IMPORTANCE OF CENTRAL CORNEAL THICKNESS WHEN STUDYING OCULAR HYPERTENSIVE EYES, GLAUCOMA SUSPECTS AND PREPERIMETRIC GLAUCOMATOUS EYES

IMPORTANCIA DEL ESPESOR CORNEAL CENTRAL EN EL ESTUDIO DE HIPERTENSOS OCULARES, SOSPECHOSOS DE GLAUCOMA Y GLAUCOMAS PREPERIMÉTRICOS

ALÍAS EG¹, FERRERAS A², POLO V², LARROSA JM², PUEYO V², HONRUBIA FM²

ABSTRACT

Purpose: To compare the central corneal thickness, measured with an ultrasound pachymeter, in normal subjects, those with ocular hypertension, glaucoma suspects and patients with preperimetric glaucoma.

Methods: 61 normal eyes (control group), 131 eyes with ocular hypertension, 62 glaucoma suspects (optic nerve head morphology compatible with glaucoma) and 36 patients with preperimetric glaucoma (abnormal short-wavelength automated perimetry) were prospectively and consecutively selected. Scatter plots of central corneal thickness, against the intraocular pressure values were calculated for each of the study groups. Ultrasound pachymetry measurements were compared between those with normal eyes and the other groups.

Results: Ocular hypertensive subjects had higher pachymetry values than the control group (p=0.009). No differences were found in the central corneal thickness between normal eyes and those who were glaucoma suspects, and between normal and preperimetric glaucomatous eyes. A mild direct logarithmic correlation was evident between central corneal thickness and the Goldmann tonometry result in the ocular hypertensive group.
Conclusions: Ocular hypertensive subjects had thicker corneas than the other groups studied. Glaucoma suspects and preperimetric glaucoma patients had similar corneal thickness to the control group (Arch Soc Esp Oftalmol 2007; 82: 615-622).

Key words: Central corneal thickness, ultrasound pachymeter, ocular hypertension, tonometry, glaucoma.

INTRODUCTION

Several studies have tried to establish a relation between IOP and CCT (1-6). The relationship between the two is not linear, so it is not easy to establish a formula to relate them. Several authors have proposed tables (7-11) to adjust IOP according to the pachymeter results, but none of them have been universally accepted.

The multicentric Ocular Hypertension Treatment Study (12,13) suggested that thin CCT was a predictive factor for the development of glaucoma. It has also been found that CCT of less than 555 μm multiplied by three the risk of developing glaucoma when compared to CCT greater than 588 μm. It seems logical to believe that thin corneas may give lower IOP readings than the actual ones. But also, thin corneas are associated to anomalous stroma collagen and lamina cribrosa that may also predispose to development of glaucoma (1). Therefore the increased risk of developing this disease in the case of thin corneas would be based on a more complex mechanism than the simple altered measurement of IOP. As a result of these and other findings, measurement of CCT has been included in the protocols for early diagnosis and examination of glaucoma, but to date, the role played by CCT is still not clear.

The objective of this study was to compare the results obtained with ultrasound pachymeter in normal subjects, those with ocular hypertension and with preperimetric glaucoma.

SUBJECTS, MATERIAL AND METHODS

Subjects

We included 254 eyes of 254 subjects, prospectively and consecutively from the outpatients depart-

ment of the ophthalmology unit at the Miguel Servet university hospital in Zaragoza.

Normal subjects were selected from hospital staff, relatives and people accompanying patients. The group of glaucoma suspects was obtained from subjects referred to the hospital’s glaucoma unit, coming from the two specialized centers attached to it.

Each subject, regardless of the classification group, had to meet the following inclusion criteria: aged 30 to 75, visual acuity greater or equal to 20/30 (Snellen scale), normal conventional automated perimetry (AP), refraction defect under 5 spherical dipters and astigmatism under 3 diopters or spherical equivalent, and transparent optical means (crystalline lens nuclear, cortical or posterior subcapsular color or opalescence <1 according to the Lens Opacities Classification System III) (14).

We excluded eyes with a history of ocular surgery or severe injuries, systemic diseases with ophthalmic impact, impossibility to conduct or assess any of the tests included in the examination protocol (perimetric study, HRT,…). For the study we looked at one eye for each subject. The choice was random, unless only one of the two eyes met the inclusion criteria.

The design of the study was accepted by the hospital’s ethics committee and all participants signed an informed consent. The study methodology followed the Helsinki Declaration guidelines.

