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A Comparative Analysis of Goldmann Tonometry Correction

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ABSTRACT

Purpose: The measurement of Intraocular Pressure (IOP) by Goldmann Applanation Tonometry (GAT) is based on assumptions about corneal parameters. To correct for variations in corneal curvature and thickness, a number of equations have been proposed. This study evaluates the in vivo accuracy of these equations from subjects with primary open angle glaucoma (POAG) comparing them to measurements taken using the Pascal Dynamic Contour tonometer (DCT) which makes no assumptions about corneal geometry or biomechanics.

Subjects and Methods: The study included 108 subjects with POAG (47 males, 61 females) with an age range of 39-81 years. Subjects were recruited from the Glaucoma Clinic at Wroclaw Medical University. A full ophthalmologic examination was conducted on all subjects. Subjects were divided into three groups depending on IOP as measured by GAT. Six formulae were applied and results compared to measurements taken with DCT.

Main Outcome Measures: To determine which formula provides the closest value to IOP measured with DCT.

Results: For IOP values $\leq$ 29 mmHg, two of the formulae show the smallest and comparable mean differences and standard deviations between corrected IOP values obtained with GAT and those measured with DCT. For IOP $\geq$ 30mmHg, the formula derived from the model of corneal applanation that takes into account corneal buckling, shows the closest agreement with measurements taken using DCT.

Conclusions: Correction formulae provide widely varying results and appropriateness can depend on the IOP values.

Key words: Intraocular pressure, glaucoma, Goldmann Applanation tonometry, Dynamic Contour tonometry, Goldmann correction

INTRODUCTION

Goldmann Applanation Tonometry (GAT) has long been accepted as the gold standard for intraocular pressure (IOP) measurement.[1-3] However, GAT applies the Imbert-Fick law which assumes an infinitely thin-walled spherical shell without intrinsic stiffness;[1] assumptions that are not applicable to the human cornea. The IOP value obtained by GAT depends on parameters of the individual eyeball: central corneal thickness (CCT), corneal radius of curvature (R) and structural corneal and scleral rigidity and this is calibrated for a cornea of R = 7.8mm, CCT = 0.55mm and an applanation diameter of 3.06 mm.[1]

As corneal parameters generally differ from those used in the calibration, this requires a correction to be made to the IOP measured with GAT (IOPG). The corrective function is referred to as the true intraocular pressure (IOPc) function.[4-9] Earlier proposals for correction only accounted for the thickness of the cornea;[10] subsequent methods also included the radius of the curvature.[11] The effect of other parameters that influence GAT have been investigated more recently (age, axial length and biomechanical parameters).[8,9,12,13] Nevertheless, none of these attempts have yielded a universally accepted correction formula.[7,9,13] The consequence of this is that there are several correction methods available rendering it difficult to make a comparative analysis between different studies.

There are indications that the source of IOPG correction discrepancies are inherent in the assumptions made about the mechanics applied to the corneal shell ie that displacement is proportional to the load. This assumption results in a linear closed-form solution model, such as that proposed by Orssengo and Pye[4], which simplifies the calculations. However, mechanical analysis of GAT has shown that applanation of a corneal shell loaded with a high IOP is accompanied by buckling as that the construct in this state is geometrically nonlinear.[15,16] Non-linear examples have been reported.[8,17,18] In a geometrically non-linear structure, it has been shown that for higher IOP values when the IOP is equal to or greater than the pressure imposed by flattening of the surface, the corneal shell loses its ability to resist the external force. Pressure from the peripheral zones facilitates the flattening of the apex as the corneal shell undergoes tension and 'buckles' rather than resists the pressure of the tonometer.[15] This is what causes the underestimation of IOP. These models of corneal applanation only account for nonlinearity in material properties which is insufficient for the buckling analysis of a structural model.[19] The phenomenon of buckling during flattening of the cornea affects the IOPc function and hence the linear form, known as the modified law of Imbert-Fick,[4] is not even a first approximation to the IOPG. Nonlinearity of the IOPc function has been reported[7,8,20] but the proposed formulae are derived from experimental results and lack mechanical analysis to justify buckling.

