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ARVO Annual Meeting Abstract | July 2018

Oral pyruvate supplementation protects against neurodegeneration in a rat model of glaucoma.

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Investigative Ophthalmology & Visual Science July 2018, Vol.59, 2618. doi:

Abstract

Purpose : Emerging evidence strongly associates retinal ganglion cell (RGC) energetic dysfunction with optic nerve degeneration in glaucoma. Pyruvate has been proposed to act as a neuroprotectant predominantly by functioning as both a metabolic substrate and potent antioxidant. Herein we test the hypothesis that oral pyruvate supplementation protects against RGC death in an experimental rat model of induced glaucoma.

Methods : Rats were randomly assigned into control (vehicle; n=18) and pyruvate treatment (administered in drinking water, dosed at 500mg/kg/day; n=19) groups. Experimental glaucoma was induced in the right eye of each animal by laser photocoagulation of the trabecular meshwork and episcleral veins at day 0. Intraocular pressure (IOP) was monitored throughout the experiment and all rats were killed on day 14. Retina and optic nerves were processed for quantification of the number of surviving RGCs and axonal injury, respectively.

Results : There was a clear pressure elevation in the right eye of all animals with no statistically significant difference in peak IOP (p=0.60), IOP exposure (p=0.54), or average IOP (p=0.74) between glaucomatous groups (pyruvate vs. vehicle). Immunohistochemical labelling of retinal wholemounts with the RGC marker Brn3a demonstrated a significant reduction (p=0.03) in the quantity of RGC loss in the pyruvate supplemented relative to the vehicle-treated glaucomatous eyes (Figure 1).

Quantitative analyses of data from distal optic nerve sections immunolabelled for

markers of axonal cytoskeletal damage (SMI32) and microglial activation (ED1) also indicated white matter protection by pyruvate, which was significant when comparing pyruvate and vehicle glaucomatous groups (p=0.03 and p=0.04 respectively).

Conclusions : Oral pyruvate supplementation reduces RGC loss and consequent optic nerve damage in our rat model of experimental glaucoma. The protecting effect of pyruvate is likely manifest via its ability to act both as a supplemental metabolic substrate and as an antioxidant. These results unveil a potential new therapy for glaucoma with the promise of translation into clinical trials.

This is an abstract that was submitted for the 2018 ARVO Annual Meeting, held in Honolulu, Hawaii, April 29 - May 3, 2018.

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