Accuracy of Goldmann, Ocular Response Analyser, Pascal and TonoPen XL Tonometry in Keratoconic and Normal Eyes

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Aim

To investigate which tonometer is practical and accurate to use in routine clinical practise for established keratoconus (KC).

Methods

A prospective study of 118 normal and 76 keratoconic eyes where intraocular pressure (IOP) was measured in random order with the Goldman applanation tonometer (GAT), Pascal® dynamic contour tonometer (DCT), Reichert® ocular response analyser (ORA) and Tono-Pen® XL. Corneal hysteresis (CH) and corneal resistance factor (CRF), as calculated by the ORA, were recorded. Central corneal thickness (CCT) was measured using an ultrasound pachymeter.

Results

The difference in IOP values between instruments was highly significant in both study groups ($p<0.001$). All other IOP measures were significantly higher than GAT except the Goldmann corrected IOP, IOPg, as measured by ORA, in normals and CH corrected IOP, IOPcc measures in KC. CCT, CH and CRF was significantly less in KC ($p<0.001$). Apart from the DCT, all techniques tended to measure IOP higher in eyes with thicker corneas.

Conclusion

The DCT and the ORA's IOPcc are currently the most appropriate tonometers to use in KC. Corneal factors such as CH and CRT may be of more importance than CCT in causing inaccuracies in applanation tonometry techniques.

Central corneal thickness (CCT), corneal curvature, axial length and the structural rigidity of the cornea are well-known sources of error in conventional applanation tonometry[1-4]. In keratoconus (KC), where there is progressive conical distortion with irregular astigmatism, axial stromal thinning and apical protrusion, measuring intraocular pressure (IOP) is known to be challenging [4-7]. Changes in ocular rigidity associated with KC influencing IOP measurements was postulated by Brooks et al [6]. Various groups studying corneal hysteresis and resistance factor have confirmed this recently. [7-9]

This study compared the Goldmann applanation tonometer (GAT), Pascal® dynamic contour tonometer (DCT), Reichert® ocular response analyser (ORA) and TonoPen® XL, in normal and keratconic eyes. The slit-lamp mounted GAT (Haag-Streit, Bern, Switzerland) is still the most widely used tonometer and was designed to measure IOP in subjects with an average corneal thickness.[3]

The ORA (Reichert Ophthalmic Instruments, Buffalo, USA) is a fully automated stand-alone non-contact tonometer with an electro-optical system that scans the central cornea. It uses a dynamic bi-directional applanation process: a precisely measured air pulse deforms the cornea inwards, past the applanation point. After the applanation point is detected the air is turned off the cornea allowed to return to normal (back through the applanation point again). Two independent pressure values are derived from these inward and outward applanation points. It then displays two IOP readings: IOPg and IOPcc. IOPg, is the average of the

two applanation pressure points, which is termed the Goldmann-correlated IOP value. IOPcc is a corneal compensated IOP value, where the difference in the two pressure readings is calculated and termed corneal hysteresis (CH) and is used to calculate the IOPcc. CH is thought to be due to the viscous damping by the cornea. The corneal resistance factor (CRF) is derived in this process and is a measurement of the both the viscous and elastic resistance to the air pulse.[9-12]

The Pascal dynamic contour tonometer (DCT) (Swiss Microtechnology AG, Bern, Switzerland) is a contemporary, slit-lamp mounted digital device that uses single use, disposable caps. It provides a direct trans-corneal measurement of IOP and detects the ocular pulse amplitude (OPA). The DCT measures diastolic IOP using the principle of contour matching with the built-in miniature SensorTip™ utilizing a solid-state pressure sensor. It displays the average diastolic IOP recorded and the mean OPA via a digital liquid crystal display. Adding the DCT's IOP reading to the OPA will give the systolic IOP.

The TonoPen XL (Reichert Ophthalmic Instruments, Buffalo, USA) is a portable hand-held instrument. It is based on the Mackay-Marg[13] principle and utilizes micro strain gauge technology. A 1.5mm transducer tip, covered by a disposable single-use cap, contacts the cornea, and displays the average of four independent readings.

The aim of this study was to assess the agreement of IOP measurement between these 4 tonometers and the effect of CCT, CH and CRF on measures of IOP to identify which is the best tonometer to use in keratoconic patients.

