Comparison of Ocular Response Analyzer Parameters in Chinese Subjects With Primary Angle-Closure and Primary Open-Angle Glaucoma

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Objectives: To evaluate corneal hysteresis (CH) and intraocular pressure (IOP) measured by the Ocular Response Analyzer in Chinese subjects with primary angle-closure glaucoma (PACG), assess their relationship with Goldmann applanation tonometry (GAT) measurements, and compare this with subjects with primary open-angle glaucoma (POAG) and normal controls.

Methods: In this prospective observational study, consecutive subjects with PACG and POAG without prior intraocular surgery were enrolled from glaucoma clinics. Normal subjects were recruited from an ongoing population-based study. One eye of each subject underwent standardized ocular examination and IOP measurement by GAT and the Ocular Response Analyzer. Corneal hysteresis and corneal-compensated IOP were compared between groups.

Results: Of the 443 subjects recruited, 131 had PACG, 162 had POAG, and 150 were normal. Corneal hysteresis was lower in PACG (9.1 mm Hg; 95% confidence interval [CI], 8.7 to 9.4 mm Hg) and POAG (9.5 mm Hg; 95% CI, 9.2 to 9.5 mm Hg) eyes compared with control eyes (10.4 mm Hg; 95% CI, 10.1 to 10.6 mm Hg; P < .001 for both), with no difference (P = .16) in CH found between PACG and POAG eyes. After adjusting for age, sex, and IOP measurement by GAT, CH persisted to be lower only in eyes with PACG in comparison with control eyes (9.4 vs 10.1 mm Hg; P = .006). Eyes with POAG had lower CH than control eyes but the difference was not statistically significant (9.6 vs 10.1 mm Hg; P = .06).

Conclusions: Corneal hysteresis was lower in eyes with glaucoma. After adjusting for age, sex, and IOP measurement by GAT, a persistently lower hysteresis was noted in eyes with PACG compared with other groups.

Arch Ophthamol. 2011;129(4):429-434
all subjects and the study had the approval of the ethics committee of the Singapore Eye Research Institute and was carried out according to the tenets of the Declaration of Helsinki. Consecutive subjects from a glaucoma clinic with PACG and POAG were enrolled. Glaucoma was defined as the presence of glaucomatous optic neuropathy (GON) (defined as loss of the neuroretinal rim with a vertical cup-disc ratio of >0.7 and/or notch-attributable to glaucoma) with an associated visual field defect, defined by the following: (1) glaucoma hemifield test result outside normal limits, (2) a cluster of 3 or more nonedge, contiguous points on the pattern deviation plot not crossing the horizontal meridian, with a probability of less than 5% of being present in age-matched control subjects (with at least 1 of the cluster points having a probability value of <1%), and (3) pattern standard deviation less than 0.05; these were repeatable on 2 separate occasions. Primary angle-closure glaucoma was defined as the presence of GON with corresponding visual field loss in association with a closed angle (presence of at least 180° of angle in which the posterior trabecular meshwork was not visible on nonindentation gonioscopy) and raised IOP and/or peripheral anterior synechiae (defined as abnormal adhesions of the iris to the angle that were present to the level of the anterior trabecular meshwork or higher). All subjects with PACG had undergone a laser iridotomy at least 1 month prior to enrollment in the study. Patients with POAG had GON and open angles and were in turn subdivided into high-tension glaucoma (HTG) and normal-tension glaucoma (NTG) groups, defined as follows:

- High-tension glaucoma was defined as GON, visual field defects consistent with glaucoma, IOP consistently higher than 21 mm Hg, and open angles on gonioscopy.
- Normal-tension glaucoma was defined as GON, visual field defects consistent with glaucoma, IOP that never exceeded 21 mm Hg during a diurnal phasing, and open angles on gonioscopy. All patients classified as having NTG had undergone at least 8 daytime diurnal IOP measurements recorded between 8 AM and 5 PM with noncontact air-puff tonometry (CT-80 Computerized Non-Contact Tonometer; Topcon, Tokyo, Japan).

