Goldmann Applanation Tonometry Versus Ocular Response Analyzer for Intraocular Pressure Measurements in Keratoconic Eyes

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Purpose: To compare intraocular pressure (IOP) measurements obtained with the Goldmann applanation tonometer (GAT) and the ocular response analyzer (ORA) in patients with keratoconus (KC) and analyze their dependence on ocular anatomic parameters.

Methods: Patients with KC were recruited prospectively. IOP was measured using GAT and ORA. The ORA provided a Goldmann correlated IOP (IOPg) and a corneal correlated IOP (IOPcc). Assessment of refractive status, visual acuity, axial length, corneal topography, and pachymetry was done.

Results: Fifty-nine eyes of 59 patients with KC (39 men, 20 women; mean age: 27.8 ± 6.8 years) were included. The differences in mean IOP values between GAT (10.9 ± 2.0 mm Hg) and IOPg (9.5 ± 2.8 mm Hg) and between GAT and IOPcc (13.3 ± 2.5 mm Hg) were statistically significant (all $P < 0.001$). Both pressure measurements provided by the ORA showed significant correlation with corneal curvature. No significant effect of corneal thickness on any of the pressures was observed.

Conclusions: IOP measurements taken with GAT and ORA in keratoconic eyes were significantly different. Although IOPcc was significantly higher, IOPg was significantly lower than GAT IOP. Unlike GAT measurements, ORA readings seemed to be affected mainly by corneal curvature. As a result of described differences, we suggest these devices should not be used interchangeably but rather in a complementary fashion to assess IOP in keratoconic eyes.

Key Words: keratoconus, intraocular pressure, Goldmann applanation tonometer, ocular response analyzer

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Achieving improved precision in measurement of intraocular pressure (IOP) has received increased interest over the last years. Growing understanding of the dependency of IOP measurements on various corneal properties, including corneal thickness, viscoelasticity, and curvature[1–5] has led to search for new methods to measure "true" IOP that is independent of these factors.

Keratoconus (KC) is an ectatic progressive corneal disorder characterized by irregular astigmatism, corneal thinning, and altered corneal viscoelasticity.[3,6] Consequently, accurate IOP measurement is even a greater challenge in keratoconic eyes than in healthy eyes.[2,3,7–9] Still, such accuracy is required when treating patients with KC and ocular hypertension or glaucoma. For over half a century, the Goldmann applanation tonometer (GAT) has been the gold-standard device for measuring IOP in everyday practice. Goldmann and Schmidt[10] calculations for the GAT were based on the law of Imbert-Fick, assuming an ideal cornea that was a dry, perfectly flexible, and infinitely thin spherical surface. Various correction algorithms have been proposed to compensate for corneal nonideality, but their inability to take into account diverse corneal structural and biomechanical properties make them unsuitable for clinical practice.[11]

The Ocular response analyzer (ORA; Reichert, Inc, Depew, NY) provides noncontact assessment of IOP as given by the parameters Goldmann correlated IOP (IOPg) and corneal compensated IOP (IOPcc) and in vivo measurements of corneal biomechanical parameters, namely, corneal hysteresis (CH) and corneal resistance factor (CRF). Reproducibility[12] and detailed description[13] of this instrument have been previously published. Briefly, the instrument measures corneal response to indentation by a rapid air pulse using an electro-optical system. The air puff causes the cornea to move inward, passing a defined point of applanation, and move into a slight concavity. After reaching the pressure peak, the pressure of the air pulse decreases, and the cornea returns to its normal configuration, passing again the defined point of applanation. The electro-optical system monitors this entire process and calculates the above parameters. CH represents the absolute difference between the 2 pressure values causing force-in (P1) and force-out (P2) applanations and provides a measure of viscous damping of the cornea. IOPg is the average of the 2 IOP measurements at the applanation points. IOPcc is a pressure measurement that uses the information provided by CH to provide an IOP that is less affected by CCT or corneal curvature.[13] IOP measurement by ORA incorporates corneal biomechanical parameters; therefore, we hypothesized that it could be used to augment our ability to assess IOP in eyes with KC.

Therefore, the aim of the present study was to compare IOP measurements by GAT and ORA in keratoconic eyes.

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Additionally, we assessed the influence of anatomic and physiologic corneal and other ocular characteristics on the measurement of IOP with 2 tonometers.

