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

NEJM 1992 February 27; 326 (9): 582 - 588

The Optic Neuritis Treatment Trial had a significant impact on the practices of both 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 using oral steroids. As such, the goal of this study was to evaluate the efficacy of oral prednisone vs. IV methylprednisolone (and both vs. placebo) in terms of improvement in visual outcomes after acute optic neuritis.

Experimental design and statistics: This was 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 had a systemic disease (including multiple sclerosis) that could cause optic neuritis. Eligible patients were then randomized to 3 treatment groups: (Grp 1) IV methylprednisolone 250mg q6h x 3 days followed by oral prednisone 1mg/kg daily x 11 days, (Grp 2) oral prednisone 1mg/kg daily for 14 days, or (Grp 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 oral prednisone (Grp 2 and placebo Grp 3) were blinded, but blinding was unavailable in the IVMP group (Grp 1). They followed these groups for 2 years after the trial, and examiners on follow-up were blinded to each patient's initial treatment allocation. The primary efficacy outcomes included visual fields and contrast sensitivity. Secondary efficacy outcomes included visual acuity and color vision.

Results: In total, the study included 457 patients randomized to the IV methylprednisolone group (N=151), the oral prednisone only group (N=156), and the placebo group (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, when comparing IV methylprednisolone to placebo, *the rate of visual recovery was greater* in the IV methylprednisolone group than in the placebo group. When comparing oral prednisone to placebo, there was no significant difference in the rate of visual recovery (**Fig 1**). Notably, visual outcome at the end of the 6-month follow-up period was only slightly better in the IV methylprednisolone group vs. the placebo group. The oral prednisone group showed no difference in 6-month visual outcome as compared to placebo. In fact, it seemed as though the oral prednisone group had a significantly HIGHER rate of new attacks of optic neuritis than the other treatment groups over time. Finally, and most notably, when analyzing each group's risk of development of multiple sclerosis within 2 years after their episode of acute optic neuritis, fewer patients in the IV methylprednisolone group had a new diagnosis of MS compared to both of the other treatment groups (14% in the IV methylprednisolone group, 24% in the oral prednisone group, 20% in the placebo group).

Conclusions: Overall, 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 are now 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 that of an untreated patient. Further, there is no benefit to oral prednisone for acute isolated optic neuritis, as it may worsen rates of recurrent optic neuritis in the future.

Summary created by Amy Li Safadi, MD