Exclusion criteria included eyes with a history of intracocular surgery, laser iridotomy within 30 days prior to enrollment, secondary glaucoma such as uveitic or neovascular glaucoma, corneal decompensation or corneal abnormalities that prevented accurate IOP measurement, previous trauma, and other nonglaucomatous optic neuropathies. Subjects with concurrent or prior use of glaucoma medications were not excluded.

A control group of normal subjects (defined as having an IOP ≤21 mm Hg with open angles, healthy optic nerves and normal visual fields, no previous surgery, and no family history of glaucoma) were recruited. These subjects were derived from an ongoing glaucoma clinic with PACG and POAG. Fifty-nine normal eyes were included in the study. No difference was noted in the mean age among the glaucoma subtypes (PACG vs POAG; P = .08), but the mean age of the control subjects was lower compared with those with PACG (P < .001) and POAG (P < .001). There were more women (73 of 131; P < .001) in the PACG group and more men (111 of 162; P < .001) in the POAG group. Eyes with PACG were less myopic than both POAG (P < .001) and control (P < .003) eyes. Mean CCT was higher in control eyes compared with POAG (P = .012) and POAG (P < .001) eyes. Bland-Altman plots (Figure 1) in-

A total of 443 eyes of 443 Chinese subjects were included in the study. This consisted of 131 subjects with PACG, 162 subjects with POAG (71 HTG and 91 NTG), and 150 normal eyes. The demographics and clinical and ocular characteristics of the study population are shown in Table 1. No difference was noted in the mean age among the glaucoma subtypes (PACG vs POAG; P = .08), but the mean age of the control subjects was lower compared with those with PACG (P < .001) and POAG (P < .001). There were more women (73 of 131; P < .001) in the PACG group and more men (111 of 162; P < .001) in the POAG group. Eyes with PACG were less myopic than both POAG (P < .001) and control (P < .003) eyes. Mean CCT was higher in control eyes compared with POAG (P = .012) and POAG (P < .001) eyes. Bland-Altman plots (Figure 1) in-

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The glaucoma groups (PACG: GAT and CH were not correlated in normal eyes (P = .20), and a weak negative correlation was noted among control eyes (r = -.05 mm Hg; 95% CI, −6.3 to 6.2 mm Hg).

Adjusted for age, sex, and IOP-GAT values.

We found CH to be lower in both PACG (9.1 mm Hg; 95% CI, −6.0 to 6.2 mm Hg) and POAG (9.5 mm Hg; 95% CI, 9.2 to 9.5 mm Hg) eyes compared with control eyes (10.4 mm Hg; 95% CI, 10.1 to 10.6 mm Hg). No correlation was noted between IOPcc and CCT in all groups. The correlation between CH and CCT was moderate in all groups (Figure 2).

On multivariate analysis (Table 3), CH was associated significantly with IOP-GAT in the PACG (β = −0.15; P = .01) and POAG (β = −0.09; P < .05) groups and with CCT in all 3 groups (β = 0.02; P < .001 for all) after adjusting for factors like age, sex, IOP-GAT, refractive error, corneal curvature, axial length, systolic blood pressure, and diastolic blood pressure. Corneal hysteresis was associated with age in control eyes (β = −0.04; P < .01) and with corneal curvature in POAG (β = −1.7; P < .01) and control (β = −1.7; P < .01) eyes.

A subanalysis of POAG (71 eyes with HTG and 91 eyes with NTG) is summarized in Table 4. Mean CH in the NTG group was higher than the HTG group but this difference was not significant.

To our knowledge, this study is the first report of ORA parameters in Asian individuals comparing PACG and POAG against normal subjects. We found CH to be lower and CH was noted in all groups (PACG r = −0.709; P < .001; POAG: r = −0.647; P < .001; control eyes: r = −0.547; P < .001). No correlation was noted between IOPcc and CCT in all groups. The correlation between CH and CCT was moderate in all groups (Figure 2).