MATERIALS AND METHODS

Patients with KC were prospectively recruited from the Outpatient Ophthalmology Clinic of the Assaf Harofeh Medical Center. This study was approved by the Institutional Review Board of Assaf Harofeh Medical Center, and a written informed consent was obtained from each subject. The diagnosis of KC was made by an experienced corneal specialist and based on a combination of the following clinical features: slit-lamp biomicroscopy signs such as Fleisher ring, corneal thinning, Vogt striae, and enlarged corneal nerves, scissoring reflex on retinoscopy and characteristic external clinical findings such as Rizzuti and Munson signs. The diagnosis was confirmed by the presence of typical topographic signs (large irregular astigmatism, steep keratometry, and inferior–superior asymmetry). We excluded subjects with active ocular inflammation, corneal epithelial defects, stromal opacity or scarring, glaucoma, known systemic illnesses, chronic use of topical ocular medications, and those who had any type of eye surgery. The participants were asked to refrain from wearing contact lenses at least 1 week before evaluation. One eye was enrolled per patient; when both eyes of the same subject had KC, only the right eye of this participant was included in the study. Attempting to minimize bias of diurnal IOP variations, we conducted all measurements between 9 AM and 2 PM.

Initially, all subjects underwent a complete ophthalmic examination including visual acuity testing and refractive error assessment, measurement of axial length (AL) with IOL Master (IOL Master; Carl Zeiss Meditec AG, Jena, Germany), and computerized corneal topography (TMS-2N; Tomey, Corporation, Nagoya, Japan). Then, each subject underwent assessment with ORA that included noncontact measurement of IOP, CH, and CRF. The ORA examination technique has been previously described.[13] For each subject, we obtained 3 readings of good quality, defined as having a waveform with 2 distinct peaks and recorded the average for each parameter as has been previously described.[12]

After the noncontact measurements, topical anesthesia with Oxybuprocaine hydrochloride 0.4% drops (Localin; Fisher Pharmaceutical Labs, Israel) was administered. Central corneal thickness (CCT) was measured with the ORA-attached handheld ultrasonic pachymeter.

Finally, applanation tonometry was performed with a Goldmann tonometer. There was approximately a 15-minute interval between IOP measurements with the 2 tonometers. One examiner, who was masked to the previously recorded ORA data, performed all measurements. Two pressure readings on the central cornea in the 90-degree apart axes were obtained, and their mean was used for analysis. Assessment of calibration of the GAT according to the manufacturer's guidelines was performed before beginning of the study.

Statistical Analysis

The Kolmogorov–Smirnov test was used to determine whether continuous parameters were normally distributed. Continuous parameters were presented as mean and SD with range (minimum and maximum values).

Correlation between GAT and both ORA measurements and other continuous parameters was calculated using Pearson coefficient. The level of agreement between the 3 sets of measurements was assessed using the Bland and Altman method.[14] According to this method, for each pair of measurements, intermeasurement differences in IOP were plotted against their mean, and the 95% limits of agreement was calculated, thereby providing a range of differences that is expected in most patients, in addition to the mean difference.

An analysis of variance with repeated measures was performed to assess the difference between the mean measurements by the 2 devices. Statistical significance was determined as $P < 0.05$. Multivariate analysis was used to compare GAT and each of the ORA's IOP parameters with sex, age, CCT, and corneal curvature as covariates. SPSS for Windows software (version 14; SPSS, Inc, Chicago, IL) was used for the statistical analysis.

RESULTS

Fifty-nine eyes of 59 patients with KC (39 males, 20 females; mean age: 27.8 ± 6.8 years) were included. Table 1 shows clinical characteristics of the study population.

The mean IOP measured using the GAT was 10.9 ± 2.0 mm Hg (range, 6.0–16.0 mm Hg), whereas those provided by the ORA were 9.5 ± 2.8 (range, 3.6–18.7 mm Hg) for IOPg ($P < 0.0001$) and 13.3 ± 2.5 (range, 9.1–20.9 mm Hg) for IOPcc ($P < 0.0001$). Multivariate analysis accounting for age, sex, corneal curvature, and CCT confirmed that observed differences were unaffected by these parameters and remained statistically significantly different. Figure 1 graphically presents measured IOP values.