Materials and Methods

KC participants involved in this prospective non-interventional study were recruited from a specialised corneal clinic. Seventy-six eyes from 39 subjects were included, 25 males and 14 females, with a mean age of 31.0 ±12.5 years (range 18-54years). All had a clinical diagnosis of KC made by an experienced corneal specialist (SS). The diagnosis was on the presence of a combination of clinical features being present: external signs such as Munson's sign or Rizzuti's sign; slit-lamp biomicroscopy signs such as stromal thinning, conical protrusion, Fleischer's ring, Vogt's striae, enlarged corneal nerves; and a characteristic retinoscopy reflex. The diagnosis was confirmed topographically with the Orbscan II (Bausch & Lomb Surgical, Rochester, New York, USA). Any eyes with a history of intraocular surgery or previously recruited for clinical studies at our unit were excluded.

Healthy subjects were recruited from the staff and relatives of patients attending outpatient clinics at the Heart of England NHS Foundation Trust between January 1st and April 1st, 2006. One hundred and eighteen normal eyes from 28 males and 35 females were analysed. The mean age of this group was 66.9 ± 15.5 standard deviation (SD) years (range 31-92 years). Only adults over the age

of 18 years were selected and all subjects had normal corneas based on slit-lamp biomicroscope examination, with no previous ocular history, trauma or surgery.

Local ethics committee approval was obtained for this study. Measurements were only taken after informed consent was taken, and the tenets of the declaration of Helsinki were observed.

To minimize the potential confounding effect of diurnal variation in IOP, all study measurements were taken in the morning. The subject was seated and topical proxymethacaine 0.5% and fluorescein (Bausch & Lomb, Rochester, New York, USA) was instilled into the study eye. Measurements were then taken, by 3 trained ophthalmologists, using the 4 tonometers. They were used in random order to allow for any variation in IOP caused by applanation. The various tonometry methods were performed according to normal clinical practice and manufacturer's guidelines, as described in referenced studies (GAT [3], DCT [8], ORA [10] and TonoPen[13]). When the GAT was used the mid-point between the systolic and diastolic IOP was recorded.

CCT measurements were recorded with a hand held ultrasonic pachymeter (DGH –550, DGH Technology Inc, Exton, PA, USA) by gently placing the

pachymeter probe in the centre of the cornea in an undilated eye. The mean of three readings was recorded as the CCT value.

Statistical analysis of data

Excel (Microsoft Corporation, Redmond, WA, USA) and SPSS (v12.0.1 Chicago, Illinois, USA) were used to analyze and present data. Pearson's correlations were used to assess the dependence of the tonometers on CCT, with stepwise modeling to determine combined factor variance. Bland-Altman[14] plots were constructed for comparisons between GAT and the other tonometry techniques. Analysis of variance was used to compare tonometer measures, with the patient's eye as a with-in subject variable to account for dependant measure bias. The level of significance was chosen at $p<0.05$.

Results

Distribution of IOP is shown in box and whisker plots for KC (figure 1a) and the normal group (figure 1b) with each tonometry technique used. The difference in IOP between techniques was highly significant in both groups (repeated measures ANOVA $F=6.4$, $p<0.001$ in normals and $F=25.3$, $p<0.001$ in KC). DCT and TonoPen measures were significantly higher than GAT in both groups. (KC mean difference $\pm$ 95% confidence interval: -2.7 $\pm$6.0 mmHg (DCT) and -3.6 $\pm$ 10.1 mmHg (TonoPen)). In the KC group the IOPcc had the greatest concordance with GAT (-0.4 $\pm$ 8.5 mmHg, table one), however the values were

wide spread. IOP values were lower in keratoconics than normals with all instruments ($p < 0.001$) except ORA IOPcc ($p = 0.11$) and TonoPen ($p = 0.40$; Bonferroni correction for multiple testing adjusting the significance level to <0.01).

Table one: Comparison of the GAT, ORA, DCT and TonoPen tonometers in IOP values and relationship to corneal structural characteristics.

	GAT	ORA		DCT	Tono-Pen®XL
		IOPg	IOPcc		
Difference from GAT (mean ± S.D.)	-	2.0 ± 5.6***	-0.4 ± 8.5**	-2.7 ± 6.0***	-3.6 ± 10.1***
Relationship with CCT (r)	0.231*	0.357**	0.188	-0.070	0.187
Relationship with CH (r)	0.138	0.167	-0.474***	0.203	-0.073
Relationship with CRF (r)	0.372**	0.631***	0.022	0.358**	0.147

*** p<0.05; ** p<0.01; *** p<0.001**

Paired T-test analysis (with a Bonferroni correction for multiple testing adjusting the significance level to <0.013) showed GAT readings were significantly different for all measures except IOPg in the normal group and significantly different from all measures except IOPcc in KC (difference 2.0 ± 5.6 mmHg; figure 2).

