A Randomized, Controlled Trial of Corticosteroids in the Treatment of Acute Optic Neuritis

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The Optic Neuritis Treatment Trial had a significant impact on the practices of ophthalmology and neurology and has been cited in more than 50 publications since 1992. Before its publication, the best treatment approach for optic neuritis remained unclear, with most neurologists and ophthalmologists prescribing oral steroids. The objective of this trial is to evaluate, therefore, was to evaluate, if treatment with either oral prednisone or IV methylprednisolone improved visual outcomes in acute optic neuritis compared to placebo.

This is a multicenter randomized control trial. Patient eligibility included 1) age of 18-46 years, 2) a history consistent with acute unilateral optic neuritis with visual symptoms lasting 8 days or less, and 3) exam findings consistent with optic neuritis (relative afferent pupillary defect and visual field defect in the affected eye). Patients were *excluded* if they had previous optic neuritis in the same eye or if they have a systemic disease (excluding multiple sclerosis) that could cause optic neuritis. They randomized patients to 3 treatment groups: (**1**) IV methylprednisolone 250mg q6h x 3 days followed by oral prednisone 1mg/kg daily x 11 days; (**2**) oral prednisone 1mg/kg daily for 14 days; or (**3**) oral placebo on the same schedule as the 2nd group. All groups were followed by a short period during which the oral dose was slowly tapered. The groups receiving prednisone (group 2) and placebo (group 3) were blinded, but blinding was unavailable in the IVMP group (group 1). They followed these groups for 2 years after the trial, and examiners on follow-up were blinded to each patient's group allocation. Primary measures of outcome were visual field and contrast sensitivity. Secondary measures were visual acuity and color vision.

In total, the study included 457 patients randomized to IV methylprednisolone group (N=151), oral prednisone only group (N=156), and placebo (N=150). The overall rate of missed visits during follow-up in the first 6 months was 3.4%. In terms of the primary outcome, they found that when comparing IV methylprednisolone vs placebo, the rate of visual recovery was greater in the IV methylprednisolone group than in the placebo group. When comparing oral prednisone vs placebo groups, there was no significant difference in rate of recovery (see **Figure 1** for an illustration of this). However, visual outcome at the end of the 6 month follow-up period was only slightly better in the IV methylprednisolone group than in the placebo group. The oral prednisone only group showed no difference in either the rate of recovery or 6 month outcome as compared to placebo. In fact, it seemed as though the oral prednisone only group had a significantly HIGHER rate of new attacks of optic neuritis than the other groups over time. Finally, and most notably, when analyzing each group's risk of the development of multiple sclerosis within 2 years after their episode of acute optic neuritis, fewer patients in the IV methylprednisolone group had a later, new diagnosis of MS compared to both of the other two groups (14% in the IV methylprednisolone group compared to 24% in oral prednisone and 20% in placebo groups).

In conclusion, this was a highly significant trial in the field of Neuro-ophthalmology, that changed our treatment protocol for acute, isolated optic neuritis. Ultimately, patients with acute optic neuritis should be treated with IV steroids to accelerate visual recovery, though it should be noted that the final outcome of visual function at 6 months may not be dramatically better than in an untreated patient. Further, there is no benefit to oral prednisone for acute isolated optic neuritis, and it can actually worsen rates of recurrent optic neuritis in the future.

Summary by Amy Li Safadi, MD