Ischemic Optic Neuropathy Decompression Trial

Twenty-Four–Month Update

Ischemic Optic Neuropathy Decompression Trial Research Group

**Objective:** To describe visual acuity outcomes of patients in the Ischemic Optic Neuropathy Decompression Trial (IONDT) after 24 months of follow-up.

**Design:** The IONDT is a single-masked, multicenter, randomized clinical trial.

**Settings:** Patients were evaluated and followed up at 25 clinical centers located throughout the United States. Data were sent to and analyzed at a central coordinating center.

**Patients:** Two hundred fifty-eight patients 50 years or older with nonarteritic anterior ischemic optic neuropathy and visual acuity of 20/64 or worse, but better than no light perception, were randomized to either a careful follow-up group (n=131) or an optic nerve decompression surgery (ONDS) group (n=127). Of these, 174 continued participation for at least 24 months, 89 in the careful follow-up group and 85 in the ONDS group.

**Methods:** Randomized patients underwent a standard visual acuity examination at 3, 6, 12, 18, and 24 months of follow-up. The primary outcome was a change of 3 lines or more of visual acuity, defined as a difference of 0.3 in logMAR scores, between baseline and 6 months of follow-up. A secondary outcome was mean change in visual acuity (in logMAR units) at 3, 6, 12, 18, and 24 months following baseline. These changes were estimated using available data from all randomized patients for whom we had data.

**Results:** Of the 258 patients randomized, 143 (55.4%) were male, and 169 (65.5%) were 65 years or older. Mean visual acuity was statistically significantly improved from baseline value at all study visits and for both treatment groups, although visual acuity declined gradually in both groups after the 3-month visit. There were no significant differences between careful follow-up and ONDS in mean change in vision from the baseline and any follow-up time point. At 24 months of follow-up, 31.0% of patients in the careful follow-up group and 29.4% of patients in the ONDS group experienced an increase of 3 or more lines of vision compared with baseline acuity; 21.8% of patients in the careful follow-up group and 20.0% of patients in the ONDS group experienced a decrease of 3 or more lines. In patients who could read at least 1 letter on the Lighthouse chart, there was a gradual decline in mean visual acuity noted over time for both treatment groups, although acuity remained significantly better than at baseline.

**Conclusion:** Analysis of visual acuity data from patients enrolled in the IONDT at 24 months of follow-up confirms that there is no benefit of ONDS compared with careful follow-up in patients with nonarteritic anterior ischemic optic neuropathy.


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PATIENTS AND METHODS

METHODS

ELIGIBILITY, ENROLLMENT, AND RANDOMIZATION

A detailed description of the methods and eligibility requirements used to enroll patients, collect data, and tabulate results has been described previously. In brief, patients who had sudden loss of vision within the previous 14 days, a relative afferent pupillary defect, optic nerve head (disc) edema, and an abnormal visual field were eligible for the IONDT. Exclusion criteria included age younger than 50 years, any medical condition that results in nonischemic optic neuropathy or excessive surgical risk, any ophthalmologic condition that precludes reliable visual acuity measurement, and inability to give informed consent. Eligible patients were randomized if, within 30 days of onset of symptoms, their visual acuity was 20/64 or worse but better than no light perception. Randomization and surgery took place within 14 days of onset of symptoms if initial visual acuity was 20/64 or worse (regular entry). When baseline visual acuity was better than 20/64, patients were followed up for up to 30 days, and those whose visual acuity decreased to 20/64 or worse were eligible to be randomized and have surgery within 4 days (≤34 days from onset of symptoms) (late entry). The ONDS procedure has been described previously.

