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CLINICAL INVESTIGATION

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Falsely elevated intraocular pressure due to increased central corneal thickness

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Abstract ● Purpose: To evaluate whether ocular hypertensive subjects have a higher central corneal thickness than other individuals. ● Methods: In this prospective study, 48 subjects with ocular hypertension, 63 patients with open-angle glaucoma, 56 nonglaucomatous patients with diabetes mellitus, and 106 control subjects were evaluated. Corneal thickness was measured by ultrasound pachymetry, and intraocular pressure was determined by Goldmann applanation tonometry. ● Results: Central corneal thickness was significantly higher in the ocular hypertensive subjects, mean ±S.D., 592±39 μm, than in the patients with glaucoma (536±34 μm), the nonglaucomatous patients with diabetes mellitus (550±31 μm), and the normal subjects (545±33 μm), $P<0.001$. The three latter groups did not vary significantly in central corneal thickness, $P>0.05$. ● Conclusion: In some individuals with increased transcorneal measurements of intraocular pressure, the cornea is thicker than in subjects with normal intraocular pressure readings or patients with glaucoma. It suggests that in ocular hypertensive subjects, corneal pachymetry should be performed to rule out an abnormally thick cornea as a reason for falsely high measurements of intraocular pressure.

Key words Central corneal thickness · Intraocular pressure · Ocular hypertension · Primary open-angle glaucoma · Diabetes

Introduction

Measurement of intraocular pressure (IOP) by Goldmann applanation tonometry assumes a normal central corneal thickness (CCT) [9]. Ehlers demonstrated that for a corneal thickness of 520 μm (called normal), the values of IOP given by the Goldmann tonometer were correct. In his study, thicker corneas gave falsely elevated IOP and thinner corneas gave falsely lower values [15]. Although these findings were published 25 years ago with optical pachymetry [15], very few studies of ocular hypertensives have included CCT as a routine part of their patient evaluations [12]. Since the IOP is the key parameter for making the diagnosis of ocular hypertension, as well as essential for following patients with known glaucoma, knowledge of the CCT would appear important to know the validity of the IOP readings.

Increased CCT has also been demonstrated in patients with diabetic retinopathy compared to patients without retinopathy and normal controls [2]. Several epidemiological studies have also pointed out the association of primary open-angle glaucoma and ocular hypertension with diabetes [4, 18].

The aims of this prospective study were to compare central corneal thickness in patients with ocular hypertension, primary open-angle glaucoma and diabetes, all compared to normal controls.

Patients and methods

Patients consenting to participate in the study were recruited successively at routine eye clinic visits. Patient data are summarized in Table 1. Subjects included in the control group were those in whom any systemic or ocular pathology could be excluded by a complete medical history and complete ophthalmologic examination. Ocular hypertension was defined as a known history of IOP greater than 21 mmHg on two successive visits, a normal Humphrey 24-2 visual field and a normal-appearing optic disk. Thirty-four patients with OHT were taking IOP-lowering medication on an ongoing basis (betablockers n=31, Latanoprost n=2, Dorzolamide one patient alone and five in combination). Patients with POAG had a known history of IOP greater than 21 mmHg without treatment, abnormal Humphrey 24-2 fields and glaucomatous modification of the optic disk, including pathological excavation, notching of the neuroretinal rim, and/or disk hemorrhages. All glaucoma patients were under antiglaucoma medical treatment or had undergone filtering surgery no less than 6 months preceding their entry into the study. Glaucoma patients were statistically older than in the other groups, $P<0.05$.

Contact lens wearers and patients with greater than 2 D of corneal astigmatism or corneal abnormalities were excluded. In the diabetic group 8 patients were insulin-dependent and 48 were taking oral hypoglycemic medication. Twenty-six diabetics had proliferative retinopathy. None of the diabetics in this study had concurrent OHT or POAG.

IOP and CCT measurements

IOP was measured twice on the same calibrated Goldmann tonometer, and the mean was stored for analysis. CCT was measured after tonometry with an ultrasonic pachymeter (KMI RK-5000 Alcon, Forth Worth, Tex.) calibrated at an ultrasound speed of 1640 m/s. After topical anesthesia, six measurements were performed at the center of the cornea. To avoid falsely elevated values by slightly off-center measurements where the cornea is thicker, only the three lowest measurements for each cornea were averaged.

Overall, IOP and CCT measurements were performed at various times of the day.

Table 1 Patient characteristics

	Controls	OHT	POAG	Diabetes
n	106	48	63	56
Male/female	37/69	29/19	29/34	33/23
Age (mean ± SD)	56±18	60±14	67±13	59±15
Age (range)	16–87	25–84	30–97	16–78

Statistical analysis

Only one eye per patient was chosen at random for analysis except in cases of unilateral disease where the affected eye was retained. Data were stored on a database and analyzed with SAS software (SAS Institute, Cary, N. C.). Descriptive analysis gave the mean value, the standard deviation, the range of values and the 95% confidence interval. In normals, linear regression analysis was performed to evaluate the association of CCT and IOP. The means of the different groups were compared globally with a one-way Anova test after checking the Gaussian distribution with a Kolmogorov-Smirnov procedure. The means were compared 2 by 2 with a Newman-Keuls post test. The level of significance was set at $P<0.05$.

