·Clinical Research·

Comparison of Diaton transpalpebral tonometer with applanation tonometry in keratoconus

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Abstract

• AIM: To investigate the added value of using a Diaton transpalpebral tonometer (DT) to measure IOP in keratoconus. Most type of tonometers use corneal applanation or biomechanical resistance to measure intraocular pressure (IOP); however, these factors can be altered by keratoconus. Specifically, we examined whether DT can detect false-negative low Goldmann applanation tonometry (AT) measurements.

• METHODS: Patients with keratoconus were recruited from our tertiary academic treatment center. Measurements included AT and DT (in random order) and Scheimpflug imaging. An age- and gender-matched group of control subjects with no history of corneal disease or glaucoma was also recruited.

• RESULTS: In total, 130 eyes from 66 participants were assessed. In the keratoconus group, mean AT was 11.0± 2.6, mean DT 11.2±5.5 (P=0.729), and the two measures were correlated significantly(P=0.006, R=0.323). However, a Bland-Altman plot revealed a wide distribution and poor agreement between both measurements. Previous corneal crosslinking, corneal pachymetry, and Krumeich classification had no effect on measured IOP.

• CONCLUSION: Measurements obtained using a Diaton tonometer are not affected by corneal biomechanics; however, its poor agreement with Goldmann AT values calls into question the added value of using a Diaton tonometer to measure IOP in keratoconus.

• KEYWORDS: Diaton; Goldmann applanation tonometry; transpalpebral tonometry; keratoconus; Bland-Altman plot

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INTRODUCTION

The presence of corneal pathology can potentially affect measurements of intraocular pressure (IOP) and several methods for measuring IOP in corneal pathology have been described [1-3]. For example, Rosentreter *et al* [1] compared rebound tonometry, applanation tonometry, and dynamic contour tonometry in pathological corneas. However, all of these devices depend upon corneal applanation and/or biomechanical resistance. Both factors can be altered by keratoconus, a progressive condition with thinning of the cornea, irregular astigmatism, and decreased biomechanical resistance [4-7]. In particular, the thinning of the cornea can be extremely severe; applanation of such a thin cornea potentially requires much less pressure and can therefore result in an underestimation of the actual IOP [8]. This effect has been observed when measuring IOP in healthy corneas with varying corneal pachymetry measurements [9], and this phenomenon was proposed as a factor in normal-tension glaucoma [10]. Specifically, the irregular shape of the cornea might prevent the Goldmann applanation tip from aligning properly, thus preventing uniform contact; this problem is not an issue with other methods (for example, rebound tonometry). Corneal rigidity can further be altered by corneal crosslinking, a widely used procedure for preventing the progression of keratoconus [11]. The effect of crosslinking on various IOP measuring methods has been studied, and these studies revealed increased IOP readings after crosslinking. It is important to note that all devices depend on corneal rigidity for their accuracy.

To circumvent this problem, the Diaton tonometer (DT, manufactured by Ryazan State Instrumental-Making Enterprise, Ryazan, Russia, http://www.diaton-tonometer.com) uses an alternate method to measure IOP; the movement pattern of a small rod falling freely onto the eyelid surface is measured and individual measurements are displayed digitally. The DT is a portable, hand-held device that measures transpalpebral IOP through the patient's upper eyelid while the patient is in a reclined or supine position. The DT has been promoted as a suitable alternative method of tonometry for patients with conjunctivitis and/or corneal

disease, or following corneal surgery [12]. Previous research found that the DT is reliable in patients without corneal disease and provides measurements that are similar to Goldmann applanation tonometry (AT); however, DT yields results with wider variation and lower correlation with repeated measurements [13-15]. Thus, the value of using DT for glaucoma screening has been questioned.

Because applanation IOP measurements in keratoconus patients can underestimate the actual IOP, and because of the claims made by the manufacturer, we investigated the added value of measuring transpalpebral IOP using DT compared to Goldmann AT in patients with keratoconus. Specifically, we examined whether false-negative (*i.e.* low) AT measurements in keratoconus can be detected using DT.

