Increased Corneal Thickness in Patients With Ocular Hypertension

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Background: Central corneal thickness greater than 0.520 mm causes true intraocular pressure to be overestimated when the technique of applanation tonometry is used to measure intraocular pressure.

Objective: To compare the corneal thickness measurements of patients enrolled in a study of ocular hypertension with those of age-matched control subjects with normal intraocular pressure.

Methods: Central corneal pachymetry using an optical pachymeter was performed on each study subject (n=55) at baseline and in an independent sample of control subjects. A 2 sample, 2-tailed t test was used to compare the 2 populations.

Results: The patients with ocular hypertension had significantly higher mean corneal thickness measurements (mean±SD, 0.594±0.037 mm) than the control group (0.563±0.027 mm) (P<.001).

Conclusion: Corneal thickness may be a confounding factor in the measurement of intraocular pressure, and this may modify the risk for progression to glaucoma in patients with ocular hypertension.


Ocular hypertension (OHT) is a diagnosis based primarily on the results obtained from the clinical measurement of intraocular pressure (IOP). The diagnosis of OHT is made when a patient has consistently elevated IOP, open angles by gonioscopy, and no clinical signs of optic nerve damage, such as pathologic cupping, disc asymmetry, or visual field changes associated with the diagnosis of glaucoma. Because the major diagnostic criterion for OHT is based primarily on the clinical measurement of IOP, any variable that can affect the measurement of IOP could lead to an errant diagnosis of OHT.

The most universally applied clinical measurement of IOP is applanation tonometry performed as first described by Goldmann and Schmidt. Although less likely to be affected by scleral rigidity, applanation tension can be affected by corneal thickness, a limitation recognized by Goldmann and Schmidt. They believed that significant variations in corneal thickness were uncommon and assumed a corneal thickness of 520 µm in calibration of the applanation tonometer. As clinical measurement of corneal thickness has become widely available, several studies have found a positive correlation between corneal thickness and applanation pressure. Manometric studies performed in animals and humans have found that pressures measured with applanation tonometry are likely to overestimate the true IOP as the central corneal thickness increases in the nonedematous cornea and underestimate the true IOP as central corneal thickness decreases.

The Ocular Hypertension Treatment Study (OHTS) is an National Eye Institute–sponsored prospective multicenter randomized study designed to determine the efficacy of early pressure-lowering intervention in patients with OHT. Mayo Clinic in Rochester, Minn, was approved by the OHTS Data and Safety Monitoring Committee and the National Eye Institute to undertake this ancillary study to investigate the corneal changes, if any, associated with OHT or its treatment.

RESULTS

Results of pachymetry are shown in Figure 1. Mean±SD left eye corneal thickness in the OHT group was 0.594±0.037 mm (range, 0.470-0.670 mm) and 0.563±0.027
PATIENTS AND METHODS

One hundred sixty-one patients were evaluated for participation in the OHTS by one of us (D.C.H.). The protocols of the OHTS and this ancillary study were reviewed and approved by the institutional review board of Mayo Clinic and informed consent was obtained for all subjects for each study before enlistment in the study. Entry criteria for the OHTS included the following: best- corrected visual acuity of 20/40 or better in both eyes; normal and reliable visual fields in both eyes as confirmed by the Visual Field Reading Center; no anterior segment abnormalities; IOP measured by Goldmann applanation tonometry with mean pressures greater than or equal to 24 mm Hg, but less than or equal to 32 mm Hg in one eye and greater than or equal to 21 mm Hg but less than or equal to 32 mm Hg in the other eye; no history of ocular trauma or surgery; no topical or systemic corticosteroid use; no ocular condition that may lead to increased IOP or cause visual field loss; and normal optic nerve appearance as confirmed by the Optic Disc Reading Center.

Of these patients, 55 were found to meet the entry criteria of the OHTS and agreed to participate in the OHTS. In addition to the studies performed for the OHTS, each subject underwent endothelial photography and central corneal pachymetry with a contact specular microscope (Keeler Instruments, Inc, Broomall, Pa) on enrollment in the study, then annually thereafter. Corneal thickness measurements of the OHTS subjects’ left eye were compared with the corneal thickness measurements of the left eye of an age-matched (±3 years) control group with normal IOP. For each patient with OHT enrolled in the study, we selected consecutive controls from an existing group of subjects previously enlisted in another study. All 55 control subjects had been carefully examined and found to have normal ophthalmic findings in all clinical respects, including anterior segment examination and dilated fundus examination. No attempt was made to match the sex, race, or refractive error of control and study subjects. To be eligible to serve as a control, the subject had to have an IOP of less than or equal to 32 mm Hg in the other eye; no history of ocular trauma or surgery; no topical or systemic corticosteroid use; no ocular condition that may lead to increased IOP or cause visual field loss; and normal optic nerve appearance as confirmed by the Optic Disc Reading Center.

