Influence of Axial Length on Intraocular Pressure Measurement With Three Tonometers in Childhood Glaucoma

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ABSTRACT

Purpose: To determine the agreement between intraocular pressure (IOP) measurements obtained using the handheld version of the Goldmann applanation (Perkins; Clement-Clarke, Haag-Streit, Harlow, United Kingdom), rebound Icare-Pro (Icare, Tiolat Oy, Helsinki, Finland), and Tonopen XL (Reichert Inc., Depew, NY) tonometers in children with childhood glaucoma and to identify factors that may affect those measurements.

Methods: Ninety-one eyes of 46 children with early-onset childhood glaucoma were included in this cross-sectional study in which IOP, ocular axial length, anterior chamber depth, lens thickness, vitreous length, and central corneal thickness measurements were obtained under general anesthesia. Agreement between tonometers was evaluated using intraclass correlation coefficients (ICCs) and the Bland–Altman method. The influence of ocular biometric parameters and central corneal thickness on IOP measurements was analyzed using multiple linear regression analysis.

Results: The mean age of the children in the current study was 29.1 months (range: 13 to 31 months). The Icare-Pro and Tonopen XL overestimated IOP measurements compared to the Perkins tonometer (Icare-Pro–Perkins mean IOP difference: 2.2 ± 3.4 mm Hg, $P < .0001$, 95% confidence interval [CI]: 1.5 to 2.9 vs Tonopen XL–Perkins mean IOP difference: 6.7 ± 7.1 mm Hg, $P < .0001$, 95% CI: 5.2 to 8.2). The Icare-Pro showed greater agreement with the Perkins tonometer than the Tonopen XL (ICC: 0.789, 95% CI: 0.697 to 0.856, $P < .0001$ vs 0.453, 95% CI: 0.272 to 0.603, $P < .0001$). Ocular axial length affected IOP measurements the most, finding increased impact on Tonopen XL (slope: 0.086, 95% CI: 0.013 to 0.16, $P = .022$ vs 0.997, 95% CI: 0.369 to 1.625, $P = .002$ vs 1.571, 95% CI: 0.541 to 2.602, $P < .0001$ for Perkins, Icare-Pro, and Tonopen XL IOP measurements, respectively).

Conclusions: Ocular axial length affects IOP measured by the Perkins, Icare-Pro, and Tonopen XL devices in patients with childhood glaucoma. The Icare-Pro shows more agreement with the Perkins tonometer than the Tonopen XL; therefore, it seems to be a more suitable option for these patients.

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INTRODUCTION

Childhood glaucoma is a potentially blinding condition. Primary congenital glaucoma is the most characteristic example of childhood glaucoma. It can occur at birth or months or years later. Primary and secondary childhood glaucoma are also responsible for an increase in intraocular pressure (IOP), which can cause misdiagnosis and suboptimal treatment and allow irreversible optic nerve damage to occur.[1-3]

Tonometry is the basis of both glaucoma diagnosis and management.[4,5] Although several tonometers have

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been assessed in adults, the results cannot always be extrapolated to children.[6,7] In recent years, some tonometers have been widely used to either diagnose or screen children suspected of having childhood glaucoma.[8-12] Goldmann applanation tonometry is the gold standard for glaucoma in adults and children. Its portable device, the Perkins tonometer (Clement-Clarke, Haag-Streit, Harlow, United Kingdom), is useful for children because it measures IOP in supine and seated positions.[13-15] However, tonometers with less corneal surface contact (eg, Tonopen XL [Reichert, Depew, NY] and Icare-Pro [Icare, Tiolat Oy, Helsinki, Finland]) have shown utility in irregular corneas[16] and good correlation with the Perkins tonometer.[9,12,17,18] Although these tonometers have been widely used in clinical practice for childhood glaucoma, ocular morphology in children differs from that in adults and presents corneal changes and higher ocular axial length due to progressive eye growth,[6,19] which could influence IOP measurement.

The purpose of this study was to evaluate concordance between the three tonometers in children with early-onset childhood glaucoma under general anesthesia and to identify possible morphometric factors that can influence the IOP measurements obtained with each tonometer.