FOLLOW-UP

Follow-up visits were scheduled at 1 week and at 1, 3, 6, 12, 18, and 24 months after randomization. The primary outcome, change of 3 or more lines of visual acuity at 6 months after randomization, was measured using Light- house charts (Lighthouse Low Vision Products, Long Island City, NY) by masked visual acuity technicians. For patients who were unable to read letters, technicians assessed the ability to count fingers, perceive hand motion, or perceive light. When visual acuity could be estimated using number of letters read on the Lighthouse chart (patients were “on chart”), we used standard methods of calculating a logMAR (logarithmic Minimum Angle of Resolution) score; otherwise (patients were “off chart”), we assigned logMAR scores of 2.0 to count fingers, 2.3 to hand motion, and 2.6 to light perception.

Patients were assigned to careful follow-up or ONDS groups via a telephone call to the coordinating center. The random allocation schedule was computer generated and stratified by clinic.

RESULTS

The numbers of patients randomized in the IONDT and for whom data are available at baseline, 6 months, and 24 months are indicated in Figure 1. There were no significant differences between treatment groups in the percentage of patients missing visual acuity measurements at any of the visits (Table 1) and no significant differences between treatment groups in the percentage of patients missing visual acuity measurements at the 24-month visit by age, sex, late entry, diabetes, hypertension, previous NAION, or baseline acuity on/off chart (data not shown).

We found few significant differences when we compared mean change in vision at 3, 6, 12, and 18 months for patients with visual acuity data at 24 months with those missing 24-month visual acuity data. In patients with visual acuity “on chart” at baseline, those without visual acuity data at 24 months had significantly poorer vision at baseline (difference of 0.14 units logMAR; P=.01) compared with those with 24-month vision data. Although visual acuity improved in both groups, the group missing 24-month vision data appeared to improve more at earlier time points. There were no significant differences in vision in patients who were “off chart” at base-
line and missing visual acuity data at 24 months compared with those with vision data, except at 12 months, where the 24-month cohort improved more (P = .04) (data not shown).

Demographic, visual acuity, and medical characteristics for the all randomized and the 24-month cohorts by treatment group are shown in Table 2. We could not compare these cohorts statistically, since the 24-month cohort is a subset of the all randomized cohort. There appears to be little difference in baseline visual acuity between the 24-month and the all randomized cohorts. A significantly higher percentage of patients in the surgery group were in the late entry category, but this was not seen in the 24-month cohort. In both cohorts, there were significantly more patients with diabetes in the careful follow-up group.

Losses to follow-up by 24 months were not differentially distributed across treatment groups nor were they associated with important differences in baseline or follow-up vision between treatment groups. In patients with “off chart” vision, those who were lost to follow-up at 24 months had significantly poorer baseline visual acuity than patients not lost to follow-up. There were no significant differences between patients with and without 24-month vision data on any of the baseline characteristics examined (data not shown). Therefore, as noted earlier, our analyses pertaining to visual acuity and other outcomes are based on the all randomized cohort.

For the primary outcome, the preliminary results of no benefit for ONDS reported for IONDT at 6 months of follow-up were confirmed for all follow-up times through 24 months (Table 3). Using logMAR scores treated as continuous variables, Figure 2 shows change in visual acuity as “mean chart lines improved” in the 2 treatment groups at the 3-, 6-, 12-, 18-, and 24-month visits for patients whose baseline visual acuity was “on chart” and “off chart,” respectively. All patients for whom data were available were included at each time point.

For the quantitative visual acuity outcome for “on chart” patients, we found that patients younger than 65 years improved significantly more than older patients (P = .02). Visual acuity was significantly improved over the baseline value at all follow-up visits, although less improvement was noted at month 24 (Figure 2, top), and the greatest improvement was seen at 3 months for both treatment groups. No significant differences were observed between groups, and patients with poorer visual acuity at baseline had greater mean improvement than did those with better baseline vision (P < .001). For “off chart” patients, statistically significant improvement from baseline visual acuity was observed for both study groups at all follow-up visits, but no decline over time was seen after the 3-month improvement (Figure 2, bottom). No differences between treatment groups were detected.