SUBJECTS AND METHODS

Patients were recruited from the cornea outpatient clinic in our tertiary academic center from October 2013 through January 2014. The inclusion criteria included a current diagnosis of keratoconus and no gross anatomical eyelid abnormalities hampering DT measurement; patients of all ages were eligible for inclusion. Corneal scarring and/or previous crosslinking treatment did not preclude patients from participating. An age- and gender-matched control group was recruited and consisted of healthy volunteers with no history of corneal disease, ocular hypertension, or glaucoma.

All measurements were collected by one examiner (Peeters N) under standardized conditions; DT measurements were taken in the supine position in accordance with the manufacturer's instructions. The DT indicates the number of measurements necessary for each eye and provides a single reading. AT was measured using standard procedures. The order of IOP measurements (*i.e.* DT followed by AT versus AT followed by DT) was randomized. All patients underwent a slit-lamp evaluation and Scheimpflug corneal imaging (Pentacam HR type 70900, Oculus GmbH) prior to the IOP measurements. All keratoconus eyes were diagnosed and graded using the Krumeich classification system [16] by one corneal specialist (Wisse RPL).

Statistical analyses were performed using SPSS version 20.0 (IBM). Box plots, scatter plots, and Bland-Altman plots were used to visualize the outcomes [17]. Differences in AT and DT readings were analyzed using the Student's t-test. A linear regression model using a generalized estimating equation (correcting for patients with two affected eyes) was used to assess the relationship between the difference in IOP and pachymetry and Krumeich classification. Normality was tested based on skewness and kurtosis, with a cut-off value of 3.29 (P<0.001).

This study was approved by our Institution's Ethics Review Board and was performed in accordance with the Declaration of Helsinki. None of the eligible participants refused to participate, and all subjects provided informed consent.

RESULTS

One hundred and thirty eyes from 66 participants were initially enrolled; 36 keratoconus patients had 70 eyes with keratoconus. Two eyes from one patient in the keratoconus group were excluded from the analysis due to missing AT measurements. The mean age (±SD) of the subjects in the keratoconus and control groups was 25.8±9.3 and 33.1±9.8y, respectively; 62% and 56% of the subjects were male in the keratoconus and control groups, respectively. Baseline characteristics did not differ significantly between the two groups. Among the eyes with keratoconus, 40 (57%) previously underwent corneal crosslinking (CXL). The grading of the keratoconus eyes (based on the Krumeich classification system [16]) was as follows: 23% were grade I, 56% were grade II, 10% were grade III, and 11% were grade IV. The mean value for thinnest corneal pachymetry was 451±57 μm. None of the patients had a history of glaucoma or ocular hypertension.

Applanation *vs* Diaton Intraocular Pressure Measurements In the keratoconus group, mean IOP measured using AT and DT was 11.0±2.6 mm Hg and 11.2±5.5 mm Hg, respectively (P=0.729). In the healthy control group, mean IOP measured using AT and DT was 12.7±2.7 mm Hg and 7.3±2.5 mm Hg, respectively (P<0.001). Thus, the mean difference between the AT and DT measurements in the keratoconus and control groups was -0.2±5.2 mm Hg and 5.5±3.5 mm Hg, respectively (P<0.001). The IOP measurements of keratoconus eyes that received CXL did not differ significantly from their untreated counterparts: AT measurements were 10.8 mm Hg *vs* 11.5 mm Hg (P=0.295), and DT measurements 11.9 mm Hg *vs* 10.2 mm Hg (P= 0.194). The mean difference between AT and DT measurements after CXL changed from 1.3±5.4 mm Hg to -1.1±4.8 mm Hg (P=0.057). Similar results were obtained regardless of whether the AT or DT measurement was taken first (data not shown). The AT and DT measurements in the two groups are summarized in Figure 1.

Correlation Between Diaton Tonometer and Applanation Tonometry Intraocular Pressure Measurements The correlation between the DT and AT measurements was low but significant in the keratoconus group (R^2=0.104 P=0.006), but not in the healthy control group (R^2=0.017, P=0.316). The measurements and their correlation coefficients are shown in Figure 2; R^2 is given for absolute IOP measurements. Trend lines are added to highlight the lack of agreement; perfect agreement would result in a trend with a 45° slope through the origin.

