung cancer in smokers.

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