PATIENTS AND METHODS

A cross-sectional, prospective study was conducted including 91 eyes of 46 patients (younger than 24 months) with consecutive early-onset childhood glaucoma. The study protocol was approved by the hospital's Human Subjects Committee and adhered to the tenets of the Declaration of Helsinki regarding research involving human patients. Informed consent was obtained from the parents of each child before being included in this study.

Diagnostic criteria of the World Glaucoma Association Consensus Meeting on Childhood Glaucoma were considered for either primary or secondary childhood glaucoma.[2] Childhood glaucoma was defined as the presence of a combination of signs consistent with high IOP (> 21 mm Hg), enlarged corneal diameter (> 11 mm in newborn, > 12 mm in an infant younger than 1 year of age, or > 13 mm in a child of any age), corneal edema, Descemet's membrane splits or Haab's striae, disc cupping of 0.3 or disc asymmetry of 0.2, progressive disc cupping, visual field defects, or progressive myopia.[2]

All patients diagnosed as having early-onset childhood glaucoma who required examination under sedation were enrolled following the usual procedure, which cannot be explored during clinical practice due to poor collaboration. Children younger than 3 years with early-onset childhood glaucoma and no ocular malformation in the anterior chamber were evaluated for primary congenital glaucoma. In both primary congenital and childhood glaucoma, secondary dense corneal edema or corneal leukoma were considered exclusion criteria. Previous ocular surgeries and number of hypotensive ocular treatments were recorded and were not considered exclusion criteria.

IOP was measured with the Perkins, Icare-Pro, and Tonopen XL tonometers. Axial length, anterior chamber depth, lens thickness, vitreous length, and central corneal thickness (CCT) were determined using ultrasound biometry and expressed as the mean of 10 consecutive measurements determined by ultrasound pachymetry and biometry (Echoscan US-50; Nidek Co. Ltd., Gammagori, Japan). IOP measurements were obtained in a single session under general anesthesia with the patient in a supine position and without an eyelid speculum. Anesthesia was induced with sevoflurane.

To minimize potential time-related anesthetic effects, IOP measurements were performed first. Because the Icare-Pro and Tonopen XL are contact devices, the exploration order was randomized using a randomization system (www.randomization.com). The Perkins tonometer was always used second to preserve the corneal deformation after applanation. Two attempts were made to obtain IOP measurement with each instrument, after which the test was considered unsuccessful. Only reliable measurements were used.

For the Icare-Pro, if the variation between measurements was within normal limits, the numerical deviation appeared in green. For the Tonopen XL, only measurements with a 95% confidence interval (CI) or higher were recorded. The mean of two measurements was considered for each procedure. The measurements were obtained by three examiners who were masked to the readings of the other tonometers. To reduce the duration of the examination and minimize the anesthetic effects, a different examiner recorded all measurements.

All measurements were taken between 9:00 PM and 12:00 AM, according to the general practice of our department to minimize the effects of diurnal variation.

Statistical Analysis

All statistical tests were performed using SPSS for Windows (version 21.0; SPSS Inc., Chicago, IL) and MedCalc (version 7.3; MedCalc, Ostsend, Belgium)

TABLE 1

Descriptive Statistics

Variable	Mean ± SD (Range)
Perkins IOP (mm Hg)	17.99 ± 6.24 (2 to 36)
Icare-Pro IOP (mm Hg)	19.3 ± 6.10 (6 to 34)
Tonopen XL (mm Hg)	23.50 ± 10.65 (2 to 54)
Central corneal thickness (μm)	573.19 ± 94.13 (465 to 1,211)
Axial length (mm)	22.84 ± 2.70 (17.32 to 29.49)
Anterior chamber depth (mm)	3.76 ± 0.66 (2.30 to 5.60)
Lens thickness (mm)	3.66 ± 0.35 (3.04 to 5.11)
Vitreous length (mm)	15.62 ± 2.25 (11.56 to 21.85)
Mean IOP difference (Icare-Pro IOP–Perkins IOP) (mm Hg)	2.18 ± 3.45 (7 to 11)
Mean IOP difference (Tonopen XL IOP–Perkins IOP) (mm Hg)	6.71 ± 7.13 (5 to 33)
Mean IOP difference (Tonopen XL IOP–Icare-Pro IOP) (mm Hg)	4.50 ± 6.06 (7 to 26)

