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Influence of Corneal Biomechanical Properties on Intraocular Pressure Differences Between a non-contact ORA Tonometer and the Goldmann Applanation Tonometer in primary congenital glacomatous children

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ABSTRACT

This study aimed at evaluating the effect of corneal properties on the difference between IOP measured with non-contact tonometer (IOPcc)and contact goldman applantation tonometer(GIOP) in children with primary congenital glaucoma(PCG) .In current study The influence of central corneal thickness (CCT), keratometry(Km),equicalent sphere of refractive error (ES) and Ocular Response Analyzer (Reichert) measurements of corneal viscoelasticity [corneal hysteresis (CH) and corneal resistance factor (CRF)] on IOP differences between tonometers was evaluated in children with PCG . The CH was calculated to be the best predictor of the differences in IOP readings between tonometers (r2=0.46; P< 0.0001 . CRF,CCT,Es and Keratometry performed very poorly as lone predictor of IOP differences. In a multiple regression model CH and CRF together accounted for 84% (r2=0.84; P< 0.0001) of the variance in IOP reading differences between tonometers. Corneal viscoelastic properties (CH)induced by either contact or noncontact tonometers was calculated to be the most determinant factor in influencing IOP differences(IOPcc-GIOP).

Key words: Primary Congenital Glaucoma(PCG), Ocular Response Analayzer (ORA), Central Corneal Thichness(CCT) , Goldmann Applanation Tonometer

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INTRODUCTION

Goldmann applanation tonometry (GAT) presents today the reference standard for assessing IOP[1 . In previous studies, the most effective factors on IOP measurement were central corneal thickness (CCT), the anterior corneal curvature, and viscoelasticity of the corneal tissue [1-3]. The exact knowledge of the relationship between these corneal features and their effects on measured IOP from a variety of contact and noncontact tonometers has not yet been thoroughly investigated. This is very important when examining patients with different CCT and corneal biomechanical properties like primary congenital glaucoma [4, 5]. Primary congenital glaucoma is not common and It is diagnosed only in 25% of the newborn infants. More than 80% of children with glaucoma have primary congenital glaucoma in their first year of life[6]. One of the most important steps in the treatment of glaucoma is precise measurement of IOP. IOP reduction plays an important role in the treatment of glaucoma,so accurate measurement of IOP plays an important role in evaluating glaucoma. Several studies had examined the IOP measured by ORA with Goldman in a normal population [7-9]. Corneal biomechanical properties were evaluated by ocular response analyser (ORA, Reichert Inc., Depew, NY, USA) . The ORA produces a rapid air puff to deform the cornea, and the process of deformation and reformation of the cornea is documented with an infrared camera. Analysis of the curve provides two parameters that are indicative of the biomechanical profile of the cornea: corneal hysteresis (CH) and corneal

resistance factor (CRF)[10]. The ORA also calculates Goldmann-correlated and corneal-compensated IOP estimates (IOPg and IOPcc, respectively). Ophthalmologists know that CCT was an important factor in accurately estimating IOP with Goldman applantation tonometer (GAT) and the more CCT, the more IOP[11]. Due to special corneal features in primary congenital glaucomatous patients, the Goldman Tonometer does not accurately assess IOP. IOPcc obtained from ORA(noncontact tonometer) and showed the corneal compensated IOP. The aim of this study was to investigate whether corneal parameters, such as CCT, keratometry (Km), spherical equivalent (SE) and corneal viscoelasticity measurements provided by the ORA, influence the IOP differences between the ORA (IOPcc) and the GAT (GIOP). This is the first work that aims to analyze the overall influence of the corneal parameters on IOP differences between an NCT (IOPcc) and the GAT (GIOP) in primary congenital glaucomatous patients.