The correction equation recently proposed by Srodka[21] is based on finite element simulation of corneal biomechanics. The results of these simulations show that when IOP is lower than 20 mmHg, the IOPG does not have to be corrected. However, above this threshold the correction is noticeably large and it rises with magnitude of IOP. For very high IOP values such as 35 mmHg, correction and calibration for central corneal thickness and radius of curvature can still leave a difference of 13 mmHg between measured and corrected values of IOP.[21]

Recently studies have reported tonometric methods that measure IOP independently of geometrical and biomechanical properties of the cornea.[22-29] One of these devices is the Pascal dynamic contour tonometer (DCT, Pascal, Ziemer Ophthalmic System AG, Switzerland) the tip of which matches the curvature of the cornea allowing it to maintain its shape when pressure on the external surface is matched to the IOP.[23,30,31] Boehm et al.[31] reported that values of IOP obtained using DCT showed good concordance with intracameral IOP, and that CCT had a negligible effect on measurements. The purpose of this study was to evaluate the in vivo accuracy of the equations[4-8,21] that have been proposed for correcting measurements of IOP made by GAT in a cohort of glaucoma patients. The corrected IOP values are compared with measurements obtained using DCT (IOP-DCT).

METHOD

Subjects

The study included 108 subjects (47 males, 61 females) with an age range of 39-81 years diagnosed with primary open angle glaucoma (POAG) who presented at the Glaucoma Clinic at the Department of Ophthalmology, Wroclaw Medical University. The POAG diagnosis was based on pathological changes in the optic nerve head to the cup/disc ratio and in cup depth with corresponding visual field defects and high or borderline IOPG in the presence of an open angle. Subjects were divided into three groups A, B and C defined in the basis of IOPG:

from 19 mmHg to 20 mmHg inclusive (Group A); from 21 mmHg to 29 mmHg inclusive (Group B) and from 30 mmHg to 42 mmHg inclusive (Group C).

Subjects were fully informed of the purpose of the study and all procedures and their requirements. Informed consent was obtained before any measurements were taken for the purposes of this study. The project was approved by the Ethics Committee of the Wroclaw Medical University (KB 481/2009) and adhered to the Tenets of the Declaration of Helsinki. Exclusion criteria were: any systemic disease or medications, intraocular surgery less than six months before the study start date, refractive surgery and corneal abnormalities such as oedema or scars. Subjects underwent an ophthalmologic examination including visual acuity, corneal topography (E300, Medmont Pty Ltd, Melbourne, Australia), central corneal pachymetry (PalmScan AP2000 A-Scan Biometer, MicroMedical Devices Inc., Calabasas, CA, USA), optic nerve head assessment with Heidelberg scanning laser ophthalmoscopy (HRT 3, Heidelberg Engineering, Heidelberg, Germany) and visual field examination using Humphrey 30-2 full threshold perimetry (Humphrey Instruments, San Leonardo, California).
The radius of curvature of the central cornea (R) was acquired by the E-300 Medmont instrument as calculated from corneal topography maps.

After the clinical examination, subjects were given a break of 60 minutes before taking measurements using the DCT (Pascal, Ziemer Ophthalmic System AG, Switzerland). These were taken with continuous IOP pulse wave recordings at a sampling rate of 100 Hz. The average (mean ± standard deviation) recording time of the IOP pulse wave for all subjects was 16.3 ±3.4 seconds and measurements were repeated until three IOP recordings with a quality score Q of three or higher were obtained. As well as providing continuous measurement of IOP, the DCT simultaneously records the ocular pulse amplitude (OPA) which indirectly provides an indication of choroidal perfusion and hence how ocular blood flow corresponds to heart pulsation. These measurements are obtained from an electronic pressure sensor which applanates the central cornea; the IOP and OPA values are computed by the instrument from the pulse curve. Measurements using GAT were then made in triplicate and the mean value used. Subjects were treated for glaucoma with either beta-blocker drops (30%), prostaglandins (36%), carbonic anhydrase inhibitor eye drops (28%) and alpha agonists (19%). Measurements were taken by Dr Asejczyk-Widlicka under supervision of Dr Krzyzanowska-Berkowska.