SD = standard deviation; IOP = intraocular pressure
The Perkins tonometer is manufactured by Clement-Clarke, Haag-Streit, Harlow, United Kingdom; the Icare-Pro tonometer is manufactured by Icare, Tiolat Oy, Helsinki, Finland; and the Tonopen XL tonometer is manufactured by Reichert, Depew, New York.

software. The Kolmogorov–Smirnov test was used to confirm the normal distribution of the quantitative data, which were provided as the mean and standard deviation. Measurements obtained using the three instruments were compared with the Student's paired *t* test. Quantitative variables were expressed as their corresponding means and standard deviations. Medians and interquartile ranges were used to describe variables showing a non-normal distribution.

The correlation between parameters and IOP measurements was assessed with the Pearson correlation coefficient. To assess the level of agreement between the methods and systemic bias, intraclass correlation coefficients (ICCs) and their 95% CIs were determined. A Bland–Altman plot was prepared to assess the difference between the Icare-Pro, Tonopen XL, and Perkins readings against the average of the three. The influence of ocular biometry and CCT on IOP was analyzed with a multiple regression linear analysis. A *P* value of less than .005 was considered significant.

RESULTS

Analysis was performed on the data obtained from 91 eyes of 46 patients. The mean age of children was 29.1 ± 26.19 months (range: 13 to 31 months); 47.3% were girls and 52.7% were boys. The mean age at childhood glaucoma diagnosis was 8.4 months (range: 10 days to 24 months). Most of the children were diagnosed as having primary congenital glaucoma (63 eyes, 69.2%), followed by Sturge–Weber syndrome (16 eyes, 17.6%), aniridia (8 eyes, 8.8%), and aphakic glaucoma (4 eyes, 4.4%). Goniotomy was the most common surgery performed to control IOP (28 eyes, 30.8%). A second goniotomy was performed in 7 eyes (7.7%). A trabeculectomy was performed in 23 eyes (25.3%) and 14 eyes (15.4%) underwent two trabeculectomies. Only 5 eyes (5.5%) required Ahmed valve implant (New World Medical, Inc., Rancho Cucamonga, CA) surgery. Of the 91 eyes, 36 used at least one glaucoma medication (39.6%).

IOP measurements with the three tonometers, ocular axial length, anterior chamber depth, lens thickness, vitreous length, and CCT are listed in **Table 1.**

A reliable measurement with the Tonopen XL could not be obtained in 2 eyes after two attempts. Biometry and pachymetry were difficult to obtain in 5 and 11 eyes, respectively. There were no complications using ultrasound pachymetry and biometry or either of the three tonometers. Mean IOP measurements were 19.3 ± 6.10 mm Hg (range: 6 to 34 mm Hg) for the Icare-Pro, 23.50 ± 10.65 mm Hg (range: 2 to 54 mm Hg) for the Tonopen XL, and 17.99 ± 6.24 mm Hg (range: 2 to 36 mm Hg) for the Perkins tonometer. The mean difference in readings between instruments was 2.18 ± 3.45 mm Hg for Perkins–Icare-Pro ($P < .0001$, 95% CI: 1.5 to 2.9), 6.71 ± 7.13 mm Hg for Perkins–Tonopen XL ($P < .0001$, 95% CI: 5.2 to 8.2), and 4.50 ± 6.06 mm Hg for Tonopen XL–Icare-Pro ($P < .0001$, 95% CI: 5.20 to 8.21), with significant differences between the readings.