On multivariate analysis (Table 3), CH was associated significantly with IOP-GAT in the PACG (β = −0.15; P = .01) and POAG (β = −0.09; P < .05) groups and with CCT in all 3 groups (β = 0.02; P < .001 for all) after adjusting for factors like age, sex, IOP-GAT, refractive error, corneal curvature, axial length, systolic blood pressure, and diastolic blood pressure. Corneal hysteresis was associated with age in control eyes (β = −0.04; P < .01) and with corneal curvature in POAG (β = −1.7; P < .01) and control (β = −1.7; P < .01) eyes.

A subanalysis of POAG (71 eyes with HTG and 91 eyes with NTG) is summarized in Table 4. Mean CH in the NTG group was higher than the HTG group but this difference was not significant.

**COMMENT**

Table 1. Demographics and Baseline Characteristics of Subjects With Primary Glaucoma and Control Subjectsa

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PACG (n=131)</th>
<th>POAG (n=162)</th>
<th>Controls (n=150)</th>
<th>P Valueb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>67.1 (9.8)</td>
<td>64.6 (10.5)</td>
<td>54.7 (8.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Female, %</td>
<td>55.7</td>
<td>31.5</td>
<td>48.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Spherical equivalent, D</td>
<td>−0.3 (1.9)</td>
<td>−1.7 (3.2)</td>
<td>−1.2 (2.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Corneal curvature, mm</td>
<td>7.6 (0.28)</td>
<td>7.6 (0.22)</td>
<td>7.6 (0.24)</td>
<td>.64</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>23.0 (0.89)</td>
<td>24.6 (1.5)</td>
<td>24.0 (1.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>IOP-GAT, mm Hg</td>
<td>16.5 (4.4)</td>
<td>14.9 (3.2)</td>
<td>14.4 (2.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CCT, μm</td>
<td>540.8 (39.4)</td>
<td>537.9 (32.3)</td>
<td>549.4 (32.5)</td>
<td>.01</td>
</tr>
</tbody>
</table>

Abbreviations: CCT, central corneal thickness; D, diopter; IOP-GAT, intraocular pressure measured by Goldmann applanation tonometry; PACG, primary angle-closure glaucoma; POAG, primary open-angle glaucoma.

a Adjusted for age, sex, and IOP-GAT values.

Table 2. Ocular Response Analyzer Parameters in Subjects With Primary Glaucoma and Control Subjectsa

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PACG (n=131)</th>
<th>POAG (n=162)</th>
<th>Controls (n=150)</th>
<th>P Valueb</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP-GAT</td>
<td>16.5 (17.2)</td>
<td>14.9 (14.5)</td>
<td>14.4 (14.9-14.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>IOPcc</td>
<td>18.1 (17.2)</td>
<td>15.9 (15.3)</td>
<td>14.4 (13.9-14.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>IOPg</td>
<td>16.4 (16.7)</td>
<td>14.4 (13.8)</td>
<td>13.7 (13.2-14.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CH</td>
<td>9.1 (8.7-9.4)</td>
<td>9.5 (9.2-9.5)</td>
<td>10.4 (10.1-10.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Adjusted CHd,e</td>
<td>9.4 (9.1-9.7)</td>
<td>9.6 (9.3-9.8)</td>
<td>10.1 (9.8-10.4)</td>
<td>.006</td>
</tr>
</tbody>
</table>

Abbreviations: CH, corneal hysteresis; CI, confidence interval; IOPcc, corneal-compensated intraocular pressure; IOPg, Goldmann-correlated intraocular pressure; IOP-GAT, intraocular pressure measured by Goldmann applanation tonometry; PACG, primary angle-closure glaucoma; POAG, primary open-angle glaucoma.

a Adjusted for age, sex, and IOP-GAT values.

b Adjusted CH (Bonferroni corrected): control eyes vs PACG eyes, P < .01; control eyes vs POAG eyes, P < .01; and PACG eyes vs POAG eyes, P = .16.
c Mean CH (Bonferroni corrected): control eyes vs PACG eyes, P < .006; control eyes vs POAG eyes, P = .6; and PACG eyes vs POAG eyes, P = .7.
d Adjusted for age, sex, and IOP-GAT values.

