Lessons From the Ischemic Optic Neuropathy Decompression Trial

A Decade Later

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Nonarteritic anterior ischemic optic neuropathy (NAION), the most common cause of acute optic nerve disease in the older population, is a peculiar disorder. It has a predilection for eyes with very small cup-disc ratios, causes predominantly inferior altitudinal visual field defects, and, like Thor’s hammer, rarely strikes the same eye twice. Vision is lost rapidly, usually within days. However, in a small fraction of patients, visual acuity or field worsens over weeks, i.e., “progressive NAION.”

The pathophysiology of NAION remains a mystery, and worse, there is no treatment established to be effective. Thus, it can be understood why there was so much hope when a 1989 publication in the Archives reported that 12 of 14 patients with progressive NAION enjoyed visual improvement after optic nerve sheath decompression.1 Patients with a progressive course compose only a small fraction of NAION cases, and it was only the progressing patients for which optic nerve sheath fenestration was suggested to be helpful. Nevertheless, this qualification failed to deter ophthalmologists from performing the procedure in both progressive and nonprogressive cases of NAION. Fortunately, several investigators decided to determine whether the procedure was truly efficacious, initiating the Ischemic Optic Neuropathy Decompression Trial (IONDT), which was funded by the National Eye Institute. The IONDT studied patients with clinically diagnosed new-onset NAION, randomizing them between optic nerve sheath fenestration or follow-up alone.

More than a decade after publication of the results of the IONDT,2 it is appropriate to consider to what extent the results of the IONDT have influenced the management of patients with NAION. At first glance, it would seem that the IONDT conclusively showed that optic nerve sheath fenestration does not improve visual acuity in patients with NAION and may also be harmful. However, a closer analysis uncovers some ambiguity. First, the IONDT did not definitively answer whether fenestration helped the group of patients for which the therapy was originally described: namely, those with progressive NAION. The 1989 article describing optic nerve sheath fenestration for progressive NAION had specifically demonstrated that it was ineffective for nonprogressive NAION. The IONDT was underpowered to specifically assess progressive NAION, and the negative findings seen in both progressing and nonprogressing cases has made it unlikely that a more adequately powered study can be performed in the future. Of the 237 randomized patients in the IONDT, only 16 patients in the surgery group and 11 patients in the follow-up group could be considered progressive by 1 clinical criterion, namely, worsening of 3 or more lines of visual acuity before randomization.2 In comparison, if one were to design a new study to have an 80% probability of detecting (at \(P = .05\)) a 50% greater improvement of 3 lines or more beyond that found in the IONDT careful follow-up group, 66 patients per group would be required. Thus, the question of whether or not optic nerve sheath fenestration might have a benefit for patients with progressive NAION has not been answered to a reasonable degree of medical certainty.

Second, including a surgical arm in an investigation of this kind adds special difficulties. This is especially true when there are many centers and surgeons involved in the investigation. Optic nerve sheath fenestration is not a new procedure, having been increasingly employed in the treatment of patients with intracranial hypertension, but it is a low-volume procedure and surgeons may...
not have achieved the surgical facility that comes with high-volume procedures. Recognizing these potential problems, the IONDT investigators went to heroic lengths to attempt surgical uniformity, including the use of questionnaires and a videotape of a fenestration operation by each study surgeon. The investigators deserve to be lauded for employing these measures. However, it is never easy to navigate between the Scylla of achieving an adequate head count in a clinical trial and the Charybdis of using data pooled from surgeons among whom skill and experience vary. Feldon and colleagues described the surgical quality-assurance methods used in the IONDT. It is clear that even within this group of experienced surgeons there were great differences in their surgical technique, including the failure to adhere to 4 of the 6 required steps in the protocol for optic nerve decompression surgery in up to 20% of centers. The other 2 required steps mandated that intervals of sustained traction on the globe be limited to 7 minutes interspersed with at least 2 minutes of “rest.” Not only was compliance difficult to assess, but it is possible that even 7 minutes of greatly elevated intraocular pressure was harmful, and this could have had 1 of the factors contributing to the worse visual outcome in the surgical arm of the IONDT.

Given these questions, how has clinical practice changed because of the IONDT? It showed that optic nerve sheath fenestration for nonprogressive NAION in the hands of most surgeons is not helpful, and thus the trial stopped an epidemic of ineffective and possibly dangerous surgery. This in itself completely changed the treatment of NAION. In addition, as reflected in an impressive list of articles published from the IONDT, our knowledge of the clinical features and natural history of the disease has been greatly expanded. The character of the visual field defects, the appearance of the optic disk, and many other elements are now better known because the trial enrolled a rigorously selected patient population who were evaluated in a uniform fashion. Based on the results of the IONDT, every ophthalmologist should know that 43% of patients with NAION experience a spontaneous improvement of at least 3 lines of visual acuity at 6 months. Although it is unclear whether improvement reflects true healing or simply improved scanning strategies, an ophthalmologist armed with this information can offer some hope to NAION patients who are overwhelmed by unexpected visual loss from an as yet untreatable disease. Meanwhile, the search for effective therapies continues.

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REFERENCES

2. 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(8):625-632.