Correction equations

The six multi-parameter equations that have been proposed as correction factors for IOPG are given below:

Orssengo and Pye:[4]

$$\mathrm{IOPc} = \frac{\mathrm{IOPG}}{\dfrac{B_c - C_c + C}{B}} \qquad (1)$$

where:

$$B = \frac{0.6\pi R\left(R - \mathrm{CCT}/2\right)\sqrt{1-v^2}}{\mathrm{CCT}^2} \text{ and } C = \frac{\pi\, R\left(R - \mathrm{CCT}/2\right)^2\left(1-v\right)}{A\ \mathrm{CCT}},$$

and B_c and C_c are calculated for $R = R_c$ and CCT = $\mathrm{CCT_c}$, and A is the applanated area.

Shimmyo et al.:[5]

$$\mathrm{IOPc} = \mathrm{IOPG} + 0.8(R - 7.85) + \exp(-0.005\ \mathrm{IOPG})10^3\ (0.55 - \mathrm{CCT})/18 \qquad (2)$$

Kohlhaas et al.:[6]

$$\mathrm{IOPc} = \mathrm{IOPG} + 23.28 - 42.3\mathrm{CCT} \qquad (3)$$

Chihara:[7]

$$\mathrm{IOPc} = \frac{\mathrm{IOPG} + 4.15}{\dfrac{1.909\ \mathrm{CCT}^2}{A\,(R - \mathrm{CCT}/2\,)} + 1} \qquad (4)$$

A is assumed to be a constant value of 0.334 $\mathrm{mm^2}$.

Elsheikh et al.:[8]

$$\mathrm{IOPc} = \frac{\mathrm{IOPG}}{A_{CCT} \cdot A_R \cdot A_{Age} \cdot A_{IOPG}} \qquad (5)$$

where

$A_{\mathrm{CCT}} = 0.68\ (\mathrm{CCT} - 0.520)^2 + 1.12\ (\mathrm{CCT} - 0.520) + 1.0$

$A_{\mathrm{R}} = 1 - 0.06\ (R - 7.8)$

$A_{\mathrm{Age}} = 0.3 \cdot 10^{-6}\ age^3 - 88 \cdot 10^{-6}\ age^2 + 0.0085\ age + 0.815$, *age* in years and

A_{IOPG} = 1.427 (IOPG + 3.373) $^{-0.119}$

Srodka:[21]

$$\mathrm{IOPc} = \left[e \left(\mathrm{CCT}_c - \frac{R}{R_c} \mathrm{CCT} \right) + 1 \right] \left(\mathrm{IOP}_{ca} + 3 \right) - 3 \qquad (6)$$

where the constant e =1mm^{-1} and

$$\mathrm{IOP_{ca}} = -1.61 + 0.94\ \mathrm{IOPG} + 0.011\ \mathrm{IOPG}^2,$$

Formulae (1) to (6) were applied using measurements of IOPG, *R* and CCT and results after the correction (IOPc) were compared with measurements IOP-DCT.

Statistical Analysis

Single factor analysis of variance (ANOVA) was used to test the hypothesis of equal means in group age, IOPG, IOP-DCT, OPA, *R* and CCT. All data were tested for normality using the Kolmogorov-Smirnov test. Agreement between IOP-DCT and IOPc and between IOP-DCT and IOPG was evaluated using the Bland–Altman analysis, where the limits of agreement were calculated to be the average difference ±1.96 standard deviation (SD). The analysis was performed with commercial software (Statistica, ver. 10, StatSoft, Inc., USA). All analyses were conducted at the 0.05 significance level.

RESULTS

The group mean age, *R* and CCT are shown in the Table 1. Significant differences between groups (p<0.05) were found in subject age. The IOPG mean values (±SD) were 20.3±0.8, 25.1±3.6 and 39.4±2.0 mmHg and mean IOP-DCT (±SD) were 21.9±3.1, 28.1±5.5 and 48.4±5.3 mmHg and OPA (±SD) were 3.6±1.5, 4.3 ± 1.4 and 4.4±0.4 mmHg for groups A, B and C respectively.

Table 1

The values of IOP-DCT and the IOPc, calculated for every subject using formulae (1) to (6), are shown in Figure 1a. For clarity of presentation, linear approximations for these points are plotted in Figure 1b.

Figure 1

The median of IOPc values in each of the three groups for the individual formulae and for IOP-DCT are shown in the Figure 2.