Studying the Bland-Altman plots (figure 2), the KC group's trend line shows that the DCT has no bias with IOP, whereas IOPcc, IOPg and TonoPen tend to overestimate IOP at lower IOPs and underestimate IOP at higher IOPs compared to GAT.

There was no difference with the eye measured (right or left) in healthy eyes and KC respectively ($F = 0.01$, $p = 0.0940$; $F = 1.6$, $p = 0.218$) or any interaction between the IOP measurement technique and eye measures ($F = 1.4$, $p = 0.221$;

F = 0.9, p = 0.484).

The mean (± SD) CCT in normals was 539.9 ± 36.0 microns (range 434-655 microns). This was significantly thicker than the KC group (453.0 ± 55.8 microns; range 342-543 microns) ($p < 0.001$). Analyzing the effect of CCT on IOP measurements in KC (figure 3) shows that, apart from the DCT, all techniques tended to measure IOP higher in eyes with thicker corneas, significantly so in GAT and IOPg measures. A summary of all devices relationships with CCT, CH and CRF is shown in Table 1.

The mean CH in normals (10.6 ± 2.2 mmHg; range 5.3-19.6 mmHg) was significantly ($p < 0.001$) greater than in the keratoconus group (8.7 ± 2.2 mmHg; range 3.1-14.3 mmHg). As expected the IOPcc is inversely related to CH, whereas all the other tonometry techniques were unaffected (table 1). CRF mean in normals (10.0 ± 2.5 mmHg; range 0.2-18.9 mmHg) was also significantly ($p < 0.001$) greater than in KC (6.9 ± 2.4 mmHg; range 1.7-13.3 mmHg). GAT, DCT and IOPg are significantly influenced by CRF (table 1) whereas IOPcc and TonoPen showed minimal relationship with CRF. The 3 corneal factors were investigated using multivariate generalized estimating equation models (Table 2).

Table two: Multivariate comparison of the GAT, ORA, DCT and TonoPen tonometers when all the corneal factors (corneal central thickness (CCT), corneal hystersis (CH) and corneal resistance factor (CRF)) were modelled.

	GAT	**ORA IOPg**	**ORA IOPcc**	**DCT**	**TonoPen ®XL**
Model	12.35-1.00CH+1.25CRF	2.99 +1.05CRF	24.30-3.44CH+2.80CRF	21.276+1.17 CRF-0.02CCT-0.73CH	19.15-1.38CH+1.35CRF
Model relationship (r)	0.530***	0.631***	1.00***	0.510***	0.436**

*** p<0.05; ** p<0.01; *** p<0.001**

Occasionally the 3 automated devices were unable to take a measurement. The number of missed IOP results from the each group from the DCT, ORA and TonoPen were 5, 2 and 8 eyes in healthy eyes and 2, 7 and 6 eyes in keratoconics, respectively (with no apparent consistency between the eyes which could not be measured with one technique or another).

Discussion

In the search of a more precise and user-friendly tonometer, manufactures have been challenged with developing an ideal device that would be unaffected by operator bias, CCT, corneal topography and rigidity, and be non-invasive; additional qualities for this futuristic device is that it has to be easy to use, cost-effective and minimize the risk of cross-contamination or prion protein transfer.[15] KC provides an extreme testing ground, as the corneas are abnormal, thin and their topography is altered.

In this study, the tonometers were used in random order to prevent bias in the average IOP reading with each instrument due to applanation. Topical proxymethacaine 0.5% and fluorescein drops were used to anaesthetize the cornea before any measurements were taken; this prevented any bias from change in the CCT or IOP due to topical anaesthetic medications that have previously been reported.[16-19] Another possible limitation of this study is the difference in the average age of the KC group compared to normals, however Doughty and Zaman [1] reported, in their meta-analysis of the world literature, there was no obvious age-dependent difference in corneal thickness.

The use of both eyes in statistical analysis remains controversial, however this was accounted for in ANOVA analysis by making eye a within subject variable. It is also of note that KC tends to be an asymmetric disease [20]. We acknowledge the degree of ectasia was not recorded in this study and is therefore a confounding factor. Additional investigations into the severity of ectasia compared to the biomechanical values are likely to be reported in the future.

