

## Clarifying the Treatment of Nonarteritic Anterior Ischemic Optic Neuropathy

Anterior ischemic optic neuropathy (AION), or optic nerve-head infarction, is the most common optic nerve disorder of the elderly except for glaucoma. There are two types of AION. The less common arteritic AION is associated with giant cell arteritis and was described more than 3000 years ago.<sup>1</sup> The pathophysiology of arteritic AION is well understood and consists of occlusion of the small posterior ciliary arteries supplying the anterior optic nerve. The diagnosis is suggested by the characteristic clinical findings of temporal ache or tenderness, polymyalgia rheumatica, and jaw claudication, as well as laboratory evidence of an elevated erythrocyte sedimentation rate. The diagnosis is proven by finding granulomatous inflammation with giant cells on biopsy of the temporal artery. Immediate high-dose corticosteroid therapy is mandatory, is usually effective prophylaxis for involvement of the other optic nerve, and may even reverse visual loss in occasional cases.

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See also p 625.

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In contrast, the far more common nonarteritic AION (NAION) was first fully delineated only 20 years ago.<sup>2</sup> The mechanism by which the anterior optic nerve becomes acutely edematous in NAION is unknown. The diagnosis is made on clinical grounds alone and typically involves acute onset of painless visual loss associated with unilateral disc edema occurring in an elderly patient. There are no pathognomonic laboratory or pathological findings. The prognosis for improvement has long been thought to be poor. And until 1989, no effective treatment had been described. In that year, Sergott and colleagues<sup>3</sup> reported that incising the optic nerve sheath in patients with NAION that progressed during 1 to 4 weeks usually resulted in an improvement in visual function.

Soon thereafter, other groups reported beneficial effects of this procedure in patients with progressive<sup>4,5</sup> as well as nonprogressive NAION.<sup>6</sup> With no other therapeutic options available, optic nerve decompression rapidly became the procedure of choice in many centers for progressive and sometimes for nonprogressive NAION. This occurred even as negative studies began to appear in the literature<sup>7-9</sup> and despite the absence of a convincing explanation for the mechanism by which the procedure might work.<sup>10-14</sup>

Fortunately, at the same time that this procedure was becoming part of clinical practice, a randomized controlled clinical study was being proposed to compare optic nerve sheath decompression with careful observation in patients with NAION. The initial proposal was submitted to the National Eye Institute in early 1991. The study was approved in late 1991, and the clinical centers were funded in the middle of 1992. Recruitment began in October 1992, a remarkably short 34 months after optic nerve decompression was first reported as a treatment for NAION. The results of the Ischemic Optic Nerve Decompression Trial (IONDT)<sup>15</sup> are reported in this issue of THE JOURNAL.

The IONDT investigators initially calculated that 300 patients would need to be randomized to detect a clinically significant effect from surgery. However, after the data from 244 randomized patients were analyzed, the Data and Safety Monitoring Committee of the IONDT halted recruitment, determining that an insignificant effect of treatment would be found even if every patient subsequently randomized to surgery improved. Specifically, at 6 months of follow-up, 32.6% of the patients who underwent optic nerve decompression improved by at least three lines of visual acuity, compared with 42.7% of patients in the careful follow-up group. In addition, 23.9% of the patients who had surgery lost three or more lines of visual acuity, compared with 12.4% of those in the careful follow-up group. Although most patients in the study did not have progressive NAION, the type reported by Sergott et al<sup>3</sup> to benefit most from optic nerve decompression, there was no beneficial effect from surgery even in the small number of patients who did have progressive disease. Finally, the study found a much higher spontaneous rate of improvement in untreated patients than had previously been recognized. Based on these findings, on January 3, 1995, the National Eye Institute issued a clinical alert to ophthalmologists and neurologists advising against the use of optic nerve decompression for NAION.

How could this procedure gain such widespread acceptance despite a lack of evidence of its efficacy or a logical explanation for its mechanism of action? There are probably two answers. First, the rate of spontaneous improvement in NAION in the IONDT was much higher than previously recognized. Therefore, patients who recovered visual function after surgery in nonrandomized retrospective studies might well have improved to a similar extent had they not been treated, leading to the erroneous conclusion that surgery is helpful. The reason that a similarly high rate of spontaneous improvement was not noted in previous studies is unclear. In the IONDT, the measurement of visual function with examiners masked to the patient's treatment assign-

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standardized conditions, and prospective criteria for patient selection were all features contributing to reliable measurement of improvement rates but were not elements of previous reports.