Figure 3 shows a Bland-Altman plot of the AT and DT measurements in the keratoconus group. Although the mean difference is extremely small (-0.21 mm Hg), a big variation of measurements is visualized. This variation exists at low

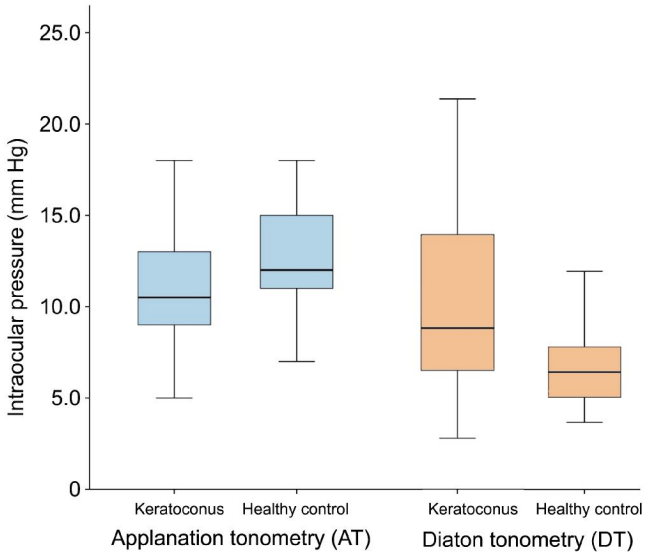

Figure 1 IOP measurements with applanation tonometry (AT) *vs* Diaton tonometry (DT) in keratoconus and healthy controls The mean IOP was comparable in the AT-group (P= 0.729), and significantly lower for healthy controls in the DT-group (P<0.001).

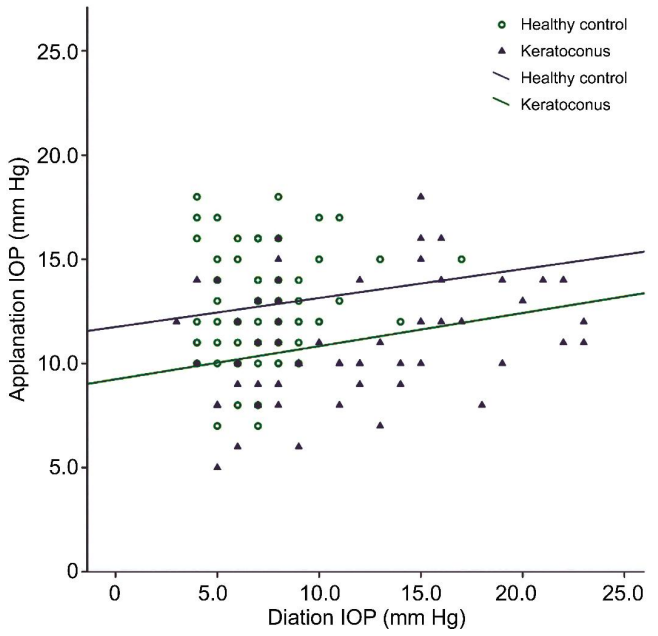

Figure 2 Correlation of applanation tonometry (AT) *vs* Diaton tonometry (DT) IOP measurements for the keratoconus group (R^2=0.104 P=0.006) and healthy controls (R^2=0.017, P = 0.316) Trend lines are given for both groups.

mean IOP levels (left side of the plot) as well as at higher mean IOP levels (right side of the plot). The SD of the difference between the AT and DT measurements is 5.2 mm Hg, which means that 27% of the DT measurements differed from their corresponding AT measurement by >1 SD. Only 16% of the measurements are within 2 mm Hg range of agreement.

Effect of Pachymetry and Keratoconus Staging on Outcomes Linear regression analysis revealed a small, non-significant effect of pachymetry on the difference between the AT and DT measurements (B: -0.011; 95% CI: -0.032 to 0.010; χ^2: 1.022; P=0.312), which means that a difference in pachymetry of 100 μm estimates a lower difference between AT and DT of 1.1 mm Hg. Krumeich classification had no effect on the difference between the AT and DT measurements (χ^2: 1.331; P=0.722).

