Surgical Treatment for Normal Tension Glaucoma

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Introduction

Normal tension glaucoma (normal pressure glaucoma; NTG) is the most prevalent subtype of glaucoma in Japan[1] and probably in other parts of Asia as well. Since there are no pathognomonic signs and symptoms for NTG, it is usually diagnosed by differentiating between diseases that mimic it. Table 1 shows the diagnostic criteria for NTG.

While the pathogenetic mechanism of this chronic disorder is not yet certain, many believe that it is not a single disease but a group of diseases that have not yet been properly differentiated.[2-7] Based on a variety of possible pathogenetic mechanisms, several treatment modalities are being investigated, including ocular hypotensive therapy and various methods of improving ocular haemodynamics.

Abnormal intraocular pressure (IOP) is believed to play a role in the development of the optic neuropathy of NTG, as it does in primary open angle glaucoma (POAG). In cases of bilateral NTG, the eye with the highest IOP tends to have the most progressive visual field changes.[8] There is no observable difference in the optic nerve head between NTG and POAG.[9]

Recent advances in surgery involving the use of antimetabolites have been successful in reducing IOP to approximately 10 mm Hg.[10-12] Moreover, the results of a multi-centered, collaborative study on the effect of surgical IOP reduction in NTG have recently been published.[13,14] Here, we discuss the findings from 2 studies conducted at our facility[15,16] and consider their implications regarding the surgical treatment of NTG.

Study 1

Change in the Mean Deviation Slope Before and After Trabeculectomy in Patients with Normal Tension Glaucoma

We compared the change in the mean deviation (MD) slope before and after trabeculectomy in patients with NTG.[15] Patients with NTG undergoing trabeculectomy with mitomycin-C who met the following criteria were retrospectively analysed:

- follow-up for more than 1 year before surgery and at least 2 years after surgery
- visual acuity of at least 6/12
- no postoperative complications that might confound an analysis of the visual field.

In patients in whom both eyes were operated on, the eye with the worse pre-operative MD was selected. 32 eyes of 32 patients were selected. The pre-operative follow-up period was 1 to 15 years (mean 3.8 years) and the post-operative follow-up period was 2 to 6 years (mean 4.5 years). The age range at surgery was 38 to 77 years. Pre-operatively, an average of 1.5 different eyedrops had been used. The MD slope was -0.97 ± 1.07 dB/year pre-operatively and -0.32 ± 0.61 dB/year postoperatively (figure 1). The difference was statistically significant ($p = 0.003$, Wilcoxon signed-rank test). The difference was more evident in patients in whom the pretreatment IOP was 15 mm Hg or higher.

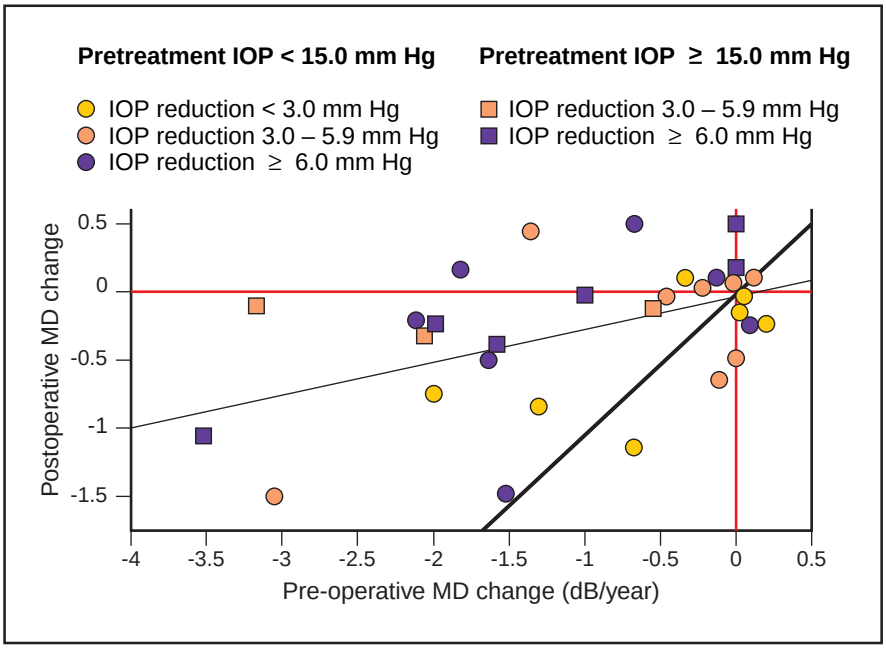
A stepwise regression analysis was performed to correlate the difference between the postoperative and pre-operative annual MD change with several clinical factors, including the difference in the pre-operative diurnal and post-operative mean IOPs, mean diurnal IOP, mean postoperative IOP, MD at the time of surgery, postoperative presence of disc haemorrhage, peripapillary atrophy, refractive error, use of calcium-channel blockers, use of ocular hypotensives, percentage recovery in a cold provocative test, blood pressure, age at surgery, and history of diabetes mellitus. We found that the amount of postoperative annual MD change deterioration (postoperative annual MD change minus pre-operative annual MD change) was positively correlated with a higher pre-operative mean diurnal IOP ($p = 0.006$), absence of diabetes mellitus ($p = 0.04$), and myopic refraction ($p = 0.116$).