All the tonometers used were compared to GAT as the latter is used almost universally in routine practice. The IOPg readings in normals showed the most agreement with GAT readings. Interestingly in KC, IOPcc measures showed the most agreement with GAT. IOPg tended to read lower than GAT in KC whereas

DCT, IOPcc and TonoPen measured higher (all tonometers read significantly higher in normals).

In both the Kc and normal groups studied, the TonoPen had the highest mean IOP value and there was a low correlation between IOP and CCT (r=0.19 in KC and normals). This is similar to other reports that the TonoPen tends to over-estimate IOP, but is relatively independent of CCT.[21,22] The GAT, ORA and TonoPen measured higher IOPs in eyes with thicker corneas. The DCT appeared not to be influenced by CCT. This is similar to the findings of Kaufmann et al [23] and Pepose et al [24] who found that IOP measurements from the DCT were not significantly changed pre- and post Laser In Situ Keratomileusis, signifying that the DCT is relatively independent of CCT and other corneal biomechanical factors.

In comparing the normals with KC, the KC corneas were thinner and had lower CH and CRF values resulting in lower IOP readings, which confirms previous reports [9,25]. Hysteresis has been shown to be a moderately independent corneal property [9-12,26] and its measurement has valid clinical implications as shown by Congdon et al [26] who found that lower CH values were associated with progressive field worsening in 230 subjects with glaucoma. More recently it has been postulated that CH may have a diagnostic role in early KC. [9,24] As expected IOPcc was inversely related to CH, since that value is derived from CH, whereas all the other tonometry techniques were not significantly affected by CH.

In contrast, GAT, DCT and IOPg were significantly influenced by CRF. Only TonoPen measures showed a minimal relationship with both CH and CRF. Interestingly, when all the corneal factors were modelled (table 2), CCT was found to be a weak to non-important factor with all instruments. CRF accounted for 12% of the variance in CCT (r=0.344), with no additional benefit of considering CH. CH and CRT may be of more importance than CCT in causing inaccuracies in applanation tonometry techniques and future studies may help to explore this.

ORA, DCT and TonoPen are objective (automatic fire and digital readout) so they are not influenced by operator bias. However they failed to measure in 5%, 4% and 7% of eyes, respectively. The TonoPen and other tonometers, such as the rebound tonometer can be used to measure IOP centrally and in the periphery which can be useful when presented with corneal pathology.[15,27,28] Hence access to alternative tonometers in clinical practice remains important.

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This study highlights the advantages and limitations of four devices and encourages the user to be cognisant of these in relation to the parameters of CCT, CH and CRF (Table 1 and 2). It is possible that the accuracy of these devices is similar in other conditions that have thin corneas, such as low-tension glaucoma and corneas that have undergone laser refractive surgery. Although no direct comparison can be drawn, further investigations would clarify this.

The TonoPen XL, although relatively independent of all three parameters investigated (CCT, CH and CRF), tends to overestimate IOP compared to GAT, in both normal and KC eyes, which is not ideal. The DCT showed no bias when compared to mean IOP measurements in the Bland-Altman plots (Figure 2), it was also not affected by CCT and CH, however the IOP values tended to by higher when compared to GAT. The ORA measures, IOPg and IOPcc, were found to be suitable in comparison to the GAT in normals and KC respectively. IOPcc was also relatively independent of CCT and CRF. Therefore the DCT and ORA (IOPcc) are probably the most accurate tonometers to use in KC at present.

Legend to figures

Figure 1: Range of IOP in (A) keratoconics and (B) normals for GAT, ORA IOPg, ORA IOPcc, DCT and TonoPen tonometers. Box limits indicate 1 S.D., black line the median, white line the mean, whiskers the 95% confidence interval and dot the data points beyond the 95% confidence interval.

Figure 2: The difference for keratoconics between tonometry with ORA IOPg, ORA IOPcc, DCT and TonoPen, and GAT, compared to their mean. Solid line indicates the mean, dashed lines the 95% confidence interval and the grey dashed line the bias. N=76.

Figure 3: The correlation for keratoconics between central corneal thickness (CCT) and ORA IOPg, ORA IOPcc, DCT and TonoPen. N=76.

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Abbreviations

CCT, central corneal thickness; CH, corneal hysteresis; CRF, corneal resistance factor; DCT, dynamic contour tonometer; GAT, Goldmann applanation tonometer; IOP, intraocular pressure; IOPcc, corneal compensated IOP measurement; IOPg, Goldmann corrected IOP measurement; KC, keratoconus; ORA, ocular response analyzer; OPA, ocular pulse amplitude.