The Bland–Altman plots show the agreement between pressure measurements obtained with ORA and GAT. This is shown in Figures 2, 3, and 4, respectively, for GAT versus IOPg (mean difference = 1.4 ± 2.7 mm Hg; 95% limits of

TABLE 1. Clinical Characteristics of the Study Population

	Mean ± SD	Range
CCT (μm)	457 ± 38	342–544
AL (mm)	24.4 ± 1.6	21.7–28.8
CH (mm Hg)	7.9 ± 1.3	4.6–12.0
CRF (mm Hg)	6.5 ± 1.6	2.6–11.0
GAT (mm Hg)	10.9 ± 2.0	6.0–16.0
IOPcc (mm Hg)	13.3 ± 2.5	9.1–20.9
IOPg (mm Hg)	9.5 ± 2.8	3.6–18.7
K_{max} (D)	53.2 ± 5.8	38.3–70.9
K_{min} (D)	44.4 ± 3.8	35.7–57.3
Mean sim K (D)	46.7 ± 4.5	36.8–59.0
SE (D)	−4.3 ± 3.3	−12.0 to 0.8
BSCVA (logMAR)	0.22 ± 0.2	0–0.8

AL, axial length; BSCVA, best spectacle-corrected visual acuity; CCT, central corneal thickness; CH, corneal hysteresis; CRF, corneal resistance factor; GAT, Goldmann applanation tonometer; IOPcc, corneal correlated IOP; IOPg, Goldmann correlated IOP; K_{max}, maximal keratometry; K_{min}, minimal keratometry; Mean Sim K, average simulated keratometry; SE, spherical equivalent.

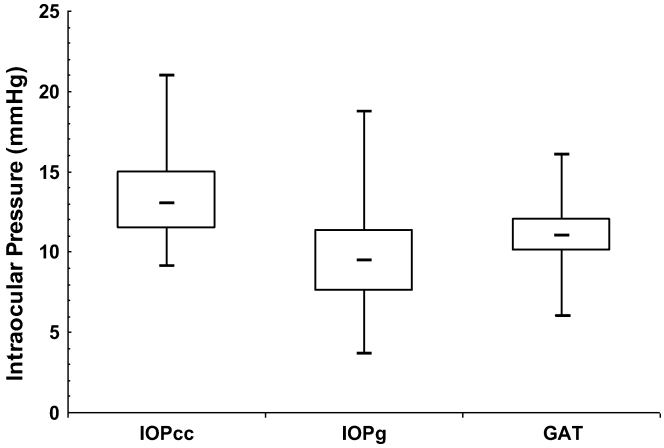

FIGURE 1. Box and whisker plots (smallest, median, and largest values with interquartile range) showing IOPcc, IOPg, and GAT IOP.

agreement = −3.9–6.8 mm Hg), GAT versus IOPcc (mean difference = −2.4 ± 2.6 mm Hg; 95% limits of agreement = −7.5 to 2.8 mm Hg), and IOPcc versus IOPg (mean difference = 3.7 ± 1.7; 95% limits of agreement = 0.4–7.1 mm Hg). Pearson correlation analysis showed weak significant correlation between the 2 devices (Table 2).

IOPg was weakly significantly correlated with CCT. Neither IOPcc nor GAT was significantly correlated with CCT (Table 2).

Whereas GAT was practically unaffected by corneal curvature, ORA-measured IOP was inversely related to *K* readings (Table 2). No significant correlation was found between standard error and IOPcc, IOPg, or GAT values (Table 2).

AL was unrelated to GAT or IOPg but was moderately significantly correlated with IOPcc (Table 2). AL was also significantly correlated with CH ($r = -0.2$, $P < 0.05$), but not with CRF or CCT.

Whereas CRF was weakly correlated with GAT and IOPcc and strongly significantly correlated with IOPg, CH showed weak negative correlation with IOPcc, weak positive with IOPg, and no correlation with GAT (Table 2).

TABLE 2. Correlation Analysis of GAT and ORA Measures and Ocular Parameters

	GAT (mm Hg)	IOPcc (mm Hg)	IOPg (mm Hg)
Age (yrs)	0.17	0.19	0.50
GAT (mm Hg)	—	0.33**	0.40**
IOPcc (mm Hg)	0.33**	—	0.80**
IOPg (mm Hg)	0.40**	0.80**	—
CCT (μm)	0.12	0.08	0.30**
K_{max} (D)	−0.01	−0.36**	−0.46
K_{min} (D)	−0.05	−0.37**	−0.41**
Mean sim *K* (D)	0.03	−0.40**	−0.49**
SE (D)	0.12	−0.06	0.07
AL (mm)	0.14	0.48**	0.26
CH (mm Hg)	0.11	−0.30*	0.25**
CRF (mm Hg)	0.28**	0.19*	0.72**

*Significance at the $P < 0.05$ level; **Significance at the $P < 0.001$ level.

AL, axial length; BSCVA, best spectacle-corrected visual acuity; CCT, central corneal thickness; CH, corneal hysteresis; CRF, corneal resistance factor; GAT, Goldmann applanation tonometer; IOPcc, corneal correlated IOP; IOPg, Goldmann correlated IOP; K_{max}, maximal keratometry; K_{min}, minimal keratometry; Mean Sim *K*, average simulated keratometry; SE, spherical equivalent.

