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Improvement in inner retinal function in glaucoma in response to nicotinamide (Vitamin B₃) supplementation: a crossover randomized clinical trial

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Abstract

Purpose : During glaucoma retinal ganglion cells sit under metabolic stress exacerbated by age and elevated IOP. Nicotinamide (NAM; an NAD⁺ precursor), is low in serum of patients with primary open-angle glaucoma and dietary NAM supplementation provides robust protection of retinal ganglion cells in preclinical glaucoma models. This crossover, double-masked, randomized pilot study aimed to determine whether NAM supplementation taken in conjunction with conventional IOP-lowering therapy led to improvement in retinal ganglion cell function in glaucoma patients.

Methods : Participants were randomized to first receive oral placebo or NAM and reviewed 6-weekly. An accelerated dosing method was utilized; participants commenced a 6-week course of 1.5 grams/day followed by 6 weeks of 3 grams/day. After 12 weeks, participants crossed over to other intervention for 12 weeks without washout. At each visit, visual function was measured using full-field flash electroretinography and white-on-white perimetry. Primary endpoint was change in inner retinal function determined a-priori as change in photopic negative response (PhNR) parameters: saturated PhNR amplitude (V_{max}), ratio of PhNR/b-wave amplitude (V_{max} ratio). Secondary endpoints were change in perimetry or optical coherence tomography.

Results : Fifty-seven participants (65.5±10.0 years, mean±SD) enrolled. Participants

demonstrated excellent treatment adherence rates (>94%) and nicotinamide was well tolerated with minimal side effects. PhNR Vmax improved beyond 95% coefficient of repeatability (COR) in 23% of participants following 12 weeks of NAM and 9% on placebo. Conversely, PhNR Vmax deteriorated in 9% on placebo and 7% on NAM. Overall, Vmax improved by 14.8% [95% CI: 2.8-26.9%], (p=0.02) on NAM and 5.2% [-4.2-14.6%], (p=0.27) on placebo. Vmax ratio improved on average by 12.6% [5.0-20.2%], (p=0.002) following NAM and 3.6% [-3.4%-10.5%], (p=0.30) on placebo. A concomitant trend for improved visual field mean deviation was observed with 27% improving ≥ 1 dB on NAM and fewer deteriorating ≥ 1 dB (4%) compared to placebo (p=0.02).

Conclusions : NAM supplementation improved inner retinal function in patients receiving concurrent IOP-lowering glaucoma therapy. Further studies are underway to elucidate the effects of long-term NAM supplementation on glaucoma progression.

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