Results

CCT and IOP results are given in Table 2. The mean CCT of the OHT group was significantly higher, 592±39 μm, compared to controls, 545±33 μm, $P<0.001$. The value for OHT was also significantly different from that of POAG and diabetics, $P<0.001$. There was no significant difference between POAG, diabetics and controls. Moreover, in nonglaucomatous diabetic patients the mean CCT was not different in patients with retinopathy (n=26) from patients without retinopathy (n=30), 548±33 μm vs 552±30 μm; difference between means 4±8 μm, 95% CI, –21 to 13 μm.

CCT in the OHT-treated group was 587±39 μm; 95% CI, 573 to 600 μm, and 603±38 μm; 95% CI, 581 to 625 μm in the OHT non-treated group. The difference between these two subgroup was not significant. In the POAG and OHT groups, a comparison was made between eyes treated with dorzolamide and eyes not receiving dorzolamide. The difference was not statistically significant in either group (Table 3).

In normals, no significant difference in central corneal thickness was found between right and left eyes, 546±32 μm vs 548±33 μm; difference between means –2±4 μm, 95% CI, –7 to 11 μm. Central corneal thickness

Table 2 Central corneal thickness and intraocular pressure in various groups of subjects and patients (*CCT* central corneal thickness, *IOP* intraocular pressure, *OHT* ocular hypertension, *POAG* primary open-angle glaucoma)

	Number of eyes	CCT (μm) Mean ± SD	95% CI[a]	Range	IOP (mm Hg) Mean ± SD	95% CI	Range
Controls	106	545±33	539–552	453–620	15.3±2.6	14.8–15.8	9–21
OHT	48	592±39	580–603	520–675	22.2±3.2	21.2–23.1	17–28
POAG	63	536±34	528–544	473–604	20.4±5.2	19.1–21.7	9–33
Diabetes	56	550±31	542–559	471–615	16.7±2.6	15.9–17.3	11–21

[a] 95% CI = 95% confidence interval

Table 3 Influence of dorzolamide on central corneal thickness in patients

	Ocular hypertension		Primary open-angle glaucoma	
Dorzolamide	Yes	No	Yes	No
Number of eyes	7	41	5	58
CCT Mean± SD (μm)	594± 41	591± 39*	514± 29	538± 33**

* $P = 0.86$
** $P = 0.12$

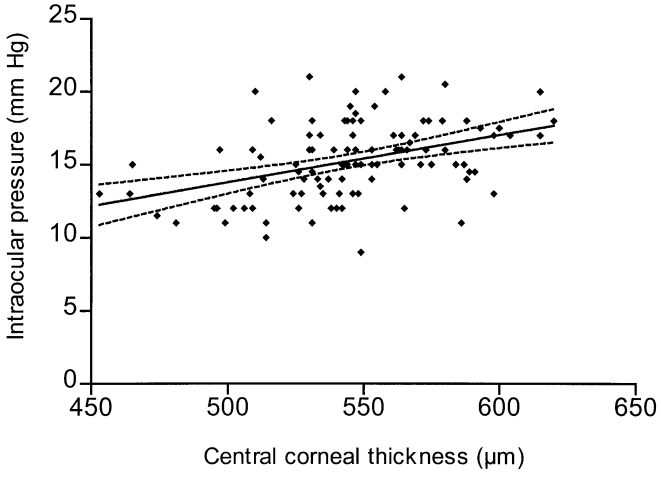

Fig. 1 Correlation of IOP and central corneal thickness in normal subjects (n=106)

was similar in men and women, 552±31 μm vs 542±34 μm; difference between means –10±6 μm 95% CI, –23 to 3 μm. No significant change in CCT was found in normals with age (0.048 μm per year; 95% CI, –0.31 to 0.41 μm). A significant association was found between CCT and IOP for normal subjects. Intraocular pressure increased linearly with greater CCT (0.32 mm Hg per 10 μm) ; 95% CI, 0.18 to 0.46 mm Hg ; $P<0.001$ (Fig. 1).

Discussion

Among the many factors that may interfere with tonometry readings, CCT would seem to play a major role [24]. A Goldmann applanation tonometer tip leads to an applanated area of 3.06 mm in diameter, so that a force of 0.1 g applied to the tip corresponds to an IOP of 1 mmHg. This relationship, however, is true only for corneas of 500 μm CCT [9, 10] and gives some approximation in measurement of the IOP since the Imbert Fick principle is not strictly followed. There is a wide variation in CCT among normal individuals: a recent study of 352 normals gave CCT values ranging from 427 to 620 μm [26].

