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Greater Impact of Corneal Biomechanics Than Central Corneal Thickness on Intraocular Pressure Measurements

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Abstract

Purpose: To evaluate the influence of corneal biomechanical properties and central corneal thickness on intraocular pressure measurements in children with aphakic glaucoma and primary congenital glaucoma. **Methods:** This comparative cross-sectional study consists of 70 eyes of 70 patients with aphakic (n=34) and primary congenital glaucoma (n=36) who referred for routine eye examinations. The intraocular pressure (IOP) and corneal biomechanical factors like corneal hysteresis (CH) and corneal Resistance Factor (CRF) were measured by Ocular Response Analyzer (ORA). Central corneal thickness (CCT) was checked by ultrasound pachymetry**. Results:** There was no statistically significant difference between the two groups for age (P=0.137), sex (P>0.05) and IOPcc (P-value=0.36). There were significant differences between CRF (p-value=0.001), CCT (p-value=0.0001) and CH (P-value=0.005) between groups. The regression equation of IOPg (goldman applantation tonometry) in aphakic group was
1.03CH (P<0.0001)+1.56CRF(P<0.0001)+0.077CCT(P=0.017) and in primary congenital glaucomatous group was -1.06CH(P<0.0001)+1.21CRF(P<0.0001)-0.03CCT(P=0.333)
Conclusion: CH, CRF, and CCT were significantly different between groups. CH and CRF were more effective than CCT for the accurate estimation of IOP in both groups.

Keywords: Glaucoma, Corneal Pachymetry, Intraocular Pressure, Corneal Hysteresis, Corneal Resistance Factor

Introduction

Knowledge of corneal biometric and biomechanic characteristics in the field of measuring intraocular presure IOP, corneal pathology and refractive surgery is very important. Central corneal thickness (CCT) is one of the most important factors in IOP measurement. The thicker and thinner CCT affected IOP measurements and led to over- and underestimation of IOP (Medeiros & Weinreb, 2006). Ocular response analyzer (ORA) is the first device that could examine the corneal biomechanic properties (viscoelastisity). Many clinical decisions in the glaucoma management is made based on the measured IOP, so accurate IOP measurement is crucial (Mathenge & Herndon et al, 2016). It had been understood that there was a large variation in the CCT between individuals and the CCT could affect the intraocular pressure (IOP) readings by tonometers. CCT and CH (corneal hysteresis) are important parameters that the examiner need to consider to accurately evaluate IOP (Perucho-González & et al, 2017). The biomechanical response of the optic nerve head is probably related to the severity of glaucoma in the primary open angle glaucoma. CCT in patients with aphakic glaucoma was higher (Simsek & et al, 2006) and in primary congenital glaucoma was equal or less than that of normal people (Wygnanski-Jaffe & Barequet, 2006)**.** Knowing the biomechanical properties of these two groups along with CCT is beneficial in the more accurate estimation of IOP. The main objective of this study was to compare corneal biomechanical factors between aphakic patients as a group with thick cornea and primary congenital glaucoma as normal corneal thickness and evaluate the effect of CH and CRF versus CCT on the IOP in aphakic group and primary congenital glaucomatous group.

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Materials and Methods

This comparative cross-sectional study was conducted on patients with established aphakic glaucoma (n=34) and primary congenital glaucoma (n=36) presenting for routine eye examinations to a Tertiary Eye Care Center in Shiraz. The study was approved by the local ethical committee and informed consent was obtained from the patients or their parents. The aphakic and primary congenital glaucomatous cases had a medically controlled glaucoma following surgery for congenital cataract or trabeculotomy surgery, respectively. In Aphakic group the patients who had medically controlled IOP, typical glaucomatous optic nerve damage followed by optic nerve head photography and cooperative patients under 20 years of age were included in the study. The patients with congenital glaucoma who met our inclusion criteria (controlled IOP level, enlarged corneal diameter>12mm, glaucomatous optic nerve cupping, Haab’s striae and cooperative patients under 20 years of age) were entered into our study. The exclusion for all groups were the presence of any corneal pathology, interference in measurements due to nystagmus, corneal edema, corneal scar, band shape keratopathy, corneal astigmatism more than 4.00 diopter, uncooperative patients and sphere component of refractive error more than ± 4.00 diopter. All patients underwent a full eye examination, including anterior segment and fundus slit lamp biomicroscopy using the Volk Superfield lens, ocular response analyzer (ORA) (Reichert Ophthalmic Instruments, Depew, NY, USA), and ultrasound pachymeter (Paxis, Biovision Inc.,Clermont-Ferrand, France). Four to five measurements were taken using an ORA tonometer and the results with the highest waveform score were used to record CH, CRF, IOPcc, and IOPg values[7]. All pachymetry measurements were performed on the central cornea. Ten measurements were taken at the center of the cornea and after excluding the outliers, the average value was regarded as CCT. Student t and Fisher-Snedecor tests, regression analysis and pearson's correlation were used for statistical analysis. A P-value less than 0.05, and a Pearson's coefficient (r) over ±0.65 were considered statistically significant.**All** statistical calculations were performed with SPSS-18® software