DISCUSSION

In this study, we compared IOP measurements as obtained with ORA and GAT in eyes with KC. Although measured GAT, IOPcc, and IOPg values were all correlated, mean IOPcc was significantly higher and mean IOPg was significantly lower than GAT values. Similar findings were previously noted in several studies regarding keratoconic eyes.[2,7,8] Interestingly, a less consistent pattern is apparent in studies of healthy nonectatic eyes. Although several studies reported principally no discrepancy between IOP measurements as obtained with ORA and GAT,[15,16] others found significantly higher IOPcc than GAT IOP.[17,18] It is plausible that the measurements of both these instruments are affected

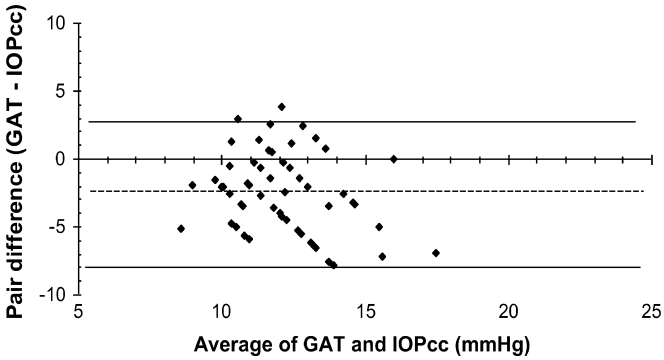

FIGURE 2. Bland–Altman plot representing the difference between GAT IOP and IOPcc versus the mean of both. The dotted line represents the mean difference between the measurements of GAT and IOPcc (−2.4 ± 2.6 mm Hg). The solid lines represent the upper (2.8 mm Hg) and lower (−7.5 mm Hg) borders of the 95% limit of agreement (calculated as mean difference ± 1.96 SD of the difference).

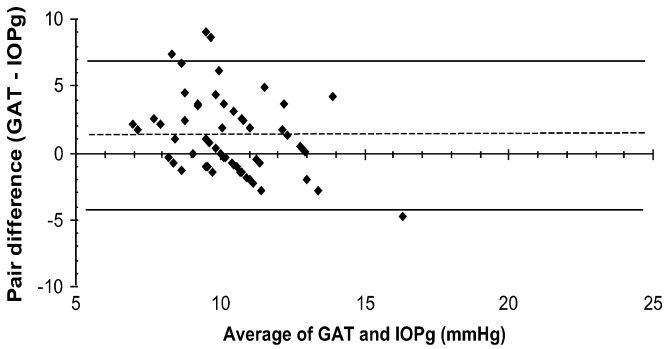

FIGURE 3. Bland–Altman plot representing the difference between GAT IOP and IOPg versus the mean of both. The dotted line represents the mean difference between the measurements of GAT and IOPg (1.4 ± 2.7 mm Hg). The solid lines represent the upper (6.8 mm Hg) and lower (−3.9 mm Hg) borders of the 95% limit of agreement (calculated as mean difference ± 1.96 SD of the difference).

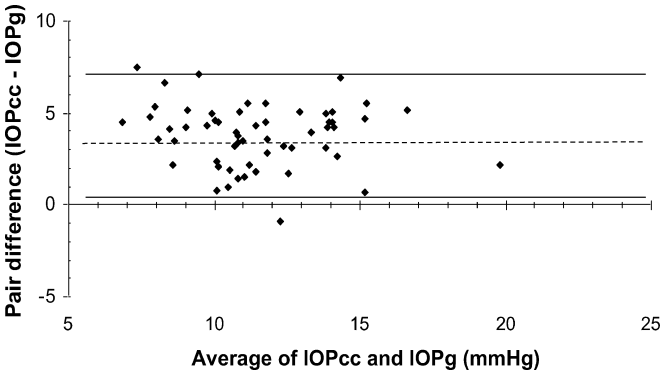

FIGURE 4. Bland–Altman plot representing the difference between IOPcc and IOPg versus the mean of both. The dotted line represents the mean difference between the measurements of IOPcc and IOPg (3.7 ± 1.7 mm Hg). The solid lines represent the upper (7.1 mm Hg) and lower (0.4 mm Hg) borders of the 95% limit of agreement (calculated as mean difference ± 1.96 SD of the difference).