Figure 2

The difference between IOP-DCT and IOPG as well as between IOP-DCT and IOPc (corrected with each formula) are shown in the Table 2. Formula (6) gave the closest reading to the IOP-DCT values out of all the other correction formulae in each of the three groups (-1.2±1.7, -0.2±2.7 and -2.0±2.5 mmHg for group A,B and C respectively). For group A, the values of IOP-DCT were higher than IOPG and the IOPc values calculated using all formulae. For groups B and C, only the Srodka[21] equation (6) gave results for IOPc that were higher than IOP-DCT.

In group A, four of the six formulae, namely: 1, 2, 3 and 4 give higher correction values (IOPc) than the IOPG values and the SD obtained with these formulae are wider than that from directly measured values (IOPG). In group B the closest agreement with IOP-DCT was found for formula (6) : 0.2±2.7 mmHg which had a slightly lower value of IOPc than the IOP-DCT values. Formula (5), the second closest IOPc value to IOP-DCT, gave a slightly higher value than the IOP-DCT: -0.8 $\pm$ 2.6 mmHg. Formulae (3) and (4) provided IOPc values that were the furthest from IOP-DCT. The greatest differences between IOP-DCT and IOPc and IOP-DCT and IOPG were found for group C (Table 2). Formula (6) again gave the IOPc value that was closest to IOP-DCT: -2.0±2.5 and the narrowest range of values (-4.1 – 5.1) with the greatest symmetry around zero.

Table 2

In order to further investigate the causal factors that may influence the discrepancy between IOP measured with different methods, a multivariate analysis was conducted[9]. The findings presented in Table 3 indicate that IOP measured with GAT and DCT are not linearly related to R or CCT. Correlations between CCT and IOPc are statistically significant for all formulae for Groups A and B and *R* and IOPc have a statistically significant correlation with IOPc for lower values of IOP (ie Group A) for formula 6. For the highest range of IOP values (Group C) there is no significamt correlation with CCT, *R* or age for any of the formulae (Table 3).

Table 3

Table 4 gives Bland-Altman analyses showing bias and limits of agreement between IOP-DCT and IOPG as well as IOP-DCT and IOPc for all formulae. The best agreement between IOP-DCT and IOPc is found using formulae (5) and (6) with slightly better agreement for the latter. IOPG has poor agreement with IOP-DCT over the entire range of IOP values (from 19 to 42 mmHg); IOPG measurements were significantly lower than those measured with DCT by an average of -2.2 mmHg (p<0.01).

Table 4

DISCUSSION

Correction of IOPG readings to account for variations in CCT has been considered since the 1970s and given due recognition by the seminal work of Ehlers et al.[10] Since then a number of studies have reported the effect of CCT on GAT readings and the correlation between the two measurements.[5,29,32-40] In recent years it has been suggested that parameters such as R, age and rheological factors should also be recognised as affecting the measurement of IOP.[8,21,41]

This has led to the number of relatively diverse formulae that correct for one or more of the factors that affect IOP and the lack of cohesion in deciding which of these factors should be given prominence or whether indeed, the predominant factor can vary depending on the individual. A further cause of discrepancy and uncertainty is the approximation to a linear approach when modelling the applanation of the corneal apex. Such a calculation does not take into account the nonlinear relationship between IOPG and IOPc[16] and the buckling of the shell that has been reported experimentally with applanation[42] and that was predicted with modelling studies.[16] The results presented in this work allow for the experimental comparison of the numerical corrections.

The linear approximations for the correlation between IOPG and IOPc (Figure 1b) indicate that formulae (1) to (3) are close to the Imbert-Fick law over the range of IOP values examined suggesting the corrections were based on this law. This tendency is not confirmed by formulae (4) and (5) which show noticeable deviations from a straight line with lower IOPc values for higher magnitudes of IOPG obtained by formula (4) and the opposite provided by formula (5). The greatest deviation from the Imbert-Fick law, particularly for high IOP values, is from formula (6). The direction of the correlation is the same as that of formula (5) ie the calculated IOPc is greater than predicted by the Imbert-Fick law for higher IOP values, but the deviation at IOPG=42 mmHg is three times higher for formula (6) compared to formula (5) (12 vs 4 mmHg). The rest of the formulae do not allow IOP to exceed the reading of the Goldman tonometer.