The relationship between CCT and IOP has been studied using optical pachymetry with the finding that CCT is greater in OHT than in controls [15] and glaucoma patients [8]. At a true IOP of 20 mm Hg a mean underestimation of 5.2 mm Hg is given by applanation tonometry in eyes with a CCT of 450 μm, and an overestimation of 4.7 mm Hg can be found with a CCT of 590 μm [7]. Similar findings were also observed with the Perkins tonometer [25].

Argus has shown similar CCT results by ultrasound pachymetry, which is believed to be more reliable than optical measurements. In comparison OHT, POAG, and controls gave mean CCT±SD of 610±33 μm for OHT compared to 557±39 μm for POAG and 567±36 μm for controls [1].

The present study confirmed the increased CCT in OHT compared to controls and POAG, although the CCT was about 20 μm less than those observed by Argus. This difference is most likely due to our selection of the three lowest readings (to avoid falsely elevated values due to off-center measurements) and the placement of the ultrasound probe at the center of the cornea instead of 1.5 mm temporal to the cornea light reflex as done by Argus. A study by Wolfs [26] using central measurement of corneal thickness found a mean CCT of 537 μm in a large number of controls, which corresponds well with the findings of the present work.

We did not find a decreased CCT in the POAG group, as shown in the Argus study. Actually, Ehlers reported a similar central corneal thickness in glaucoma patients and normals. He also found a higher CCT in pseudoexfoliation, but this difference was not statistically significant [8]. More recently, Herndon et al. confirmed the results of the above-mentioned studies: OHT patients had a significantly greater CCT than controls and glaucomatous patients [12]. CCT may be reduced in normal-tension glaucoma compared to OHT and controls [5]. This was confirmed very recently [19].

The role of corneal curvature was not investigated in our study. Mark has shown that an increase of 1 D in keratometry is associated with an increase of 0.34 mmHg in IOP [17]. However, this finding has not been confirmed by other authors [7].

We did not measure a thicker cornea in eyes receiving dorzolamide in the POAG and OHT groups.The effect of topical carbonic anhydrase inhibitors remains controversial since some authors have observed a significant effect of dorzolamide on CCT [12], and some authors did not [13]. However, the number of patients receiving dorzolamide was too small to draw any conclusions.

A positive statistical association has been shown between CCT and IOP in normal subjects, 0.19 mm Hg per 10 μm in Wolfs' study [26], and 0.32 mm Hg per 10 μm in the present study. However, the correlation coefficient between central thickness and IOP was rather poor (r=0.41), suggesting that others factors of variation

are involved in the assessment of IOP by applanation tonometry (stroma hydration, corneal architecture [21]).

In most studies diurnal variations of IOP and central thickness were not considered, although the magnitude of CCT diurnal variation has been recently evaluated to vary from 2.1 to 14.3% [11]. However, no association between CCT and time of examination was found in the above-mentioned study. CCT has been assessed in several other clinical situations. For instance, in angle-closure glaucoma, CCT was demonstrated to be higher than in controls (580 μm vs 569 μm on average) [23]. The relation between CCT and IOP has been also investigated in retinal detachment [6]. In corneal grafts, the rise of IOP after surgery has been documented [14]; however, few data are available correlating IOP and CCT of the graft. Corneal thinning has even been observed among patients with the highest IOPs during the early postoperative period [20].

The modification of CCT in photorefractive keratectomy (PRK) may lead to some changes in the measurement of IOP, which is a critical point in patients receiving corticosteroids and who are prone to an elevation of IOP. In a recent paper involving 1320 patients undergoing PRK for myopia, a statistically significant decrease was observed in IOP before and after treatment. The difference was related to the degree of myopia treated, i.e., to the thinning of the cornea [3]. The same findings were reported in a more recent study [16].

Several epidemiological studies have reported the association of POAG and OHT with diabetes mellitus [4, 18]. Many hypotheses have been drawn, varying from genetics to hydrostatic considerations related to elevated blood-glucose levels. However, the potential swelling of the cornea in diabetics, as was described in early diabetes mellitus, has not been taken into consideration when measuring the IOP in these patients. A later study using ultrasound pachymetry showed an increase CCT in patients with retinopathy when compared to patients without retinopathy [22]. In our study we failed to demonstrate a difference in CCT between diabetics and the control group, and in patients with or without diabetic retinopathy.

It is our impression based on the present findings that CCT should be routinely performed in evaluation of patients with a diagnosis of ocular hypertension. CCT measurement can also be of great value in all types of glaucoma, especially where the visual fields and optic disk morphology over time do not appear to correlate with the IOP level.

Correlating CCT with IOP in eyes having had PRK may be just as important in the future since the onset of glaucoma may be masked in myopic eyes with artificially thinned corneas where IOP readings will be falsely low [21].

Although the findings of the present study are not new, we feel it is important to point out their clinical relevance again. Studies of OHT should include CCT to avoid treating those with abnormally thick (but still normal) corneas for a risk of glaucoma they do not have. Also, by excluding normal corneas with high CCT, long-term studies on the evolution of OHT should yield more meaningful results.

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