Similarly, the stepwise regression

Table 1. Diagnostic criteria for normal tension glaucoma

- Untreated intraocular presure ≤ 21 mm Hg at all times, including 24-hour phasing
- Normal open angle
- Presence of typical glaucomatous optic nerve changes and corresponding visual field changes
- No ocular, rhinologic, neurological, or systemic disorders responsible for the optic neuropathy

Figure 1. **The postoperative change in the annual mean deviation (MD) change after trabeculectomy.[15] Modified from Daugeliene *et al*. with permission.**



analysis revealed that negative pre-operative visual field change (annual MD change) was highly correlated with a higher mean IOP during the 24-hour phasing (p = 0.012), history of disc haemorrhages (p = 0.015), myopic refraction (p = 0.061), and greater age (p = 0.141).

Study 2

Comparison of Visual Function in Patients Undergoing Unilateral Trabeculectomy

A prospective study of unilateral trabeculectomy in 21 patients with bilateral NTG was conducted.[16] The enrollment criteria were as follows:

- established bilateral NTG following an intensive diagnostic process
- visual acuity of at least 6/9
- IOP difference between both eyes of less than 2.0 mm Hg
- no history of intraocular surgeries
- documented progressive visual field defects
- presence of a threat to fixation with the presence of absolute scotomas near the fixation.

After obtaining informed consent, an antimetabolite trabeculectomy was performed unilaterally in the more progressed eye. All surgeries were conducted between July 1991 and September 1993. There were 7 males and 14 females and the postoperative follow-up period ranged from 29 to 84 months (mean 56.9 months). Age at surgery was 41 to 73 years (mean 57.3 years). Perimetry was performed at least once every 6 months using the Central 30-2 programme of the Humphrey Field Analyzer.

In the operated eyes, the IOP was significantly reduced from 14.8 ± 1.8 mm Hg (range 11.3 - 17.6 mm Hg) pre-operatively to 9.6 ± 3.9 mm Hg (range 5.0 - 19.0 mm Hg) postoperatively (p = 0.0002), while the IOP in the fellow eyes was 14.7 ± 1.9 mm Hg (range 10.0 - 17.6 mm Hg) pre-operatively and 14.2 ± 1.8 mm Hg (range 10.3 - 17.7 mm Hg) postoperatively (p = 0.3945). The post-operative IOP was significantly different between the treated and the untreated eyes. In the treated eyes, the MD was -12.69 ± 6.41 dB (range -23.18 to -1.84 dB) pre-operatively and -14.70 ± 5.49 dB (range -23.17 to -5.20 dB) post-operatively, while in the untreated eyes, the MD was -7.85 ± 5.65 dB (range -21.34 to -1.03 dB) pre-operatively and -11.15 ± 5.62 dB (range -26.21 to -3.32 dB) postoperatively. There was a statistically significant deterioration in the visual field in both treated and untreated eyes (p = 0.0239 and p = 0.0002, respectively).

If visual field deterioration was defined as an MD deterioration of ≥ 3.00 dB, 6 of the 21 treated eyes and 10 of the untreated eyes showed deterioration. Of the 6 treated eyes, MD deterioration was caused by cataract in 3 eyes and by glaucoma progression in 3 eyes.