Results

The Demographic information of the participants, CCT, CH, CRF and IOP of patients is shown in table 1. There was no statistically significant difference between the groups for age (P-value=0.137) and sex (P-value=0.086). Only the two groups of aphakic glaucoma and congenital glaucoma were the same in IOPcc (P-value=0.36). There were significant differences between CRF (p-value=0.001), CCT (p-value<0.001) and CH (P-value=0.005) .The regression equation was written in each of the groups with respect to the effect of CH, CRF, and CCT on the IOP. The effect of CH, CRF, and CCT on the IOPcc in regression equation of each group is shown in Table 2. The coefficients of regression equation on the effects of CH, CRF, and CCT on IOPg in each groups are shown in Table3. In each group, the Pearson's correlation between CH, CRF, and CCT was investigated. A significant relationship was observed between CH and CRF in the three groups (Pearson's correlation=0.78, p-value<0.0001 in group 1), and (Pearson's correlation=0.66, p-value<0.0001 in group 2). The correlation between CH and CCT in the groups was investigated, but this correlation was significant only in group 1 (Pearson's correlation=0.48, p-value=0.006 in group 1) and (Pearson's correlation=- 0.19, p-value=0.31 in group 2). The correlation between CRF and CCT in the groups was investigated, but this correlation was significant only in group 1 (Pearson's correlation= 0.56, p-value=0.001 in group 1). The correlation between the differences in the two types of intraocular pressure (IOPg-IOPcc) and CCT, CH, and CRF was investigated. In the aphakic group, which CCT was significantly more than the other group (P-value=0.0001), there was a significant correlation between CCT and IOPg-IOPcc (Pearson's correlation=-0.55, p-value=0.001); meaning that in this group, the decrease in the thickness of CCT increased the differences in intraocular pressure. In this group, the difference is strongly more with decreasing CH and CCT (p-value<0.0001, Pearson's correlation=-0.96 / p-value<0.0001, Pearson's correlation=-0.93). In the primary congenital group, the data show that the lower the CH and CRF, the greater the difference between intraocular pressure (p-value<0.0001, Pearson's correlation=-0.95 / P-value<0.0001, Pearson's correlation=-0.87). The differences between the biomechanical properties (CRF-CH) were calculated and compared between groups. It was observed that in both glaucomatous groups, CRF-CH difference ranged from 2 to 3 mmHg.

