



Published in final edited form as:

Arch Ophthalmol. 2008 July ; 126(7): 994–995. doi:10.1001/archophth.126.7.994.

Treatment of Acute Optic Neuritis:

A Summary of Findings From the Optic Neuritis Treatment Trial

Roy W. Beck, MD, PhD,

Robin L. Gal, MSPH

Jaeb Center for Health Research, Tampa, Florida.

Corticosteroids have been used as treatment for optic neuritis since these drugs were introduced into clinical practice in the 1950s. Numerous anecdotal reports and clinical experience suggested that they were effective but early randomized trials did not demonstrate a benefit, although they were all inconclusive because of small sample size. In the 1980s, the Optic Neuritis Treatment Trial was developed to evaluate corticosteroid treatment for optic neuritis. This multicenter randomized clinical trial, supported by the National Eye Institute, was designed to answer the following questions: (1) Does treatment with either oral prednisone or intravenous methylprednisolone followed by oral prednisone improve the visual outcome of acute optic neuritis? (2) Does either treatment speed recovery of vision? and (3) Are the complications of treatment insignificant in relation to the magnitude of the treatment effect? Long-term follow-up of the cohort was performed to investigate the relationship between optic neuritis and the development of multiple sclerosis (MS).

STUDY DESIGN

The study design has been previously described in detail.^{1–3} Patients were entered into the study subject to the following criteria: presence of acute unilateral optic neuritis with visual symptoms lasting 8 days or less, aged between 18 and 45 years, no previous history of optic neuritis in the affected eye, no evidence of a systemic disease other than MS that might be associated with the optic neuritis, and no previous treatment with corticosteroids for MS or optic neuritis. Fifteen clinical centers throughout the United States participated in the Optic Neuritis Treatment Trial, recruiting 457 patients between July 1, 1988, and June 30, 1991. The mean age of the patients at study entry was 32 years; 77% were female and 85% were white.

Each patient was randomly assigned to 1 of 3 treatment regimens: (1) oral prednisone (Deltasone; Upjohn Co, Kalamazoo, Michigan) (1 mg/kg/d for 14 days; referred to as the prednisone group); (2) intravenous methylprednisolone (Solu-Medrol; Upjohn Co) (250 mg every 6 hours for 3 days) followed by oral prednisone (1 mg/kg/d for 11 days) (referred to as the intravenous group); or (3) oral placebo (for 14 days; referred to as the placebo group). Each regimen was followed by a short oral dosage taper consisting of 20 mg of prednisone

(or placebo) on day 15 and 10 mg of prednisone (or placebo) on days 16 and 18. Through randomization, 150 patients were assigned to the placebo group, 151 to the intravenous group, and 156 to the prednisone group. Most patients (97%) completed the full treatment course, and adverse effects from the treatments were generally mild.¹ Two patients in the intravenous group had serious adverse effects (one patient had an acute transient depression that required psychotropic drugs and the other had acute pancreatitis) that resolved without sequelae. Minor adverse effects were more common in both steroid groups than in the placebo group and included reports of sleep disturbance, mild mood change, stomach upset, facial flushing, and mild weight gain.⁴

Patients were evaluated at 7 follow-up visits during the first 6 months, at 1 year, then yearly through 1997, in 2001 through 2002, and finally in 2006. The primary outcome for the treatment group comparison was at 6 months. At baseline and during follow-up, measurements of best-corrected visual acuity were made with the charts developed for the Early Treatment Diabetic Retinopathy Study, contrast sensitivity was measured with the Pelli-Robson chart, visual field was measured with the Humphrey Field Analyzer program 30-2 (Carl Zeiss Meditech Inc, Dublin, California), and color vision was measured with the Farnsworth-Munsell 100-hue test. Neurologic examinations were performed at baseline, 6 months, and all subsequent visits. A vision-specific quality-of-life questionnaire was completed at the 6-month visit.⁵

RESULTS

The study found that most patients experienced rapid visual recovery within 2 weeks after onset of symptoms in all of the 3 treatment groups. In many patients, complete recovery often occurred by 4 to 6 weeks, although improvement for up to 1 year was observed. Severity of visual loss at the initial visit was the only predictor of the 6-month visual outcome⁶; however, even with severe visual loss, visual recovery was generally good.⁷

Vision recovered faster in the intravenous group than in the placebo group ($P < .001$ for visual field, $P = .02$ for contrast sensitivity, and $P = .09$ for visual acuity), with the greatest difference between the 2 groups occurring on days 4 and 15. The difference between these 2 groups decreased after 15 days, although at 6 months, contrast sensitivity ($P = .03$), visual field ($P = .05$), and color vision ($P = .03$) were still slightly better in the intravenous group, whereas visual acuity ($P = .66$) was not. When the prednisone group was compared with the placebo group, there were no significant differences in the rate of recovery or the 6-month outcome for any of the visual function measures. The visual function questionnaire results suggested that patients in the intravenous group perceived their vision to be better than the patients in the other groups did.