Pointwise visual field progression was defined as the occurrence, at 2 consecutive perimetric examinations, of a visual field deterioration of at least 2 contiguous points by ≥ 10 dB and/or deterioration of at least 3 contiguous points by ≥ 5 dB with at least 1 of them being ≥ 10 dB. Pointwise comparison for progression demonstrated that the untreated eyes had a more progressive field than did the treated eyes (p < 0.05, McNemar test). If deterioration in visual acuity is defined as a change of ≥ 2 lines, then 6 of the treated eyes and 5 of the untreated eyes showed deterioration in visual acuity. Of the 6 deteriorated eyes in the treated group, 5 were due to cataract.

Comments

Previously, the study by the Collaborative Normal-Tension Glaucoma Study Group revealed several important aspects of NTG, including the following findings:

- progression is slow
- 30% IOP reduction is accomplished

Table 2. Indications for surgery for patients with normal tension glaucoma

Factors	Indications for surgery	Surgery less indicated
Visual field	Progression confirmed Advanced defects Threat to fixation imminent Defects in the inferior hemifield	Progression not confirmed Mild to moderate defects No threat to fixation
Symptoms	Severe	Mild to none
Pretreatment IOP	≥ 15 mm Hg	< 15 mm Hg
Effect of medication	None or minor IOP reduction	IOP reduction > 3 mm Hg
Age	70 years or younger	80 years or older

in approximately 50% of patients using medical and laser therapy

- surgical treatment does prevent visual field progression, but may cause complications, particularly cataracts
- IOP plays some pathogenetic role in the disease.[13,14]

The IOP criteria employed in the study is different from that in our study (table 1) in that they used the median of baseline IOPs measured 10 times after a 4-week washout period, of which 6 were taken between 08:00 hours and 18:00 hours on a single day. Their definition is that the median of baseline IOPs is ≤ 20 mm Hg, with no IOP reading > 24 mm Hg and no more than one reading of 23 to 24 mm Hg. Their IOP criteria are higher than that used in many Asian studies. Moreover, there were only 12 ethnic Asian subjects enrolled. These important differences should be taken into account before applying their findings to an Asian population. Nevertheless, their findings support treating NTG with higher IOP.

Our results are compatible with those of the study. If we can achieve sufficient IOP reduction by surgical intervention, then there may be less progression, or even stabilisation, of optic neuropathy for some patients. Likewise, the findings from studies by Abedin *et al.*[17] and de Jong *et al.*[18] are also compatible with ours, since the positive effect of surgery on the visual field is greater when the pretreatment IOP is higher.

Clearly, reducing the IOP yields the most favourable effect. Thus, if an identical IOP reduction is achieved by other treatment modalities, such as medication or laser trabeculoplasty, a similar effect would be expected. Since NTG is a chronic disease, and especially since most patients with NTG may well survive beyond 2010, it is important to keep in mind that alternative treatment strategies will be developed in the future and that any current strategy should not obviate the possibility of an alternative approach.

There is some disagreement as to the target IOP for the appropriate management of NTG. Abedin *et al.* recommended an IOP of 12 mm Hg, with an ultimate goal of ≤ 10 mm Hg.[17] de Jong *et al.* stated that an IOP reduction of > 20% is preferable.[18] According to our data, a target IOP of between 10 and 12 mm Hg or less is recommended. Of course, since it is difficult to achieve this by medical treatment alone, we consider surgical intervention to be the best method of achieving this level of reduction.

However, several issues prevent us from recommending surgery for every patient. Several postoperative complications may lead to vision deterioration, including cataract, corneal astigmatism, hypotony, maculopathy, and late-onset bleb-related infection. Cataract development is especially common following successful filtering surgery, although recent improvements in surgical technique can minimise this problem.

Further, not all patients have a reduction in the progress of visual field abnormality, even with 'sufficiently' reduced IOP following surgery. Without long-term intensive follow-up, we cannot predict whether a particular patient will benefit from surgical intervention.

In our opinion, the indication for surgery should be limited in patients where there is a severe threat to visual function and each patient should be considered on an individual basis. Table 2 presents some of the factors we use when considering surgical intervention.

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