Discussion

There were significant differences between CRF (sig=p-value=0.001), CH (P-value=0.005) and CCT (sig=p-value <0.001) between groups. CH and CRF were more effective than CCT for the accurate estimation of IOP (table2, 3) and the higher the difference between CRF and CH, the greater the measured IOPg (r = 0.98, P-value<0.0001 in group1) (r = 0.96, P-value<0.0001 in group2) and IOPcc (r = 0.96, P-value<0.0001 in group1) (r = 0.93, P-value<0.0001 in group2). Faramarzi et al found significant difference in CCT, CH and CRF between the two groups of Aphakic glaucoma and normal groups (Faramarzi, Feizi & Maghsoodlou, 2017). According Gonza´ lez et al (Perucho González & et al, 2017), the values of CH and CRF between the two groups of primary congenital glaucoma and normal had a significant difference but CCT between the two groups did not differ significantly. CH and CRF were likely to be affected by CCT, such that in these two groups, in addition to the difference in CCT, there are differences in CH and CRF. Comparison of the average CCT and CRF between groups showed that these two variables had the same behavior and this was consistent with the results of Touboul et al (Franco & Lira 2009; Touboul & et al, 2008) who concluded that CCT played an important role in the process of corneal damping and was effective in elastic properties According to Luce (Luce, 2005), corneas with low CH were less capable of gripping energy than normal eyes and they may be prospects for several ocular diseases. Moreover, low CRF showed that the overall corneal rigidity was lower than the normal. Nejabat et al (Nejabat & et al, 2016) revealed that CCT is thinner in Persian children than in most other racial groupings. Less CH and CRF values indicate changes in the corneal response in relation to glaucoma (Dascalescu & et al, 2016) .In glaucomatous patients, an accurate estimate of IOP will result in deciding on the treatment process. CCT affected the accuracy of measuring IOP using Goldman Applantation Tonometer (GAT). More CCT caused more pressure and the lower CCT resulted in lower measurement. Ehlers et al (Ehlers, Bramsen & Sperling 1975; Ehlers, HANSEN & Aasved, 1975). performed some studies of the effect of CCT on Goldman Applantation Tonometer (IOPGA) measurement and concluded that the IOPGA was determined precisely when the CCT was about 520 microns and the difference from this amount led to an estimation of more or less IOP, so with each 100 µm changes in CCT, IOP changes by 7 mm. These studies had influential constraints, including the relatively small volume of patients and the racial homogeneity of the population; nonetheless, the findings encouraged other investigations which suggested that CCT-induced GAT error might be important in ocular hypertension and normal tension glaucoma (Argus, 1995; Johnson & et al, 1978; Liu & Roberts, 2005) Liu et al., in a biomechanical model of the cornea, showed that corneal biomechanical properties had a significant effect on IOP measurement. In the present study, IOP data in the groups showed that corneal biomechanical properties (CH and CRF) have a greater effect than CCT in the IOP measurement. In the regression equation, the effect of CH on IOPcc in the groups was negative (P-value=0.0001, R=-1.45 in group 1), (P-value=0.0001, R=-1.25 in group 2), but the CRF had a positive effect on IOPcc (P-value=0.0001, R=1.50 in group 1) (P-value=0.0001, R=0.99 in group2) (Table 3). In other words, IOPcc increased by decreasing CH. This was similar to the findings of Mathenge et al (Mathenge & Herndon, 2016). who said that CH seems to have a greater effect than CCT on IOP measurement. Mangouritsas et al (Mangouritsas & et al, 2009). stated that corneal hysteresis in eyes with primary open-angle glaucoma was less than non-glaucomatous and they showed that CH has a weak positive relationship with CCT. In the present study, there was no correlation between biomechanical properties and CCT in groups 2. There was a weak correlation in the positive direction only in group 1. It can therefore be assumed that factors in addition to CCT affected the corneal biomechanical properties. Corneal deformability presented a summation of the real IOP, surface pressure, corneal curvature, and elastic properties (Liu & Roberts, 2005) Corneal elasticity was affected by corneal thickness, collagen structure, hydration, and extracellular matrix that certainly fluctuate between individuals (Mathenge & Herndon, 2016). Lui et al. showed that in a biomechanical model of the cornea, biomechanical properties had a great effect on IOP measurement. This model used a value called Young's modulus, which named it a modulus of elasticity. They used a modulus of 0.1 to 0.9 for Young's modulus, which assumed constant CCT and curvature of the cornea. Modulus difference 0.1 to 0.9 for Young’s modulus created 17 mmHg differences in predicting IOP measurements. A more significant coefficient was also obtained in CH and CRF versus CCT in regression equations for the prediction of IOP in the groups. There was a significant difference in CH between groups (P-value=0.005). It can be said that the CCT in the aphakic group caused increase in CRF, which had significant difference with the group2 (P-value=0.0001). Shah et al. reported that there was a positive correlation between increasing the CCT and increasing CRF. In the present study, a significant positive correlation was also observed between CCT and CRF in group 1 (Pearson's correlation=0.56, P-value=0.001), but there was no significant correlation between these two values in group 2 (P-value=0.82). A significant correlation was observed between CH and CCT in group 1 (Pearson's correlation=0.48, P-value=0.006<0.01) and there was no significant correlation in group 2 (P-value=0.31). CH is corneal biomechanical behavior and is not a stable physical characteristic like corneal thickness. It had been shown that CH in different types of glaucoma was lower than the normal eyes (Deol, Taylor & Radcliffe, 2015). In the present study, significant less CCT was found in group 2 as compared to group 1 (P-value=0.000<0.001). The results were in agreement with the results obtained by Perucho-González et al. and the results obtained from Mendes et al., who studied the distribution of CCT and its connection with other biometric data in patients with PCG and concluded that the patients presented a reduced mean keratometry when compared with the controls (Mendes, Sakata & Betinjane, 2011). IOPg-IOPcc was found to understand which factor was more relevant to this difference and the data showed that in the groups the effective factor was the CH and CRF, such that this difference (IOPg-IOPcc) decreases by increasing CH and CRF(table 4). The less the CH measured, the more likely the difference in IOPg with IOPcc. Since IOPcc took into account the viscoelastic nature of the cornea to assess the "corneal-compensated IOP, " a substantial difference should be expected between IOPcc and IOP GA when tissue viscous damping was abnormal. Under the low “viscous-damping” capacity (low CH), mechanical applanation was easier as compared to over “viscous-damping” capacity (high CH). As a result of this, IOPg should be underestimated in corneas with low “viscous-damping” capacity. This finding could be important in glaucoma screening process or IOP measurements after corneal refractive surgery. lower values of CH were found at the eyes with higher IOP and this amount was normalized by decreasing the IOP of the eyes (Deol & et al, 2015; Mendes, Sakata & Betinjane, 2011). Kamiya et al. reported IOP as an important explanatory variable relevant to CH, while Gonzalez-Meijome et al. reported a significant correlation between changes in IOP and changes in CH during the day in healthy patients. Medeiros and Weinreb (Medeiros & Weinreb, 2006), reported that GAT IOP was significantly associated to CCT and significantly affected by CRF, while IOPcc was not, and similar results have recently been confirmed by others (Touboul & et al 2008; Lau & Pye, 2011; Bayoumi, Bessa & El Massry, 2010). Therefore, the effect of CCT on IOP overestimation may be explained by CRF and the resistance against deformation of the cornea which was also higher in eyes with higher IOP values (Lau & Pye, 2011). There was a significant strong correlation between CRF-CH and both IOPg ($P<0.0001, r = 0.98$ in group1) ($P<0.0001, r = 0.98$ in group2) and IOPcc($P<0.0001, r = 0.96$ in group1) ($P<0.0001, r = 0.97$ in group2) in the groups. Our study result is in agreement with a study which showed that the combination of CH and CRF better explains the difference between a Goldman tonometer and other tonometers in normal eyes the present study limitation was that Goldman's eye pressure was not mached between groups and there was not any normal group for comparison. Although the two groups of aphakic glaucoma and primary congenital glaucoma matched in IOPcc, IOP was not measured with the Goldman applantation tonometer. In conclusion, biomechanical properties (CH, CRF) and CCT in aphakic group were significantly more than these values in primary congenital glaucomatous group. CH and CRF were more effective than CCT in the accurate estimation of IOP in both groups.