Recurrences of optic neuritis occurred more commonly in the prednisone group than in either of the other 2 groups. Within the first 5 years of follow-up, the probability of a recurrence in either eye was almost 2-fold higher in the prednisone group than in either the placebo group ($P = .004$) or the intravenous group ($P = .003$).⁸

Among 389 patients who were not diagnosed as having probable or definite MS at baseline, definite MS developed within 2 years at a lower rate in the intravenous group (8%) compared with the placebo group (17%) ($P=.03$) but was not significantly different between the prednisone group (15%) and the placebo group ($P=.54$). Most of the apparent intravenous treatment group benefit on development of MS was observed in patients with abnormal brain magnetic resonance imaging results at baseline because the rate of MS among patients without baseline magnetic resonance image lesions was so low that therapeutic efficacy could not be determined. The beneficial effect of intravenous methylprednisolone treatment on the development of MS lessened after 2 years.⁹ By 5 years, the treatment had no significant effect on the development of MS.¹⁰

CONCLUSIONS

The Optic Neuritis Treatment Trial showed that high-dose intravenous methylprednisolone followed by oral prednisone accelerated visual recovery but did not improve the 6-month or 1-year visual outcome compared with placebo, whereas treatment with oral prednisone alone did not improve the outcome and was associated with an increased rate of recurrences of optic neuritis. An unexpected finding was that those who received intravenous corticosteroids followed by oral corticosteroids had a temporarily reduced risk of development of a second demyelinating event consistent with MS compared with subjects who received oral placebo or treatment with oral corticosteroids only.

The study investigators concluded that for patients with acute optic neuritis and a clinical profile similar to that of the patients who were enrolled in the trial, (1) both no treatment and treatment with intravenous methylprednisolone followed by oral prednisone are viable options and (2) there is not a role for oral prednisone alone in standard doses.

Funding/Support:

This work was supported by cooperative agreement U10 EY09435 from the National Eye Institute, National Institutes of Health.

REFERENCES

1. Beck RW, Cleary PA, Anderson MM Jr, et al. ; Optic Neuritis Study Group. A randomized, controlled trial of corticosteroids in the treatment of acute optic neuritis. *N Engl J Med*. 1992;326(9):581–588. [PubMed: 1734247]
2. Cleary PA, Beck RW, Anderson MM Jr, Kenny DJ, Backlund JY, Gilbert PR. Design, methods, and conduct of the Optic Neuritis Treatment Trial. *Control Clin Trials*. 1993;14(2):123–142. [PubMed: 8500302]
3. Optic Neuritis Study Group. The clinical profile of acute optic neuritis: experience of the Optic Neuritis Treatment Trial. *Arch Ophthalmol*. 1991;109(12): 1673–1678. [PubMed: 1841573]
4. Chrousos GA, Kattah JC, Beck RW, Cleary PA; Optic Neuritis Study Group. Side effects of glucocorticoid treatment: experience of the Optic Neuritis Treatment Trial. *JAMA*. 1993;269(16):2110–2112. [PubMed: 8468765]
5. Cleary PA, Beck RW, Bourque LB, Backlund JC, Miskala PH. Visual symptoms after optic neuritis: results from the Optic Neuritis Treatment Trial. *J Neuroophthalmol*. 1997;17(1):18–28. [PubMed: 9093956]

6. Beck RW, Cleary PA, Backlund JC; Optic Neuritis Study Group. The course of visual recovery after optic neuritis: experience of the Optic Neuritis Treatment Trial. *Ophthalmology*. 1994;101(11):1771–1778. [PubMed: 7800355]
7. Beck RW, Cleary PA; Optic Neuritis Study Group. Recovery from severe visual loss in optic neuritis. *Arch Ophthalmol*. 1993;111(3):300.
8. Optic Neuritis Study Group. Visual function 5 years after optic neuritis: experience of the Optic Neuritis Treatment Trial. *Arch Ophthalmol*. 1997;115(12): 1545–1552. [PubMed: 9400788]
9. Beck RW, Cleary PA, Trobe JD, et al. ; Optic Neuritis Study Group. The effect of corticosteroids for acute optic neuritis on the subsequent development of multiple sclerosis. *N Engl J Med*. 1993;329(24):1764–1769. [PubMed: 8232485]
10. Optic Neuritis Study Group. The 5-year risk of MS after optic neuritis: experience of the Optic Neuritis Treatment Trial. *Neurology*. 1997;49(5):1404–1413. [PubMed: 9371930]