These six formulae were verified by comparing IOPc to IOP-DCT measurements which are not dependent on corneal geometry. The IOP-DCT has been compared against intracameral IOP, treating the latter as the reference IOP, on patients undergoing phacoemulsification.[31] The investigation conducted on 75 eyes was set using a manometer at three pressure levels: 15, 20 and 35 mmHg. At the lower two levels. 15 and 20 mmHg, there was no statistically significant difference between IOP-DCT and reference IOP. At 35 mmHg the difference was statistically significant but the magnitude of this difference was only -0.84 $\pm$ 1.90 mmHg.[31] Given these findings, DCT can be deemed to provide a reliable measure over the range of IOP values tested in this study. The values of IOP-DCT in this study are closest to the IOPc obtained using formula (6).

The shape of the function for formula (6) shows that up to just over 20 mmHg, the approximation to a linear relationship between IOPc and IOPG can be made. For higher values of IOP, this relationship no longer holds as for given increments in IOPG, the increments of IOPc are greater. The reason for this has been explained as the capillary or adhesion forces created within the tear film between the measurement tip and the cornea[22]. However, the numerical solutions of the nonlinear model indicate different causes for the deviation from linearity: the models predict a buckling of the corneal shell during the applanation.[16] Such a deviation from linearity is seen in Figure 1a) for measurements obtained with the DCT and those produced for IOPc corrected using equation (6). This cannot be explained by the influence of an adhesive or the tear film force both of which are constant.

The results of this study suggest limited clinical utility for most of the current correction formulae. This confirms the analysis of Ang et al.[14] who found, on a population of Caucasian patients with glaucoma and those with suspected glaucoma, that the agreement with DCT measurements was better when IOPG remained uncorrected than when the values were corrected using six different correction formulae.

The equation proposed by Srodka[21], formula (6), is the only one of the formulae that shows close agreement with DCT. In group C, where the average difference between IOPG and IOP-DCT is 6.1±4.0mm Hg, the difference between IOPc calculated using formula (6) and IOP-DCT is -2.0±2.5. Bland–Altman analysis shows that over the range of IOP (from 19 to 42 mmHg), there is good agreement with IOPc using this formula and IOP-DCT with a limit of agreement between -4.5 to 4.9 mmHg and differences that were not statistically significant. Boehm et al.[31] reported limits of agreement between -3.5 to 2.8mmHg for IOP-DCT and intracameral IOP over an IOP range between 15 to 35 mmHg. This study suggests that correction of GAT measurements with five of the formulae in the literature may be misleading if the real value of IOP is underestimated. Only the formula proposed by Srodka[21] can be used even for higher values of IOP (> 30 mmHg). It should be noted that this formula has not been evaluated previously and these promising theoretical findings should be tested in future studies with further experimental validation. The limitations of this study are that although the formulae are tested for a relatively wide range of IOP, this did not cover the widest possible range ie below 19mmHg and above 42mmHg. This notwithstanding, ultimately the clinical significance needs to be considered and at such high values of IOP, it may be argued that the precise value is less important than the fact the IOP poses a high risk to vision if not treated. It should also be noted that investigations pertained to the adult eye; the eyes of children and the changes with growth and development remain to be tested.

CONCLUSIONS

The numerical model of corneal applanation that takes into account buckling of the corneal shell provides a correction to IOPG that is closest to the IOP value obtained with DCT. This is a method that does not depend on corneal parameters and that has been verified against intracameral IOP.

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FIGURE LEGENDS

Figure 1. Relationship between IOPc and IOPG, a) values for DCT and IOPc calculated for individual patients according to equations (1) to (6), the three IOPG ranges are separated with vertical lines, b) the approximations of these points. The dashed line illustrates the Imbert-Fick law. For clarity of presentation, linear approximations for these points are plotted in Figure 1b.

Figure 2. Box plots and median values for IOPc calculated with formulae (1) to (6) for the three groups categorized according to IOPG measurements a) group A (19 $\leq$ IOPG $\leq$ 20 mmHg), b) group B (21 $\leq$ IOPG $\leq$ 29 mmHg) and c) group C (30 $\leq$ IOPG $\leq$ 42 mmHg).