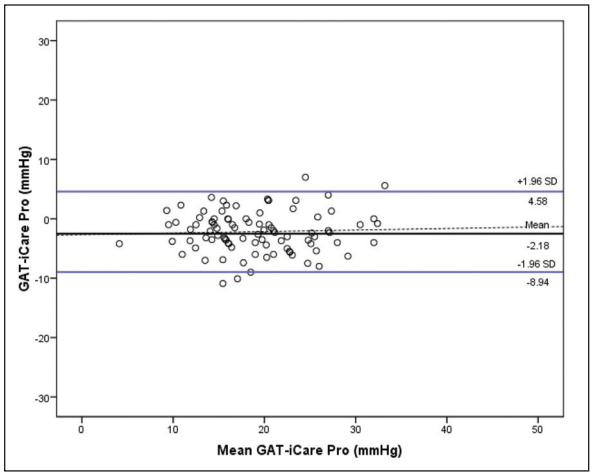

Figure 1. Bland–Altman plot. Measurement of intraocular pressure (IOP) with Perkins versus Icare-Pro versus the mean of both (slope: 0.26; P = .676). The handheld Goldmann applanation tonometer (GAT) (Perkins) is manufactured by Clement-Clarke, Haag-Streit, Harlow, United Kingdom, and the Icare-Pro is manufactured by Icare, Tiolat Oy, Helsinki, Finland.

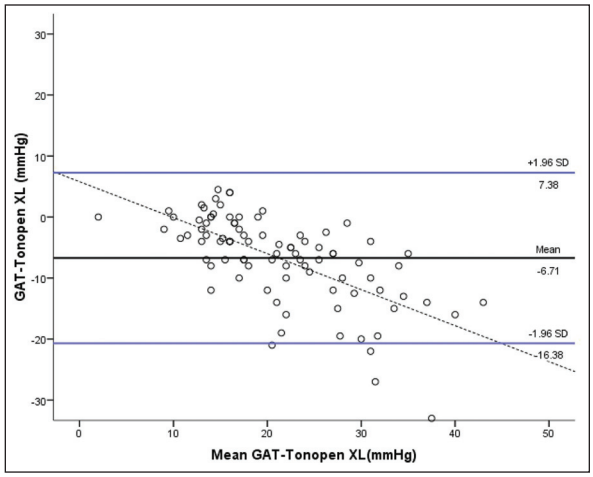

Figure 2. Bland–Altman plot. Measurement of intraocular pressure (IOP) with Perkins versus Tonopen XL versus the mean of both (slope: -0.590; P < .0001). The handheld Goldmann applanation tonometer (GAT) (Perkins) is manufactured by Clement-Clarke, Haag-Streit, Harlow, United Kingdom, and the Tonopen XL is manufactured by Reichert Inc., Depew, NY.

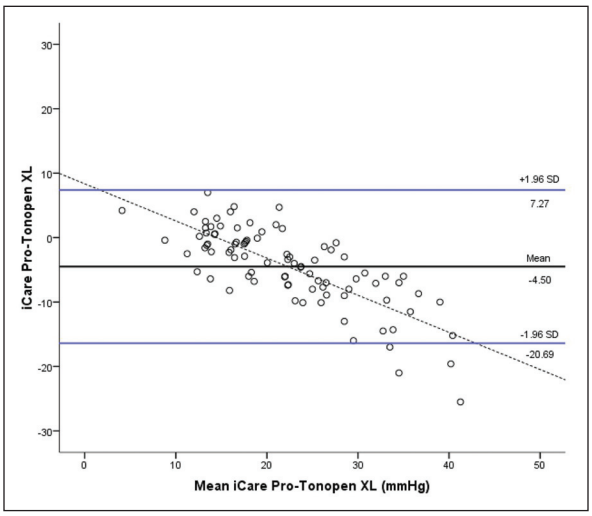

Figure 3. Bland–Altman plot. Measurement of intraocular pressure (IOP) with Icare-Pro versus Tonopen XL versus the mean of both (slope: -0.576, P < .0001). The Icare-Pro is manufactured by Icare, Tiolat Oy, Helsinki, Finland, and the Tonopen XL is manufactured by Reichert Inc., Depew, NY.

Good linear correlation was observed between the readings of the three instruments (Perkins–Icare-Pro: r = 0.844, P < .0001 vs Perkins–Tonopen XL: r = 0.764, P < .0001 vs Icare-Pro–Tonopen XL: r = 0.877, P < 0.0001). The Icare-Pro showed greater concordance with the Perkins tonometer than the Tonopen XL (ICC: 0.789, 95% CI: 0.697 to 0.856, P < .0001 vs 0.453, 95% CI: 0.272 to 0.603, P < .0001), indicating good agreement between the tonometers.

