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We Should Treat Fewer Patients With Elevated Intraocular Pressure Now That We Know the Results of the Ocular Hypertension Treatment Study

THE OCULAR HYPERTENSION Treatment Study (OHTS), a landmark trial in glaucoma therapy, has definitively answered the question “Does lowering intraocular pressure (IOP) in persons with elevated IOP but no glaucoma damage reduce the incidence of glaucoma?”, confirming what most ophthalmologists knew—that treatment works.

However, even the most ardent supporters of treatment to lower IOP would concede that the results of the study do not suggest that all persons with ocular hypertension should be treated.^{1,2} After all, only 9.5% of the subjects who were observed without therapy developed glaucoma during a mean follow-up period of 6 years. As the authors of the study themselves conclude in their article, “The results of the OHTS do not imply that all individuals with elevated IOP should be treated with ocular hypotensive medication.”^{3(p708)} Others may look at the OHTS results with a “number needed to treat” perspective⁴ and

conclude that to prevent glaucoma damage in 1 person with ocular hypertension, 20 persons need to be treated.

If the OHTS investigators had supplied us with this information only, we would be hard pressed to know how to apply it to our clinical practice. Fortunately, they have provided us with an analysis of risk factors for the development of glaucoma that allows us to think more critically about whom we decide to treat.⁵ Of greatest importance is the role of central corneal thickness (CCT) as a risk factor for the development of glaucoma. The investigators of the OHTS were able to stratify risk based on a combination of IOP and CCT. They demonstrate that for untreated subjects in the OHTS with IOP ranging from 24 to 32 mm Hg, the risk of incident damage varied 18-fold. Subjects with an IOP of 23.75 mm Hg or lower and a CCT of 588 μ m or less had a 2% incidence, whereas subjects with an IOP of higher than 25.75 mm Hg and a CCT of 555 μ m or less had an incidence of 36%.

The relatively low risk of damage shown in the OHTS for eyes with relatively low elevated IOP and the influence of CCT on the risk profile should lead to the treatment of fewer patients with elevated IOP. Before the OHTS, data on the rate of conversion to glaucoma in patients with ocular hypertension were limited. Without firm data, many practitioners probably felt that it was better to treat all subjects with elevated IOP because the risk of developing glaucoma damage might be very high (even in the absence of a proven treatment effect). With the OHTS data, we can now find good reason not to treat many individuals with elevated IOP measurements only.

Suppose that one's practice pattern was to treat select individuals with an IOP lower than 21 mm Hg but treat all patients with an IOP of 21 mm Hg or higher (it would not surprise me if this were a common practice among ophthalmologists). Based on the OHTS, we now know that some of these individuals with an IOP of 21 mm Hg or higher have thick corneas, suggesting that their

Theoretical Sample of 10 Subjects With Ocular Hypertension and With Normal Visual Fields*

Intraocular Pressure, mm Hg	Central Corneal Thickness, μm	Cup-to-Disc Ratio	Treat Before OHTS	Estimated Risk of Conversion to Glaucoma Across 6 Years, % [†]	Treat Knowing OHTS Results
30	550	0.7	Y	36	Y
29	490	0.5	Y	36	Y
28	570	0.8	Y	13	Y
27	620	0.4	Y	6	N
26	650	0.3	Y	6	N
25	480	0.6	Y	12	Y
24	500	0.9	Y	12	Y
23	580	0.6	Y	2	N
22	600	0.5	Y	2	N
21	470	0.7	Y	17	Y

Abbreviation: OHTS, Ocular Hypertension Treatment Study.

*Before the OHTS results, all 10 of these individuals with elevated intraocular pressure might have been treated. Armed with the OHTS results, only individuals with a risk of conversion of greater than 1% per year (6% across 6 years) are treated. This results in 4 (40%) (shaded rows) of 10 fewer subjects being treated.

[†]Liberalized adapted from Gordon et al.⁵

“true” IOP is lower. Some of these individuals have a low risk of developing damage and don’t need to be treated. Therefore, on the basis of the results of the OHTS, one might treat fewer subjects with an IOP of 21 mm Hg or higher because their risk of glaucoma damage is so low. The **Table** presents a theoretical sampling of 10 subjects with ocular hypertension with normal visual fields. Whereas before the OHTS results, one might have treated all 10 of these individuals, knowledge of the OHTS results leads to treatment of only 6 of the 10. Of particular note is the treatment of the patient with an IOP of 21 mm Hg and a CCT of 470 μm and the discontinuation of therapy in the patient with an IOP of 27 mm Hg and a CCT of 620 μm .

There is a flip side to the treatment of fewer patients with ocular hypertension because of the OHTS results and that is the likelihood of treatment of more patients without glaucoma whose IOP is within the normal range. Although not tested in the OHTS, one might infer that subjects with unremarkable measured IOP but thin corneas may be at a high enough risk of glaucoma to merit treatment. For instance, a person with an IOP of 18 mm Hg but a corneal thickness of 450 μm may be at high enough risk to merit treatment. However, this person would not fall under our general conception of ocular hypertension and hence would not be an additional pa-

tient with ocular hypertension that we had decided to treat on the basis of the OHTS.

Although based on the OHTS results, we will treat fewer patients who have false-positive results for ocular hypertension and are at low risk for development of glaucoma, and hopefully, we will treat more patients who have false-negative results and patients with normal IOPs who are actually at considerable risk for the development of glaucoma. It is hard to predict if the overall total number of patients treated will be greater or less based on the OHTS results. Ideally, application of the results of the OHTS will result in more treatment of the most susceptible individuals and less treatment of those at low risk.

Finally, one should consider that the prevention of first visual-field loss or disc change is not necessarily the be-all and end-all of glaucoma treatment. Subjects who experienced threshold visual-field loss in the OHTS were asymptomatic. An informed patient might elect to forego treatment until a disc or visual-field change has occurred, particularly if the patient’s life expectancy is relatively short.

Before the OHTS results, all 10 of the individuals in the Table with elevated IOP might be treated. Armed with the OHTS results, one might elect to treat only individuals with a risk of conversion to glaucoma of greater than 1% per year (6% across 6 years). This would result in 4 (40%)

of 10 fewer subjects (the shaded rows in the Table) being treated.

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