MATERIALS AND METHODS

This 24-month prospective, comparative study was conducted among patients who referred to the tertiary glaucoma Eye Care Center for follow up. This cross-sectional study was conducted after approval from the local Ethics Committee. Informed consent was obtained from the patients and the parents of the enrolled children during the study. The study included 47 eyes of 28 patients under twenty years old with primary congenital glaucoma. Inclusion criteria included cooperative patients with PCG (elevated IOP, enlarged corneal diameter > 12 mm, Haab's striae, and typical glaucomatous optic neuropathy). Uncooperative patients, subjects with corneal pathology (corneal edema, corneal scar, or band shape keratopathy), secondary glaucoma, and congenital optic neuropathies were excluded. The participants had undergone trabeculotomy as the first surgical procedure for glaucoma. Those with uncontrolled IOP following initial surgery were on medications or had received shunt surgery. All patients underwent a full eye examination, including slit lamp biomicroscopy and fundus slit lamp biomicroscopy using the Volk Superfield lens, gonioscopy using a Sussman gonio lens (for uncooperative patients; we used their gonioscopy records during surgical procedures or examinations under anesthesia), and fundus slit lamp biomicroscopy using a Volk Superfield lens . An autokerato-refractometer (KR-8900; Topcon Co., Tokyo, Japan) was employed to determine mean power and mean curve. Refractive examination was done and refracteve error and best single corrected visual acuity and spherical equivalent was recorded. All pachymetry were performed on the central cornea using an ultrasound pachymeter (Paxis, Biovision Inc., Clermont-Ferrand, France). Ten measurements were taken at the center of the cornea and after excluding the outliers, the average value was regarded as CCT. To minimize the potential confounding effects of diurnal IOP variation, all study measurements were taken between 9:00-11:00 AM. Four to five measurements were taken by an ORA tonometer and the results with the highest waveform score were used for recording CH, CRF, IOPcc, and IOPg values[12] . Two GAT measurements were obtained by an experienced specialist using a calibrated GAT (Haag-Streit, Köniz, Switzerland), averaged and noted as the GAT-IOP. Measurements were taken randomly to compensate for any variation in IOP caused by corneal applanation. . All data were tabulated in an SPSS17 Statistical analysis (SPSS Inc., Chicago, IL, USA). Data were analyzed by the authors and by a statistician team from Shiraz University of Medical Science. The Kolmogorov– Smirnov test was used to confirm normal distribution for all collected data. Relationships between CCT, CH, CRF,Km and ES were investigated by Pearson's correlation coefficient. Significance was set at $p < 0.05$. Regression analysis was used to study the effect of CH, CRF ,CCT and p on IOP . The difference between GIOP-IOPcc was calculated . Regression analysis was performed to examine the effect of CH, CRF ,CCT and p on GIOP-IOPcc.

RESULTS

The mean and range of variables studied in this study are summarized in Table 1. Pearson correlation CH, CRF, CCT, Km and ES were investigated. A significant strong correlation was found between CH snd CRF (r=0.75,P=0.000) There were weak significant correlation between CH,Km (r=0.44,P=0.006) and CRF, Km(r=0.35,P=0.031). In a single linear regression model, CH was the best predictor of IOP differences (GIOP-IOPcc), explaining 46% of the differences between GIOP (by goldman applantation tonometer) and IOPcc (by ORA) corneal (r2=0.46; P=0.000<0.01). Effects of other variables like CRF (r2=0.013, P=0.52), CCT (r2=0.004, P=0.28), Km (r2=0.004, P=0.23) and SE (r2 =0.04, P=0.04) were not significant. Single

linear regression equations were investigated between each of the indicators of IOP (IOPg, IOPcc and GIOP) and any of the variables(CCT, CH, CRF, Km, SE) that may affect IOP. Km and SE did not have a significant effect on IOP. A multiple linear regression model, containing CRF, CH, and CCT, performed slightly better than single models, explaining 83% of the variance in IOP differences (GIOP-IOPcc). Adding Km did not improve the prediction efficacy of the multivariate model. The results of multiple stepwise regression models are shown in Table 2.

Table 1: Characteristics of subjects included in the study

Variables	Mean(SD)	Rang
Age, year	9.50 ± 3.57	4-20
CH, mmHg	8.67 ± 3.20	2.3-15.7
CRF, mmHg	10.28 ± 3.28	4.30 ± 16.80
CCT, µm	594.5 ± 65.5	444-850
KM , D	41.16 ± 2.4	34.75-48
IOPcc, mmHg	21.68 ± 7.47	12-41
IOPg,mmHg	19.96± 7.26	7.6-39.5
GIOP, mmHg	17.05 ± 3.93	8-27
SE, D	-1.29 ± 2.80	-9-+9

CH: corneal hysteresis; CRF: corneal resistance factor; CCT: central corneal thickness; KM: Mean Keratometry; IOPcc: corneal compensated intraocular pressure; IOPg : Goldmann-correlated intraocular pressure ; GIOP: Goldmann intraocular pressure; SE: spherical equivalent