Examination procedure

All subjects underwent a full ophthalmological examination, which included a biomicroscopy with slit lamp, gonioscopy, measurement of baseline intraocular pressure level (IOP) with applanation tonometry (mean of 3 recordings on different days without hypotensive treatment), central corneal ultrasound pachymeter, eye fundus evaluation with
indirect ophthalmoscope and slit lamp (−78 diopter Volk lens), papilla stereophotographs, at least one reliable AP and one short-wavelength automated perimetry (SWAP).

AP was performed with a Humphrey 750 perimeter (Zeiss Humphrey Systems, Dublin, CA) and Standard 24-2 SITA strategy. Altered perimetry was considered when the pattern deviation map showed a group with at least 3 altered points with a probability lower than 5% or a group with at least 2 altered points with a probability lower than 1% (we excluded points located at the blind spot poles) (15) and/or standard deviation of the mean (SDM) with a probability lower than 5%; and/or a glaucoma hemifield test outside normal boundaries. If any of these did not meet the validity criteria defined by the perimeter itself (false positives, false negatives and loss of binding), the test was repeated. When the first reliable AP was normal, the test was not repeated, otherwise it was, to diminish the learning effect (16,17). If the second AP was normal, the subject was included in the study, but if the second AP continued presenting a consistent defect in the visual field, the subject was excluded from the study.

SWAP was performed with a Humphrey 750 perimeter (Zeiss Humphrey Systems, Dublin, CA) and the full 24-2 threshold strategy. A criterion of perimetric anomaly was the presence in the pattern deviation map of a group with at least 4 altered points with a probability of less than 5% or a group with at least 3 altered points with a probability of less than 1% (we excluded points located at the blind spot poles) (18) and/or SDM with a probability of less than 5%. We used the same reliability criteria as for AP. When a SWAP presented a defect in the visual field, it was repeated to ensure there was a reproducible defect not explicable by any other cause.

An ultrasound pachymetry was conducted with a DGH 500 pachymeter (DGH Technology, Exton, AP). Three central measurements were taken and the mean of the three was considered.

Clinical evaluation of the optic nerve was conducted by two glaucoma specialists masked with regard to the subject’s clinical history. Discrepancies between the evaluators were resolved by consensus. We defined an optic nerve compatible with glaucoma when there was a thinning of the neuroretinal rim, focal or diffuse with increased excavation, presence of notches or both (24).

**Classification into groups**

Control group (n = 61 eyes): IOP < 21 mmHg, normal papillary morphology and normal AP.

Ocular hypertension group (n = 131): IOP > 21 mmHg with normal AP, regardless of papillary morphology.

Glaucoma suspects group due to papillary morphology (n = 62 eyes): IOP > 21 mmHg with normal AP and papillary morphology compatible with glaucoma.

Preperimetric glaucoma (n = 36 eyes): IOP > 21 mmHg with normal AP and altered SWAP.

**Statistical analysis**

To conduct statistical analysis we used the statistics programs SPSS (version 15.0; SPSS Inc., Chicago, IL) and MedCalc (version 9.2.1.0 MedCalc Software, Belgium).

The Kolmogorov Smirnov test was used to verify the adjustment of a normal distribution of the data analyzed.

To compare quantitative variables of the normal group with the other groups studied (patients with ocular hypertension, glaucoma suspects due to papillary morphology and preperimetric glaucoma) we used Student’s t test. The descriptive variables of the groups analyzed were age, improved corrected visual acuity, baseline IOP, excavation/vertical disk ratio assessed with stereophotographs, mean deviation of AP, and SDM of AP. The main variable studied was CCT. Significant differences were accepted when the p value was lower than 0.05.

Scatter plots and trend lines were calculated between CCT and applanation tonometry for the various sub-populations which included normal subjects and subjects from the other groups. The relationship between the two variables was evaluated with an r² regression coefficient.

**RESULTS**

The group of normal subjects was comprised of 61 subjects with an average age of 60.38 SD 10.21 years (table I). The group of patients with ocular hypertension included 131 subjects with an average age of 59.98 SD 8.85 years. The group of glaucoma suspects due to papillary morphology consisted of
62 subjects with an average age of 60.68 SD 10.05 years. The group with preperimetric glaucoma included 36 patients with an average age of 61.89 SD 10.53 years. No significant differences were observed related to age or improved corrected visual acuity between the normal group and the other three groups.

Table I shows mean values for visual acuity, IOP, excavation, automated perimetry and CCT in each group.

IOP and the excavation/vertical disk ratio assessed with stereophotographs were lower in the normal group than in the other three groups. As for AP rates, mean deviation was lower (more negative) in the normal group than in the ocular hypertension subjects (p<0.001) and the glaucoma suspects (p=0.037). SDM was greater in the normal subjects than in those with ocular hypertension (p=0.039). Despite these differences in perimetric rates, normal subjects, those with ocular hypertension and glaucoma suspects presented normal AP.

