A Randomized, Double-Masked, Placebo-Controlled Trial of the Efficacy of a Novel Neuroprotective Combination for Reversing Mitochondrial Dysfunction in Glaucoma

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PURPOSE
To determine whether a combination of over-the-counter supplements with anti-oxidant and mitoprotective properties could reverse mitochondrial dysfunction in treated glaucoma patients by reducing mitochondrial flavoprotein fluorescence compared to placebo.

METHODS
Retinal Metabolic Analysis (RMA) (OcuMet Beacon, OcuSciences, Inc. Ann Arbor, MI) measures adjusted mitochondrial flavoprotein fluorescence (aFPF) and its average curve width (ACW), which are markers of mitochondrial oxidative stress. Fourteen patients (28 eyes) were randomized into two groups: 1) placebo and 2) a combination of curcumin, Ginkgo biloba extract, citicoline, coenzyme-Q10 (ubiquinol, Cognizin™), N-acetyl-cysteine, alpha-lipoic acid, grape seed extract, and green tea extract (GlaucoHealth™). The study was performed under an IND from the FDA. Patients were tested with visual fields (VF), optical coherence tomography (OCT), and RMA at baseline, 1 month, and 3 months after randomization. Hierarchical mixed effects linear models were tested for changes in VF, OCT, and RMA indices over time.

RESULTS
Table 1 shows the clinical characteristics of the treatment and placebo groups. None of the variables differed significantly between groups (all P > 5%).

During follow-up, there were no significant changes in VF (MD, PSD) or OCT (macular RGC) indices over time in either group (all P > 5%).

There was a significant decrease in optic nerve aFPF and ACW from baseline to 1 month in patients treated with GlaucoHealth™ (β = -39, P = 0.003; β = -25, P = 0.01; respectively) but not in patients treated with placebo (P = 0.47 and 0.25) (Tables 2 and 3).

Mitochondrial dysfunction and death are increasingly implicated in retinal ganglion cell death in glaucoma and neuronal death in other neurodegenerative disorders. Mitochondria become dysfunctional and die prior to neuronal cell death. Formulations with IOP-independent neuroprotective effects could be additive in slowing progression rates by reversing mitochondrial dysfunction. Stabilizing mitochondria could shift the treatment paradigm to an earlier stage of disease, prior to retinal ganglion cell death. In this study, a combination of mitochondrial protectants and anti-oxidants reversed mitochondrial metabolic dysfunction as measured with RMA. This finding serves as a proof-of-concept for future trials testing the neuroprotective effect of supplement combinations in glaucoma.

CONCLUSIONS
GlaucoHealth™ reverses mitochondrial dysfunction and may be neuroprotective in glaucoma. This finding serves as a proof-of-concept for future trials testing the neuroprotective effect of supplement combinations in glaucoma.

REFERENCES

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