by the biomechanical features specific to KC. The keratoconic cornea is characterized by reduced thickness, rigidity, and CH compared with the healthy cornea.[3,7–9,19–21] The mean values of biomechanical parameters in our study were in good accordance with those reported in previous studies of KC.[3,7,8,20] CCT, as was measured in our group of keratoconic eyes (457 ± 38 μm), was also in good agreement with previously published data regarding KC.[8,9,20–22] GAT measurements do not take into account variations in corneal thickness and rigidity. GAT is most accurate for CCT of 520 μm and assumes that the pressure inside the eye equals the force necessary to flatten determined surface area of corneal surface.[10] Plausibly, reduced thickness and rigidity of keratoconic cornea allow easier applanation and thus underestimation of true IOP. This is possibly the reason for the consistent reports of lower readings of GAT in KC.[2,7,8,22] IOPcc, however, is a pressure measurement that uses the information provided by CH to provide an IOP that is less affected by corneal parameters such as CCT or corneal curvature.[13] This is likely the reason for the results in our study and others[2,7,8] showing IOPcc values higher than GAT values in KC.

Although analyses of means and correlations are commonly used for comparison of measurements by different devices, Bland and Altman[14] proposed a more informative method to evaluate actual interdevice agreement. Besides graphical presentation, numerically, the 95% limits of agreement gives the clinician an indication of how much the devices may differ in 95% of cases, that is, in most of his or her patients. Bland–Altman plots of our data (Figs. 2–4) show that, although there is no invariable bias evident between each pair of methods, the 95% limits of agreement demonstrate a relatively large range of intermethod differences, possibly precluding use of GAT and ORA interchangeably.

GAT in our study did not show significant correlation with CCT. Such independent behavior of GAT regarding CCT has been previously shown in keratoconic eyes.[9,21,23,24] One recent study reported that changes in CCT may influence GAT measurements, but such influence was much less in keratoconic than in healthy eyes.[22] We can hypothesize that the abnormally low rigidity of KC corneas is different to such an extent from that of healthy corneas as to cancel the well-known relationship between GAT and CCT.

Independence of GAT from corneal curvature as presented in our study was also previously demonstrated in keratoconic eyes.[21,22,24] In other studies of healthy eyes, however, GAT measurements were shown to be affected by corneal curvature and strong positive correlation was described.[4,5] The nature of these differences is not completely understood, and perhaps other additional corneal properties of keratoconic eyes, such as altered rigidity and elasticity, influence more GAT measurements.

We report that ORA-measured IOP showed more dependence on corneal curvature than GAT IOP. Both IOPcc and IOPg were moderately to strongly inversely correlated to corneal curvature. This dependency may result from the asymmetric deformation of the irregular central cornea during ORA's evaluation. ORA measures IOP through corneal deformation using an air pulse causing corneal applanation and electro-optical infrared detection system consisting from light emitter and light detector. An irregular corneal surface likely undergoes uneven deformation during the applanation process and results in disturbed signal reflection toward the ORA's detector. Similar phenomenon was previously described by Kerautret et al[25] in post–laser in situ keratomileusis corneal ectasia. Furthermore, we found an association between IOP measured by ORA and between corneal biomechanical parameters as expressed by CH and CRF. Mollan et al[8] previously described dependence of IOP measured by ORA on corneal viscoelasticity, but their study did not assess corneal topography and its influence on ORA measurements. In this regard, our study showed that topographical properties of KC, in addition to internal corneal viscoelasticity, exert a major influence on ORA's IOP evaluation, unlike an influence of CCT on ORA's performance.

We showed that IOPcc was moderately significantly correlated with AL. The nature of such a correlation is not clear. Longer eyes do not necessarily have thinner cornea, and the present study showed no correlation between CCT and AL, consistent with some previous observations.[26,27] Furthermore, longer eyes in our study were characterized by low CH, and CH itself was inversely correlated to IOPcc. Recently, Schen et al[28] showed a similar association in elongated myopic eyes. They showed higher IOPcc, lower CH, and similar CCT in highly myopic eyes compared to normal eyes. Therefore, it is plausible that the association between increased IOPcc values and eye elongation derived from intrinsic corneal biomechanics.

In summary, we found that IOP measurements taken with GAT and ORA in keratoconic eyes were significantly different, with IOPcc higher and IOPg lower than GAT IOP. IOP measured with ORA was more influenced than GAT IOP by corneal curvature. We did not perform intracameral manometry; therefore, we cannot decide which device is more precise and provide "true IOP" measurements. We recommend that these devices should not be used interchangeably but rather in a complementary fashion to assess IOP in keratoconic eyes.

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