The second reason for the rapid acceptance of optic nerve decompression for NAION is that physicians caring for these patients have long been handicapped by a lack of therapeutic options. Faced with a patient acutely blinded in one eye by a disease for which there is no known treatment, a compassionate physician might well consider any reasonable option, especially one for which the literature gives assent. That the natural history of the disease was thought to be so poor reinforced this sense of desperation. With this background, it is understandable that so many patients were offered surgery for NAION. In fact, it is fortunate that there were enough physicians and, more important, enough patients who were willing to take part in a clinical trial in which half of the subjects received no treatment at all. If not for them, optic nerve decompression may de facto have eventually become so accepted as a treatment for NAION that a study comparing it with observation alone would have been impossible. If that had happened, we may well have permanently added a useless and possibly harmful therapy to our armamentarium.

Clearly, the system worked. The results from this study, although negative, bear witness to the immense power of the prospective randomized controlled clinical trial. The fact that a rigorous clinical study of a new therapy for a blinding disease was able to be proposed, funded, and carried out so rapidly kept an ineffectual procedure from becoming an es-

1. Miller NR. *Walsh and Hoyt's Clinical Neuro-Ophthalmology*. 4th ed. Baltimore, Md: Williams & Wilkins; 1991:2601.
2. Boghen DR, Glaser JS. Ischaemic optic neuropathy: the clinical profile and natural history. *Brain*. 1975;98:689-708.
3. Sergott RC, Cohen MS, Bosley TM, Savino PJ. Optic nerve decompression may improve the progressive form of nonarteritic ischemic optic neuropathy. *Arch Ophthalmol*. 1989;107:1743-1754.
4. Spoor TC, Wilkinson MJ, Ramocki JM. Optic nerve sheath decompression: treatment of progressive nonarteritic ischemic optic neuropathy. *Am J Ophthalmol*. 1991;111:724-723.
5. Spoor TC, McHenry JG, Lan SL. Progressive and static nonarteritic ischemic optic neuropathy treated by optic nerve sheath decompression. *Ophthalmology*. 1993;100:306-311.
6. Kelman SE, Elman MJ. Optic nerve sheath decompression for nonarteritic ischemic optic neuropathy improves multiple visual function measurements. *Arch Ophthalmol*. 1991;109:667-671.
7. Jablons MM, Glaser JS, Schatz NJ, Siatkowski RM, Tse DT, Kronish JW. Optic nerve sheath fenestration for treatment of progressive ischemic optic neuropathy: results in 26 patients. *Arch Ophthalmol*. 1993;111:84-87.
8. Yee RD, Selky AK, Purvin VA. Outcomes of surgical and nonsurgical management of nonarteritic ischemic optic neuropathy. *Trans Am Ophthalmol Soc*. 1993;91:227-240.
9. Glaser JS, Teimory M, Schatz NJ. Optic nerve sheath fenestration for progressive ischemic optic neuropathy: results in second series consisting of 21 eyes. *Arch Ophthalmol*. 1994;112:1047-1050.
10. Seiff SR, Shah L. A model for the mechanism of optic nerve sheath fenestration. *Arch Ophthalmol*. 1990;108:1326-1329.
11. Sadun AA, Heller KB, Feldon SE. Model for optic nerve sheath decompression: Bernoulli's principle applied. *Arch Ophthalmol*. 1991;109:612.
12. Bazarian RA, Burde RM. Mechanism of optic nerve sheath fenestration. *Arch Ophthalmol*. 1991;109:613.
13. Hayreh SS. The role of optic nerve sheath fenestration in management of anterior ischemic optic neuropathy. *Arch Ophthalmol*. 1990;108:1063-1065.
14. Flaherty PM, Sergott RC, Lieb W, Bosley TM, Savino PJ. Optic nerve sheath decompression may improve blood flow in anterior ischemic optic neuropathy. *Ophthalmology*. 1993;100:297-302.
15. The Ischemic Optic Neuropathy Decompression Trial Research Group. Optic nerve decompression surgery for nonarteritic anterior ischemic optic neuropathy (NAION) is not effective and may be harmful. *JAMA*. 1995;273:625-632.