Regarding IOP measurements and their relation to CCT, our results showed a low nonsignificant correlation with the Perkins tonometer IOP measurements (Perkins vs CCT: r = 0.129, P = .293). Similarly, our results showed a low nonsignificant correlation with the IOP measurements obtained by the Perkins tonometer, Icare-Pro, and Tonopen XL and their relation to anterior chamber depth or lens thickness (Perkins vs anterior chamber depth: r = 0.170, P = .127; Perkins vs lens thickness: r = 0.117, P = .311; Icare-Pro vs anterior chamber depth: r = 0.120, P = .282; and Icare-Pro vs lens thickness: r = 0.153, P = .185). However, CCT values were significantly correlated with both Tonopen XL and Icare-Pro measurements (Tonopen XL vs CCT: r = 0.461, P < .0001; Icare-Pro vs CCT: r = .277, P = .022).

Axial length measurements and vitreous measurements affected the Perkins, Icare-Pro, and Tonopen XL IOP measurements. Greater axial length and vitreous length resulted in greater IOP. The three sets of readings also showed good linear correlation (Perkins vs axial length: r = 0.395, P < .0001; Perkins vs vitreous length: r = 0.378, P = .001; Icare-Pro vs axial length: r = 0.470, P < .0001; Icare-Pro vs vitreous length: r = 0.463, P < .0001; Tonopen XL vs axial length: r = 0.410, P < .0001; and Tonopen XL vs vitreous length: r = 0.433, P = .001).

Perkins–Icare-Pro concordance was stable in all IOP measurements (**Figure 1**) (slope: 0.26, P = .676). The Tonopen XL overestimated IOP compared with the Perkins tonometer (slope: -0.590, P < .0001, **Figure 2**) and the Icare-Pro (slope: -0.576, P < .0001, **Figure 3**), being more remarkable if the measurements obtained with the Perkins tonometer were greater than 20 mm Hg. In the 34 eyes with Perkins tonometer measurements greater than 20 mm Hg, the mean dif-

ference in IOP readings between the Tonopen XL and the Icare-Pro was 8.31 ± 5.73 mm Hg. In the 55 eyes with Perkins tonometer measurements of 20 mm Hg or less, the mean difference in IOP readings between the Tonopen XL and the Icare-Pro was 2.15 ± 5.0 mm Hg.

Bland–Altman plots showed that IOP measurements in 87 of 91 eyes (95.6%) (**Figure 1**), 86 of 89 eyes (96.6%) (**Figure 2**), and 85 of 89 eyes (95.5%) (**Figure 3**) were within the limits of agreement for Perkins–Icare-Pro, Perkins–Tonopen XL, and Icare-Pro–Tonopen XL concordances, respectively. Of the patients whose Icare-Pro readings were higher than the Perkins measurements, the greatest difference recorded was 11 mm Hg. In patients showing a higher IOP with the Perkins tonometer, the difference was 7 mm Hg. Regarding the Perkins–Tonopen XL agreement, the greatest difference recorded was 33 mm Hg in patients whose Tonopen XL IOP readings were higher than those of the Perkins tonometer. In patients showing a higher Perkins tonometer IOP, the difference was 5 mm Hg.

Multiple regression linear analysis was used to determine the influence of biometry parameters (axial length, vitreous length, lens thickness, and anterior chamber depth) and CCT on IOP measurements. A greater influence on IOP corresponded to greater axial length, with the greatest effect on the Tonopen XL (slope: 0.086, 95% CI: 0.013 to 0.16, $P = .022$ vs 0.997, 95% CI: 0.369 to 1.625, $P = .002$ vs 1.571, 95% CI: 0.541 to 2.602, $P < .0001$ for Perkins, Icare-Pro, and Tonopen XL IOP measurements, respectively).

DISCUSSION

In many patients with childhood glaucoma, it is difficult to evaluate visual fields and changes in the optic nerve head. Therefore, a reliable IOP assessment is an essential step in examining these patients because the decision to perform surgery mostly depends on the IOP measurement. Also, general anesthesia often is required to measure IOP in non-compliant and young children.