Corneal thickness measurements for the OHTS group were made at the study randomization visit (REPRINTED) ARCH OPHTHALMOL / VOL 119, MAR 2001 WWW.ARCHOPHTHALMOL.COM ©2001 American Medical Association. All rights reserved.

Figure 1. Corneal thickness measurements for the Ocular Hypertension Treatment Study (OHTS) group and the control group. Mean corneal thickness in the OHTS group was 0.594 mm, mean corneal thickness for the control group was 0.563 mm (P<.001).

Figure 2. Plot of corneal thickness vs intraocular pressure (IOP) for the Ocular Hypertension Treatment Study (OHTS) group and the control group. Correlation between corneal thickness and IOP for the 2 groups together is statistically significant. (r = 0.37, P < .001). Correlation for the OHTS group is also significant (r = 0.28, P = .04). There is no correlation between corneal thickness and IOP in the control subjects (P = .99).

When comparing the right eye between groups. Mean±SD left eye IOP in the OHTS group was 25.2±2.0 mm Hg (range, 21.0-29.0 mm Hg) and 15.4±2.9 mm Hg (range, 9.0-21.0 mm Hg) in the control group. A comparison between corneal thickness and IOP for each group is illustrated in Figure 2. The correlation between corneal thickness and IOP was significant in the OHT group (r = 0.28, P = .04). There was no correlation between corneal thickness and IOP in the control group (P = .99). When the groups are pooled, the correlation between corneal thickness and IOP is also significant (r = 0.37, P < .001).

The pharmacological reduction of IOP by at least 20% in the treatment group did not affect the corneal thickness of these subjects (P = .25), when pretreatment corneal thickness was compared with posttreatment corneal thickness.

COMMENT

Ocular hypertension is a condition for which the major diagnostic criterion is IOP. Previous studies have dem-
onstrated the correlation between increased corneal thickness and IOP as measured by applanation tonometry. Subjects with OHT have statistically greater mean corneal thickness than matched control subjects and subjects with the diagnosis of glaucoma.\textsuperscript{5-6} Results of the present study, performed on a group of carefully selected subjects with OHT, confirm those of prior investigations. These studies taken together suggest that corneal thickness may be a significant confounding factor in the diagnosis and classification of OHT.

Most studies of OHT have assumed that, after careful examination and testing, the measured IOP is one of the primary determinants of risk for progression to glaucoma. However, clinical experience with these patients has shown that it is difficult to accurately predict which patients will eventually develop field loss and optic nerve changes, qualifying them for the diagnosis of glaucoma.\textsuperscript{8-10} Studies of early treatment of subjects with OHT have had varying results, with some suggesting that early pressure-lowering intervention was beneficial, while others demonstrated no clinical effect of intervention.\textsuperscript{11-15} None of these studies have considered corneal thickness as a factor, which, depending on the corneal thickness distribution of the sample studied, may have allowed the selection of non-homogeneous groups with respect to the true IOP. Increased corneal thickness may also have allowed some subjects to be classified as OHT when in fact their true IOP may have been less than the entry criteria for the study. This would have decreased the statistical power of the study to show a difference between treated and untreated subjects. The OHTS will be measuring the corneal thickness in all enrolled subjects.

Several authors, through manometric studies, have devised nomograms for correcting a pressure measured by Goldmann applanation tonometry to true manometric IOP.\textsuperscript{5,6} These studies, individually and collectively, measured a relatively small number of eyes, and it is difficult to determine whether these conversion factors can be applied to the individual patient with accuracy. Experiments by Ehlers and colleagues\textsuperscript{5} suggest that a central corneal thickness of 0.59 mm may cause IOP measured by applanation tonometry to overestimate true IOP by as much as 5 mm Hg. Eyes previously studied by manometric IOP manipulation were known to have increased corneal thickness at normal IOPs. The role of increased true IOP as a cause of increased corneal thickness in the normal cornea has not been determined, although corneal thickness is unchanged in the patients in our study whose pressures have been reduced pharmacologically by at least 20%. Corneal thickness measurements in a large group of patients with OHT may help to determine whether corneal thickness plays a clinically significant role in OHT and the progression to glaucoma in some subjects.\textsuperscript{16}

In summary, a sample of carefully selected subjects with OHT was found to have greater average corneal thickness than a sample of age-matched controls. Further study is needed to determine what role, if any, corneal thickness plays in the conversion of OHT to glaucoma.

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