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Corneal hysteresis was negatively associated with age in normal subjects and is in agreement with prior reports. This association, however, was not seen in the glaucoma subtypes in this study. Kotecha et al have reported an age-related decrease in corneal constant factor (a parameter derived from CH) in their sample of eyes. These differences may be because we did not exclude subjects who were using IOP-reducing medications. The role of medications influencing CH has been contemplated and needs to be explored further.1

There are few studies to compare our findings. Sun et al22 also reported a lower CH in their group of 40 Chinese subjects with chronic PACG with uncontrolled IOP at initial presentation. They reported a recovery of CH in eyes with PACG after IOP reduction but it continued to remain lower than normal controls in their study. In a subanalysis of POAG (HTG and NTG) eyes, we found a marginally higher (but not statistically significant) CH value in eyes with NTG compared with HTG. Prior reports about differences in CH between NTG and POAG (HTG) groups have been variable. Ang et al23 reported a higher CH among NTG eyes but Shah et al24 found a lower CH when compared with subjects with HTG.

Figure 1. Bland-Altman plots for agreement between corneal-compensated intraocular pressure (IOPcc) in comparison with intraocular pressure measured by Goldmann applanation tonometry (IOP-GAT). A, Primary angle-closure glaucoma: positive mean difference of 1.6 mm Hg; 95% confidence interval, –6.4 to 9.6 mm Hg. B, Primary open-angle glaucoma: positive mean difference of 1.0 mm Hg; 95% confidence interval, –5.3 to 7.4 mm Hg.
tions on corneal biomechanical properties is unknown. For example, prostaglandin eye drops are known to have effects on the extracellular matrix of ocular tissues via expression of matrix metalloproteinases. It is thus possible that these eye drops may have an influence on corneal biomechanics. Additionally, all our PACG cases had previous laser iridotomy, which was performed at least 1 month before study recruitment. Whether this has an effect on the ORA measurements is not known. Finally, the sample size was relatively small and hence statistical values may have to be interpreted with caution.

In summary, we found lower CH in Asian eyes with glaucoma (PACG and POAG) compared with control eyes and no difference in CH between PACG and POAG. After adjusting for age, sex, and IOP-GAT, a persistently lower hysteresis was noted in eyes with PACG. Further evaluation is required with respect to the clinical implications of these factors in specific glaucoma subtypes.

Submitted for Publication: March 8, 2010; final revision received April 26, 2010; accepted June 16, 2010.