IOP measurements are influenced by anesthesia,[20] but corneal changes can also affect these measurements.[6,7] Although several studies have demonstrated that repeat exposure to sevoflurane for less than 45 minutes does not affect cognitive child development,[21] all experts in childhood glaucoma know that the number of exposures and the time exposed to general anesthesia should be minimized. With the development of new tonometers (eg, Tonopen XL and Icare-Pro), sedation is needed less frequently.

Several studies have examined various techniques of IOP measurement in children. Bordon et al.[22] concluded that the Tonopen XL and Perkins tonometers may be reliable for children aged 1 to 60 months. Levy et al.[23] found that the Tonopen XL overestimated IOP compared with the Perkins tonometer when IOP measurements were greater than 16 mm Hg. Concordance was found between the results of the current study and those obtained by the only study that compared the Icare-Pro and Tonopen XL in anesthetized children with and without glaucoma.[24] In McKee et al.'s study,[24] IOP measurements with the Tonopen XL were 2 mm Hg higher than the Icare-Pro, with a greater difference in eyes with corneal edema or corneal abnormality. One hundred eyes were included in their study and only 33 were diagnosed as having glaucoma. The current study included 91 eyes of 46 children diagnosed as having childhood glaucoma who required surgery. If we had included younger children in our study, implying early diagnosis and surgical treatment, our results may have shown greater IOP differences between the Tonopen XL and Icare-Pro or the Perkins tonometer.

In the most recent study in which agreement between Goldmann applanation tonometry, Icare-Pro, and Tonopen XL was evaluated, the Tonopen XL showed the worst agreement.[25] In the current study, good agreement was found between the Perkins tonometer and the Icare-Pro, but concordance between Tonopen XL–Perkins and Tonopen XL–Icare-Pro was lower, showing a strong trend toward overestimation. The frequency of higher values may indicate that the Icare-Pro is the best option for IOP measurement in patients when the Perkins tonometer is not available. Recent studies performed using the Ocular Response Analyzer (Reichert Technologies, Inc.) in patients with primary congenital glaucoma found that corneal changes in those patients could influence IOP measurements.[6,7] The correlation between CCT and IOP shows the influence of pachymetry on IOP measurements, which is greater in the Tonopen XL. It is possible that patients with corneal scars, leukoma, or corneal pathology secondary to primary congenital or childhood glaucoma present a greater tendency toward IOP overestimation with the Tonopen XL. Because patients included in this study were young, corneal hysteresis could not be determined.

A multiple regression linear analysis was used to identify possible risk factors that affect IOP measurements determined with different tonometers. Although pachymetry affected the IOP measurement of the three

tonometers, multiple regression linear analysis showed that axial length affected IOP measurement the most. For every 1 mm increase in axial length, IOP measured with the Tonopen XL increased 1.5 mm Hg and IOP measured with the Icare-Pro increased approximately 1 mm Hg. However, this effect was almost nonexistent when measuring with the Perkins tonometer. For each 1 mm increase in axial length, IOP increased 0.086 mm Hg, which was not statistically significant. Axial length determination by A-scan ultrasound is helpful in both diagnosing the disease and determining response to treatment while the sclera remains vulnerable to the effects of elevated IOP.[26] The observation of significant progressive myopia indicates inadequate IOP control, especially if observed in the setting of progressive axial length increase. The mean axial length in our patients was greater than expected according to mean age.[26,27] The influence of axial length on IOP has been previously described.[19,26,27] Patients with greater axial length present worse evolution and visual prognosis. In these patients, it is possible that the Tonopen XL may not be as exact in IOP determination as the Perkins tonometer or the Icare-Pro.

Our study had limitations. The number of patients is small and both eyes were included in several patients. Because childhood glaucoma is an infrequent disease, it is difficult to increase the sample size.

The Icare-Pro may become a useful tool for tonometry in children due to its concordance with the Perkins tonometer. The influence of axial length on IOP measurements with the Tonopen XL should be taken into account in children with childhood glaucoma to avoid IOP overestimation.

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