Abstract Title: Phenytoin is Neuroprotective in Acute Optic Neuritis: Results of a Phase 2 Randomized Controlled Trial

Press Release Title: Epilepsy Drug May Preserve Eyesight for People with MS

Objective: Partial blockade of voltage-gated sodium channels is neuroprotective in experimental models of inflammatory demyelination. In this phase 2 clinical trial we assessed whether sodium channel blockade with phenytoin is also neuroprotective in acute optic neuritis (AON).

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Background: AON is a common and often presenting feature of multiple sclerosis (MS), and attacks can lead to persistent visual impairment through neuroaxonal damage in the retina and optic nerve. As with other relapses of MS, corticosteroids hasten recovery, but do not improve its final extent. Hence, there is an unmet need for neuroprotective therapy to prevent residual disability from relapses.

Design/Methods: 86 people with AON were randomized within two weeks of symptom onset to receive either phenytoin (4 mg/kg/day) or placebo for three months. Retinal nerve fiber layer (RNFL) thickness and macular volume (MV) were measured at baseline, and then six months later, using optical coherence tomography. Visual function (logMAR, low contrast acuity, colour perception), optic nerve imaging, and visual evoked potentials were also measured. The primary outcome was RNFL thickness in the affected eye at six months, adjusted for fellow eye RNFL thickness at baseline.

Results: Five participants were lost to follow up. In the remaining 81, intention to treat comparison showed that average adjusted affected eye RNFL thickness at six months was 7.15 um higher in the active group (n=39) vs placebo (n=42, p=0.02), a 30% protective treatment effect. Adjusted MV was 0.20 mm^3 higher in the active group (p=0.005), a 34% protective treatment effect. Similar, significant treatment effects were also found in the per protocol comparisons. Vision generally recovered well, with no significant difference in visual outcomes between the treatment groups.

Conclusions: Treatment with phenytoin protects the RNFL and macula from neurodegeneration in AON, raising the possibility that blockade of voltage-gated sodium channels may be neuroprotective in relapses of MS in general.
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