Table 3. Multiple Linear Regression Model of the Factors Associated With CH

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PACG Unadjusted</th>
<th>PACG Controls</th>
<th>POAG Unadjusted</th>
<th>POAG Controls</th>
<th>Controls Unadjusted</th>
<th>Controls Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>−0.04 (−0.08 to −0.01)</td>
<td>−0.05 (−0.07 to −0.02)</td>
<td>−0.03 (−0.08 to 0.01)</td>
<td>−0.01 (−0.04 to 0.01)</td>
<td>−0.04 (−0.07 to −0.01)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>−0.02 (−0.71 to 0.67)</td>
<td>0.38 (−0.09 to 0.85)</td>
<td>0.94 (0.46 to 1.41)</td>
<td>−0.25 (−1.2 to 0.69)</td>
<td>0.27 (−0.27 to 0.82)</td>
<td>0.46 (−0.19 to 0.70)</td>
</tr>
<tr>
<td>IOP-GAT</td>
<td>−0.27 (−0.31 to −0.22)</td>
<td>−0.24 (−0.29 to −0.19)</td>
<td>−0.28 (−0.35 to −0.21)</td>
<td>−0.15 (−0.26 to −0.03)</td>
<td>−0.09 (−0.16 to −0.02)</td>
<td>0 (−0.32 to 0.17)</td>
</tr>
<tr>
<td>CCT</td>
<td>0.17 (0.09 to 0.02)</td>
<td>0.01 (0.01 to 0.02)</td>
<td>0.02 (0.01 to 0.03)</td>
<td>0.02 (0.01 to 0.02)</td>
<td>0.02 (0.01 to 0.02)</td>
<td>0.02 (0.01 to 0.02)</td>
</tr>
<tr>
<td>Refractive error</td>
<td>−0.11 (−0.29 to 0.30)</td>
<td>0 (−0.06 to 0.07)</td>
<td>0.01 (−0.09 to 0.7)</td>
<td>−0.23 (−0.57 to 0.11)</td>
<td>0.09 (0.03 to 0.22)</td>
<td>0.01 (−0.11 to 0.13)</td>
</tr>
<tr>
<td>Corneal curvature</td>
<td>−1.0 (−2.2 to 0.18)</td>
<td>−0.5 (−1.5 to 0.44)</td>
<td>−2.1 (−3.0 to −1.1)</td>
<td>−0.9 (−3.4 to 1.5)</td>
<td>−1.7 (−3.0 to −0.4)</td>
<td>−1.7 (−2.6 to −0.16)</td>
</tr>
<tr>
<td>Axial length</td>
<td>0 (−0.39 to 0.38)</td>
<td>−0.02 (−0.17 to 0.12)</td>
<td>−0.25 (−0.45 to −0.06)</td>
<td>0.2 (−1.1 to 0.58)</td>
<td>0.16 (−0.13 to 0.47)</td>
<td>−0.15 (−0.40 to 0.30)</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>−0.01 (−0.03 to 0.0)</td>
<td>−0.01 (−0.02 to 0.0)</td>
<td>−0.01 (−0.03 to 0.1)</td>
<td>0 (−0.02 to 0.03)</td>
<td>0 (−0.01 to 0.01)</td>
<td>0 (−0.02 to 0.01)</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>0 (−0.05 to 0.04)</td>
<td>−0.01 (−0.04 to 0.0)</td>
<td>−0.01 (−0.05 to 0.01)</td>
<td>0 (−0.06 to 0.07)</td>
<td>−0.01 (−0.04 to 0.01)</td>
<td>0 (−0.02 to 0.02)</td>
</tr>
</tbody>
</table>

Abbreviations: BP, blood pressure; CCT, central corneal thickness; CH, corneal hysteresis; CI, confidence interval; IOP-GAT, intraocular pressure measured by Goldmann applanation tonometry; PACG, primary angle-closure glaucoma; POAG, primary open-angle glaucoma.

Adjusted for all variables in the Table.

Correlations significant at P < .05.

Table 4. Comparative Analysis of Ocular Response Analyzer Parameters Between POAG Subgroups: HTG and NTG

| Parameter       | HTG (n=71) | NTG (n=91) | P Value
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>63.3 (10.3)</td>
<td>65.3 (10.2)</td>
<td>.78</td>
</tr>
<tr>
<td>IOP-GAT, mm Hg</td>
<td>15.8 (3.7)</td>
<td>14.2 (2.5)</td>
<td>.05</td>
</tr>
<tr>
<td>IOPcc, mm Hg</td>
<td>16.8 (4.4)</td>
<td>15.2 (2.9)</td>
<td>.001</td>
</tr>
<tr>
<td>IOPg, mm Hg</td>
<td>15.3 (4.1)</td>
<td>13.7 (2.6)</td>
<td>.001</td>
</tr>
<tr>
<td>CH, mm Hg</td>
<td>9.4 (1.5)</td>
<td>9.6 (1.3)</td>
<td>.10</td>
</tr>
</tbody>
</table>

Abbreviations: CH, corneal hysteresis; HTG, high-tension glaucoma; IOPcc, corneal-compensated intraocular pressure; IOPg, Goldmann-correlated intraocular pressure; IOP-GAT, intraocular pressure measured by Goldmann applanation tonometry; NTG, normal-tension glaucoma; POAG, primary open-angle glaucoma.

N = 162.

P Values determined using an independent-samples t test.
REFERENCES


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