Table 2: The results of multiple stepwise regression models

Variable	IOPg B (p-value)	IOPcc B (p-value)	GIOP B (p-value)	IOPcc- GIOP B (p-value)
CH	-2.85 P=0.000	-3.50 P=0.000	-0.86 P=0.001	+2.67 P=0.000
CRF	+3.35 P=0.000	+2.85 P=0.000	+1.13 P=0.000	-1.74 P=0.000
CCT	+0.001 P=0.036	+0.001 P=0.000	-0.004 P=0.691	-0.003 P=0.755
Constant	10.81 P=0.0000	23.28 P=0.000	14.13 P=0.020	-9.16 P=0.119
R2	1	1	0.46	0.84

CH: corneal hysteresis; CRF: corneal resistance factor; CCT: central corneal thickness; IOPcc: corneal compensated intraocular pressure; IOPg : Goldmann-correlated intraocular pressure ; GIOP: Goldmann intraocular pressure; GIOP-IOPcc: differences between goldman applantatiopn tonometry-corneal compensated intraocular pressure

CONCLUSION

Knowledge of Corneal Biomechanics characteristics in the field of measuring IOP, corneal pathology and refractive surgery was very consequential. It has been long debated whether the Goldmann tonometer is sensitive and specific enough to be used for patiants with special cornea properties like primary congenital glaucoma. CH and CRF vary between patients with PCG and normal people[4]. In normal group, the mean of CH was obtained about 10.7 in the study of Shah et al.[9, 13] and approximately 10.24 in the study of cabonaro et al [14]. Sullivan et al. [15] showed that CH in POAG was significantly lower than that of normal people,glaucoma suspect and ocular hypertention. Mean CH (8.6 mmHg) obtained in this study was less than that of the normal group. Experience in POAG showed that IOPcc provided more accurate information on IOP and Goldman Tonometer has always been considered as the standard method for measuring IOP.The critical purpose of measuring IOP was in the diagnosis and management of IOP in glaucomatous patients. In this study, the influence of various corneal parameters on IOP differences between an ORA NCT (IOPcc) and the GAT was evaluated. In our previous study [16], we found that the mean IOPcc measured with ORA (21.1 mm Hg) was statistically significantly higher than that obtained with the GAT (15.3 mmHg). The 95% limit of agreement amplitude between the 2 tonometers was calculated to be wide, ranging from 0.6 to 10.8 mm Hg. In a view to identify the major(s) corneal parameters capable to influence the differences in IOP readings between the 2 tonometry methods, in this study we performed a linear regression model including the Km, the CCT, and the viscoelasticity parameters provided by the ORA (CH and CRF), other than the age and sex of subjects included in the study. CH and CRF were measured to be the best predictor of IOP differences between instruments, explaining 84% of the differences NCT (ORA) and GAT(table2) . Mean Km values revealed to be the worst predictor of IOP differences between the instruments tested .When considered as lone predictors; CRF and CCT were calculated to be less effective than CH in predicting differences between tonometers, explaining approximately 45% of the variance in IOP differences. we chose to use the ORA parameters as estimates of the corneal biomechanical properties, as the ORA was the only device to provide this information in the clinical setting. The CRF value was in general measured to be significantly correlated to CCT [17]. Significant correlation between CH, CCT(r=0.023, P=0.895) and CRF, CCT(r=0.272, P=0.114) werenot found and this was probably due to lower CCT in this group than normal. Farvardin et al.[18]performed a meta-analysis in the normal group and achieved a significant correlation between IOP and CCT. Nejabat et al [19] examined CCT in normal Iranian children and

found that the CCT was lower in Iranian normal children than in other racial groups. They achieved a weak correlation between IOP and CCT. In non- glaucomatous groups, the biomechanical properties was heavily influenced by CCT But had a little effect on glaucomatous eyes[20]. CH could be a useful tool for diagnosis of glucomatous patients [20]. In our regression equation, we obtained a significant positive correlation between CH and IOPcc-GIOP, It can be concluded that the difference in CRF and CH in this group makes more difference in IOPcc-GIOP. The numerical value of corneal biomechanical properties due to its high variation in healthy individuals and glucomatous patiants did not give us complete information And it was even said that CH is corneal biomechanical behavior and was not a fixed property like thickness[17]. In normal group,With increasing CRF, the amount of CH increased and was linked together. True IOP was underestimated by Goldmann applanation tonometry in underdampened corneas (lower CH) and should be an interesting factor in glaucoma management. The difference in CH compared to other variables has a greater effect on IOPcc-GIOP.

Conflict of interest
None declared.

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