When results from similar analyses using the 24-month cohort were compared with analyses using the all randomized cohort, the 24-month cohort showed somewhat less improvement over time. This result is consis-

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**Table 1. Participants With Visual Acuity Measurement by Treatment Group and Follow-up Visit**

<table>
<thead>
<tr>
<th>Visit</th>
<th>Careful Follow-up</th>
<th>Optic Nerve Decompression Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visit</td>
<td>No. With Data</td>
<td>No. (%) Missing Data</td>
</tr>
<tr>
<td>Total randomized</td>
<td>131</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Baseline</td>
<td>129</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>3 mo</td>
<td>123</td>
<td>8 (6.1)</td>
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<tr>
<td>6 mo</td>
<td>124</td>
<td>7 (5.3)</td>
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<tr>
<td>12 mo</td>
<td>116</td>
<td>15 (11.5)</td>
</tr>
<tr>
<td>18 mo</td>
<td>107</td>
<td>24 (18.3)</td>
</tr>
<tr>
<td>24 mo</td>
<td>89</td>
<td>42 (32.1)</td>
</tr>
</tbody>
</table>

*a* No significant differences observed between treatment groups in percentage missing for any follow-up visit using χ² test.

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tent with the fact that those missing data at 24 months had significantly worse baseline vision and patients with poorest baseline vision improved most.

The IONDT remains the only multicenter, randomized study of a large number of patients with NAION. Although other studies have provided important information on the natural history of NAION, the IONDT is still the best source of comprehensive, prospective data on this disease process based on its experimental design.

There were no significant differences between the careful follow-up and ONDS groups in mean changes in visual acuity at the 24-month follow-up. These results support the IONDT Research Group’s conclusion at the 6-month follow-up that ONDS is not of value in treating NAION. For patients “on chart” at baseline, both treatment groups improved significantly over the mean enrollment baseline visual acuity by the 3-month assessment, followed by a gradual decline over time (Figure 2, top). Despite this decline, at 24 months mean visual acuity in both treatment groups was still significantly better than that at baseline. A similar decline in visual acuity...
population. The IONDT intends to follow up enrolled pa-
sibility over time was not seen in either treatment group for patients “off chart” at baseline (Figure 2, bottom).

Although the average change in vision for the 2 groups is toward improvement over baseline at every subsequent time point, it is highest at 3 months. This average change should not be interpreted to mean that vision in patients with NAION declines generally during the follow-up period. A possible explanation for a decrease in average improvement is that some individuals experience a large decrease in vision, whereas others experience no change or improvement. Indeed, the median improvement for the 2 groups should not be interpreted to mean that vision in patients “off chart,” ie, sufficiently good to be measured with a standardized chart. Results were adjusted for baseline visual acuity, age (<65 years or ≥65 years), and diabetes. Improvement is indicated by positive values. Bottom, Mean change from baseline in visual acuity in patients with baseline visual acuity “off chart,” ie, count fingers, hand motion, or light perception. Results were adjusted for baseline visual acuity. Improvement is indicated by positive values. ONDS indicates optic nerve decompression surgery.

Figure 2. Top, Mean change from baseline in visual acuity in patients with baseline visual acuity “on chart,” ie, sufficiently good to be measured with a standardized chart. Results were adjusted for baseline visual acuity, age (<65 years or ≥65 years), and diabetes. Improvement is indicated by positive values. Bottom, Mean change from baseline in visual acuity in patients with baseline visual acuity “off chart,” ie, count fingers, hand motion, or light perception. Results were adjusted for baseline visual acuity. Improvement is indicated by positive values. ONDS indicates optic nerve decompression surgery.

history of NAION in an attempt to answer this and other important questions.

Therapy to treat acute NAION successfully, reduce the gradual decline in the visual improvement noted in some of these patients, and protect the fellow eye from NAION is not yet available. Neuroprotective agents, reduction of vascular risk factors, aspirin or other antiplatelet medication, dopaminergic medication, and other agents are potential avenues for investigation.14-18 Regardless of any new treatment strategy that is considered, the 6- and 24-month follow-up results of the IONDT underscore the importance of testing any new therapy with a randomized clinical trial before widespread use.

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