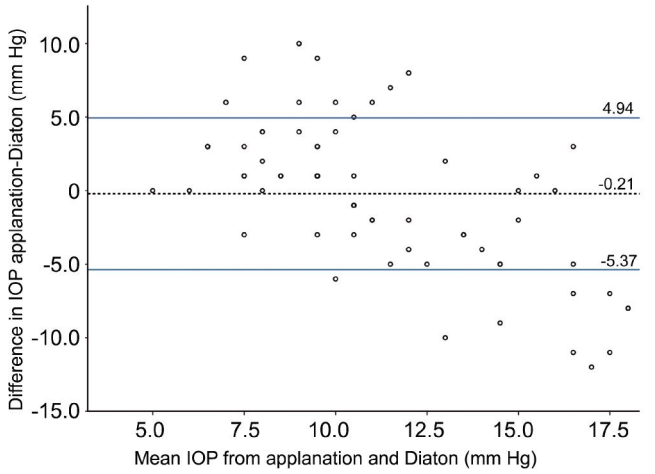

Figure 3 Bland-Altman plot of the agreement of applanation tonometry (AT) *vs* Diaton tonometry (DT) in keratoconus patients (n=70) The dashed line represents the mean difference (-0.21 mm Hg); The solid lines represent the ±1 SD of the mean difference (±5.2 mm Hg). Note the high spread number of measurements; 16% of measurements are within a 2 mm Hg range of agreement.

DISCUSSION

In this study, we investigated the added value of performing transpalpebral tonometry versus Goldmann AT to measure IOP in keratoconus. The small mean difference of IOP measurements in keratoconus between both instruments suggest that DT could be an alternative for AT. However, the wider variability of DT measurements and their poor correlation to AT renders the use of the Diaton tonometer in keratoconus debatable.

These findings are consistent with two large studies in which Diaton tonometry was used to measure IOP in eyes without corneal disease [13-14]. Both studies reported remarkably poor agreement between DT and AT measurements and concluded that DT is not a feasible substitute for AT in routine clinical practice. However, patients generally favor DT over AT, particularly young patients [13-14]. Nevertheless, Goldmann AT remains the gold standard for measuring IOP, although other devices have been studied extensively and are considered suitable alternatives [2,18-20]. The ocular response analyzer in particular combines IOP measurements with information on central corneal thickness and corneal hysteresis[20].

It is important to note that all IOP measurements were within the normal range; the highest recorded IOP was 23 mm Hg. We cannot draw conclusions for higher IOP ranges. In our measurements, we did not account for eyelid abnormalities due to allergic papillary conjunctivitis, which is a potential

confounding factor for transpalpebral tonometry in keratoconus. All patients were treated for concomitant ocular allergy; however, eyelid eversion was not performed routinely. Another consideration regarding DT is that the measurements are rather cumbersome to perform, as the patient must be in a supine or reclined position. In addition, the Diaton device has a steep learning curve; however, this was not likely to have affected the outcome, as the examiner in this study (Peeters N) had extensive experience performing DT prior to the start of the study. The significant difference between DT measurements in keratoconus and healthy eyes (with a mean difference of -5.5±3.5 mm Hg) could not be explained and is not consistent with previous studies [13-15]. A quarter of the DT measurements in healthy eyes were <5 mm Hg, which is not compatible with the distribution of IOPs in a normal population[21]. The initial patient records and the study database were checked for erroneous data entries, but these were not found. We can only hypothesize on the origin of this difference; statistical chance is highly unlikely based on the solid significance. A calibration deficit might have clouded the measurements, though the apparatus was calibrated before every measurement according to the manufacturers instruction. Regardless of the origin of this deficit we state that these data do not support our hypothesis that DT can potentially identify false-negative IOP measurements in keratoconus eyes.

The prevalence of glaucoma increases in eyes following penetrating keratoplasty (PK), and AT can be difficult to perform in these cases [22]. Although no post-PK eyes were included in this study, we recommend using a device that has been shown to be reliable for measuring IOP in keratoconus and/or post-PK eyes.

The Diaton device is specifically advertised for use in patients with corneal disease; however, although the device is portable, well tolerated by patients, and not influenced by corneal biomechanics, our results suggest that it does not measure IOP reliably in patients with keratoconus.

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