

Randomized, double-blind, placebo-controlled study of zeaxanthin and visual function in patients with atrophic age-related macular degeneration:

The Zeaxanthin and Visual Function Study (ZVF) FDA IND #78, 973

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Abstract

Background

The purpose of this study is to evaluate whether dietary supplementation with the carotenoid zeaxanthin (Zx) raises macula pigment optical density (MPOD) and has unique visual benefits for patients with early atrophic macular degeneration having visual symptoms but lower-risk National Institute of Health/National Eye Institute/Age-Related Eye Disease Study characteristics.

Methods

This was a 1-year, $n = 60$ (57 men, 3 women), 4-visit, intention-to-treat, prospective, randomized controlled clinical trial of patients (74.9 years, standard deviation [SD] 10) with mild-to-moderate age-related macular degeneration (AMD) randomly assigned to 1 of 2 dietary supplement carotenoid pigment intervention groups: 8 mg Zx ($n = 25$) and 8 mg Zx plus 9 mg lutein (L) ($n = 25$) or 9 mg L ("Faux Placebo," control group, $n = 10$). Analysis was by Bartlett's test for equal variance, 3-way repeated factors analysis of variance, independent t test ($P < 0.05$) for variance and between/within group differences, and post-hoc Scheffé's tests. Estimated foveal heterochromic flicker photometry, 1° macular pigment optical density (MPOD QuantifEye[®]), low- and high-contrast visual acuity, foveal shape discrimination (Retina Foundation of the Southwest), 10° yellow kinetic visual fields (KVF), glare recovery, contrast sensitivity function (CSF), and 6° blue cone ChromaTest[®] color thresholds were obtained serially at 4, 8, and 12 months.

Results

Ninety percent of subjects completed ≥ 2 visits with an initial Age-Related Eye Disease Study report #18 retinopathy score of 1.4 (1.0 SD)/4.0 and pill intake compliance of 96% with no adverse effects. There were no intergroup differences in 3 major AMD risk factors: age, smoking, and body mass index as well as disease duration and Visual Function Questionnaire 25 composite score differences. Randomization resulted in equal MPOD variance and MPOD increasing in each of the 3 groups from 0.33 density units (du) (0.17 SD) baseline to 0.51 du (0.18 SD) at 12 m, ($P = 0.03$), but no between-group differences (Analysis of Variance; $P = 0.47$). In the Zx group, detailed high-contrast visual acuity improved by 1.5 lines, Retina Foundation of the Southwest shape discrimination sharpened from 0.97 to 0.57 ($P = 0.06$, 1-tail), and a larger percentage of Zx patients experienced clearing of their KVF central scotomas ($P = 0.057$). The "Faux Placebo" L group was superior in terms of low-contrast visual acuity, CSF, and glare recovery, whereas Zx showed a trend toward significance.

Conclusion

In older male patients with AMD, Zx-induced foveal MPOD elevation mirrored that of L and provided complementary distinct visual benefits by improving foveal cone-based visual parameters, whereas L enhanced those parameters associated with gross detailed rod-based vision, with considerable overlap between the 2 carotenoids. The equally dosed (atypical dietary ratio) Zx plus L group fared worse in terms of raising MPOD, presumably because of duodenal, hepatic-lipoprotein or retinal carotenoid competition. These results make biological sense based on retinal distribution and Zx foveal predominance.

Keywords: [Zeaxanthin](#), [Lutein](#), [Carotenoids](#), [Macular pigment](#), [Atrophic age-related macular degeneration](#)