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Table 1. Demographics, CCT, CH, CRF and IOP of patients included in study

groups	Aphakic glaucoma (n=34)	Primary congenital glaucoma (n=36)	
	Mean ± SD (rang)	Mean ± SD (rang)	P
Age	15.5 ± 3.8 (6.5-20)	14.2 ± 2.6 (10-20)	P=0.137> 0.05
IOPcc	25.5 ± 7.8 (11.5-47)	23.9 ± 8.7 (12-46.5)	P=0.357>0.05
IOPg	26.5 ± 8.7 (11.7-53.7)	22.1 ± 8.1 (12-44.8)	p=0.013<0.05
CH	10.3 ± 3.2 (3.4-16.5)	8.3 ± 3.3 (2.3-13.9)	P=0.005<0.01
CRF	13.7± 3.9 (8.1-23.2)	10.6 ± 3.1 (4.3-16.1)	P=0.000<0.0001
CCT	651.6 ± 43.2 (586-758)	565 ± 40.7 (444-616)	P=0.000<0.0001

CCT, central corneal thickness; CH, corneal hysteresis; CRF, corneal resistance factor; IOPcc, corneal compensated intra ocular pressure; IOPg, goldman intracorneal pressure

Table 2- The effects of CH, CRF and CCT on IOPcc in regression equation of each group

IOPcc	CH	CRF	CCT	R Square
1[a]	P<0.0001 R = -1.45	P<0.0001 R= 1.5	P=0.092 R =0.92	0.997
2[b]	P<0.0001 R= -1.25	P<0.0001 R=0.99	P=0.404 R= -0.002	1.00

CH, corneal hysteresis; CRF, corneal resistance factor; CCT, central corneal thickness; IOPcc, corneal compensated intraocular pressure

[a]Aphakic glaucomatous group considered as 1.

[b] Primary congenital glaucomatous group considered as 2

Table 3 - The effect of CH, CRF and CCT on IOPg in regression equation of each group.

IOPg	CH	CRF	CCT	R Square
1[a]	P <0.0001 R= -1.03	P <0.0001 R= 1.56	P =0.077 R= 0.017	1.00
2[b]	P<0.0001 R= -1.06	P<0.0001 R= 1.21	P=0.333 R= -0.03	1.00

CH, corneal hysteresis; CRF, corneal resistance factor; CCT, central corneal thickness; IOPg, goldman applantation tonometer

[a]Aphakic glaucomatous group considered as 1.

[b] Primary congenital glaucomatous group considered as 2.

Table 4 - Correlation between IOPg-IOPcc and CH, CRF , CCT in each group.

IOPg-IOPcc	CH	CRF	CCT
1[a]	P <0.0001 r= - 0.96	P <0.0001 r= - 0.93	P =0.001 r= -055
2[b]	P<0.0001 r= -0.95	P<0.0001 r= -0.86	P=0.438 r= -0.147

CH, corneal hysteresis; CRF, corneal resistance factor; CCT, central corneal thickness; IOPg, goldman applantation tonometer

[a]Aphakic glaucomatous group considered as 1.

[b] Primary congenital glaucomatous group considered as 2.