

The Ocular Hypertension Treatment Study

Primary open angle glaucoma (POAG) is one of the leading causes of blindness worldwide. People with elevated intraocular pressure (IOP; ocular hypertension) are at increased risk for developing POAG. However, a substantial proportion of optic nerve fibre may be lost before glaucomatous visual field defects can be detected. There is, therefore, a need for early detection and treatment. The Ocular Hypertension Treatment Study (OHTS) was designed to evaluate the safety and efficacy of topical ocular hypotensive medication in delaying or preventing the onset of POAG in individuals with elevated IOP.

Patients and Methods

Eligibility criteria included age from 40 to 80 years, IOP between 24 mm Hg and 32 mm Hg in 1 eye and between 21 mm Hg and 32 mm Hg in the other eye, gonioscopically open angles, 2 normal visual field tests per eye, and normal optic discs. In this multicentre study, patients were randomised to either a medication group or an observation group.

Patients randomised to receive medication began treatment to achieve a target pressure of 24 mm Hg or less and a minimum 20% reduction in IOP from the average of the qualifying IOP and from IOP at baseline. Topical medication was changed or added to until these goals were met or the patients were receiving maximum tolerated therapy. The primary outcome was POAG in one or both eyes.

The medications given included prostaglandins, β -adrenergic antagonists, topical carbonic anhydrase inhibitors, α_2 -adrenergic agonists, parasympathomimetic agents, and epinephrine/dipivefrin.

Results

1636 patients were enrolled in the study between February 1994 and October 1996. Patients were randomised to receive topical ocular hypotensive medication (n = 817) or observation (n = 819) and 702 and 706 patients, respectively, completed the trial.

The baseline and follow-up IOPs for patients in the medication and observation groups are shown in Table 1. The IOP

goal was met in both eyes at 87% of the follow-up visits by the medication participants and in 1 eye at 7% of visits.

At 60 months, 2 or more topical ocular hypotensive medications were prescribed for 39.7% of patients receiving medication and 3 or more medications were prescribed for 9.3%. Thirty six of the patients (4.4%) in the medication group developed POAG compared with 89 patients (10.9%) in the observation only group (Table 2). During the course of the study, the cumulative probability of developing POAG was significantly lower for patients in the medication group compared with the observation group (hazard ratio, 0.40; 95% confidence interval [CI], 0.27-0.59; $p < 0.0001$). A treatment benefit was observed for reproducible visual field abnormality attributed to POAG (hazard ratio, 0.45; 95% CI, 0.27-0.76; $p = 0.002$) and for reproducible optic disc deterioration attributed to POAG (hazard ratio, 0.36; 95% CI, 0.23-0.56; $p < 0.0001$).

Discussion

This study has shown that topical ocular hypotensive medication is effective for reducing the incidence of glaucomatous visual field loss and/or optic nerve deterioration for patients with elevated IOPs between 24 mm Hg and 32 mm Hg. This is the largest randomised study of the safety and efficacy of ocular hypotensive medication for delaying or preventing the onset of POAG in individuals with ocular hypertension. After 5 years, the cumulative probability of developing POAG was 4.4% for patients taking medication and 9.5% for those in the observation group.

Interestingly, approximately 55% of the initial POAG endpoints involved optic disc deterioration in the absence of visual field abnormalities. With longer follow-up, it may be possible to ascertain how many of the patients with optic disc deterioration go on to develop visual field loss.



Table 1. Intraocular pressure (IOP) at baseline and follow up for patients with ocular hypertension receiving medication or observation

	Medication group (n = 817)	Observation group (n = 819)
IOP at baseline (mm Hg)	24.9 ± 2.6	24.9 ± 2.7
IOP average for follow-up visits (mm Hg)	19.3 ± 2.2	23.9 ± 2.9
IOP reduction from baseline (%)	-22.5 ± 9.9	-4.0 ± 11.6

Table 2. First primary open angle glaucoma endpoint for each participant.

	Medication group (n = 817)	Observation group (n = 819)
Visual field	15	29
Optic disc	18	51
Visual field and optic disc	3	9

SHORT COMMUNICATION

This trial also demonstrated that moderate IOP reductions could be attained and maintained for a median follow-up of 6 years. During the course of the trial, 87% of patients receiving medication achieved the target IOP reduction in both eyes, and an additional 7% did so in 1 eye.

In terms of safety of the medications, there was no evidence of excess risk in the medication group for patient-reported symptoms according to the Glaucoma Symptom Scale or SF-36. There was no evidence of excess risk in the medication group for the overall number of new medical conditions, worsening of pre-existing conditions, admissions to hospital, or mortality. Patients in the medication group had a similar mean visual acuity to those in the observation group throughout the study.

Overall, the decision to recommend medical treatment for patients with ocular

hypertension should take several factors into consideration, including the following:

- the low overall incidence of POAG in individuals with ocular hypertension
- the burden of long-term treatment
- the individual's risk of developing POAG
- the individual's likelihood of being helped by medication
- the individual's health status and life expectancy.

Baseline factors that predict which patients in the Ocular Hypertension Treatment Study developed POAG have been published,¹ and may be useful for clinicians caring for patients with ocular hypertension.

Conclusion

For years, there has been doubt about whether lowering IOP is useful in POAG. This study provides clear proof of the

benefit of lowering IOP and, when these results are taken together with results of other studies, there is now strong evidence that lowering IOP preserves vision in POAG.

Reference

1. Gordon MO, Beiser JA, Brandt JD, et al. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. *Arch Ophthalmol* 2002;120:714-720.

This article was summarised from: Kass MA, Heuer DK, Higginbotham EJ, et al, for the Ocular Hypertension Treatment Study Group. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. *Arch Ophthalmol* 2002;120:701-713.