CCT differences were only found between the group with ocular hypertension and the normal group (p=0.009). The group with ocular hypertension presented the highest pachymetric values.

Figure 1 shows the scatter plot for CCT and IOP values in the normal group and the ocular hypertension group. A slight direct logarithmic relation was observed between CCT and IOP (r² value was 0.021).

Figure 2 shows the scatter plot for CCT and IOP values in the normal group and in glaucoma suspects due to papillary morphology. The trend line indicates a direct logarithmic regression with an r² value =0.0005.

Figure 3 contains the scatter plot for CCT and IOP values in the normal group and in preperimetric glaucoma (r² =0.0014). Just as in the previous case, we observed a slight direct logarithmic relation (r² =0.0014).

Table I. Clinical characteristics of the various study groups. Column p shows the results of Student’s test between the normal group and each one of the other groups

<table>
<thead>
<tr>
<th>Descriptive statistics</th>
<th>Normal groups</th>
<th>OHT</th>
<th>Glaucoma suspects due to papilla</th>
<th>Preperimetric glaucoma by SWAP</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean 60.38</td>
<td>SD 10.21</td>
<td>Mean 59.98</td>
<td>Mean 60.68</td>
<td>10.05</td>
</tr>
<tr>
<td>VA</td>
<td>0.89</td>
<td>0.10</td>
<td>0.91</td>
<td>0.89</td>
<td>0.13</td>
</tr>
<tr>
<td>Baseline IOP</td>
<td>14.30</td>
<td>2.28</td>
<td>22.98</td>
<td>22.63</td>
<td>3.30</td>
</tr>
<tr>
<td>E/D</td>
<td>0.30</td>
<td>0.16</td>
<td>0.41</td>
<td>0.69</td>
<td>0.10</td>
</tr>
<tr>
<td>MD</td>
<td>-1.29</td>
<td>2.42</td>
<td>-0.24</td>
<td>-0.50</td>
<td>1.31</td>
</tr>
<tr>
<td>SDM</td>
<td>1.42</td>
<td>1.59</td>
<td>1.03</td>
<td>1.00</td>
<td>0.73</td>
</tr>
<tr>
<td>Pachymetry</td>
<td>551.26</td>
<td>28.55</td>
<td>564.37</td>
<td>549.61</td>
<td>33.85</td>
</tr>
</tbody>
</table>

VA = improved corrected visual acuity; OHT= ocular hypertension; E/D excavation/vertical disk ratio in stereophotographs; SD=standard deviation, MD=mean deviation of conventional automated perimetry; SDM=standard deviation of the mean of conventional automated perimetry; H= statistically significant differences between the normal group and the ocular hypertension group; S=statistically significant differences between the normal group and glaucoma suspects; P=statistically significant differences between the normal group and preperimetric glaucoma; N=number.
plots of the various groups, the best $r^2$ regression coefficient was seen in the normal group and in the one of OHT ($r^2 = 0.021$), which indicates that 2.1% of the IOP variance would be predicted by changes in CCT.

This difficulty to establish a valid correction algorithm between IOP and CCT has led to the appearance of new ways of measuring IOP that are not so influenced by the CCT value, such as the dynamic contour tonometer and others (22-25). This opens new perspectives when assessing IOP, although the clinical applicability of these tonometers is still to be proven.

Various studies (4,20,26) have observed that eyes with less CCT have a greater risk of developing visual field losses in subjects with normotensive glaucoma. Lower CCT has also been highlighted as a risk factor for developing glaucoma (27-29). This is why CCT has become an important biometric factor and it is an essential component of examinations of glaucomatous patients.

In our study we have evidenced that patients who began presenting glaucomatous changes (glaucoma suspects and preperimetric glaucoma) had less CCT than the control group. With our results we cannot confirm that diminished CCT is a factor predisposing to the development of the disease. However, the ocular hypertension group presented thicker corneas than the others. Probably, many of the subjects included in the hypertensive group would stop being considered as such if an IOP correction algorithm was applied according to pachymeter values. These results are consistent with other studies (4,5), although some of them go even further. Herman et al (6) have suggested that CCT increases slowly in eyes with ocular hypertension and decreases slowly if IOP is reduced with topical medications, so that according to them, high IOP would lead to greater CCT and not the opposite.

To be able to establish more precisely the value of CCT in the development and progression of glau-
coma, new longitudinal studies with a higher number of cases are necessary.

REFERENCES


