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Corneal Biomechanical Properties and Thickness in Primary Congenital Glaucoma and Normal Eyes: A Comparative Study

Athar ZAREEI [1*], Mohammad Reza RAZEGHINEJAD [1,2], Ramin SALOUTI [1]

[1] Poostchi Ophthalmology Research Center, Department of Ophthalmology, Shiraz University of Medical Sciences, Shiraz, Iran
[2] Glaucoma Service, Wills Eye Hospital, Philadelphia, PA, United States

ABSTRACT

The correct estimation of Intraocular Pressure (IOP) is the most important factor in the management of various types of glaucoma. Primary congenital glaucoma is a type of glaucoma that can cause blindness in the absence of control of the IOP. In this retrospective observational study, 95 eyes, including 48 healthy eyes and 47 eyes with Primary Congenital Glaucomatous (PCG) were studied. Two groups were matched for age, gender, and Goldman Applanation Tonometry (GIOP). Corneal Hysteresis (CH), Corneal Resistance Factor (CRF), and Goldman intraocular pressure were measured by ORA (IOPg), and corneal compensated Intraocular Pressure (IOPcc) was measured for each patient using the Ocular Response Analyzer (ORA). Central Corneal Thickness (CCT) was measured by ultrasonic pachymetry. For each patient, one eye was selected randomly. Student's t-test and analytical regression were used for statistical analysis. The two groups were matched for age (P = 0.34), gender (P = 0.47), and GIOP (P = 0.17). Corneal hysteresis and CRF were significantly lower in PCG than in normal eyes (P < 0.0001), yet CCT was significantly thicker in PCG than normal eyes (P < 0.0001). The regression equation on the effect of CH, CRF, and CCT on GIOP in the PCG group showed that CH and CRF (P-value = 0.001 and P-value<0.0001) also had a significant effect yet CCT did not (P-value = 0.691). A significant decrease in CH and CRF was found in the PCG group compared to the normal controls. In the PCG group, the CCT was greater than normal. These results showed the usefulness of biomechanical properties (CH, CRF) in order to interpret IOP measurements. Furthermore, GIOP measurement may not be confined to consideration of CCT alone. A low CH and CRF value could be responsible for under-estimation of GIOP in the PCG group, in comparison to the normal controls.

KEY WORDS

Central Corneal Thickness; Corneal Biomechanics; Goldman Applanation Tonometer; Primary Congenital Glaucoma

Correspondence to:

Athar Zareei, MSc, Poostchi Ophthalmology Research Center, Shiraz University of Medical Sciences, Zand Street, Shiraz, Iran. E-mail: opt.zareei@gmail.com

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INTRODUCTION

Central Corneal Thickness (CCT) has always been investigated for glaucoma and thinner CCT was related to the condition of glaucomatous damage [1]. There has been differences in the description of the relationship between CCT and risk of glaucoma. One hypothesis is that thinner CCT leads to lower IOP measurements, thus, less intensive treatment is done, and results in a greater risk of glaucoma damage. Another hypothesis is that the

thinner cornea is associated with the response of the corneoscleral shell and ocular vasculature to increased IOP measurements. Central corneal thickness and Corneal Hysteresis (CH) are used to assess IOP [2]. Recent evidence has demonstrated that CH provides important information for glaucoma management [3, 4]. It has been shown that IOP measurement influences CH [5-7] and with increasing IOP, the CH decreases [8]. This study examined two groups of normal and congenital glaucomatous subjects, who were matched for age, gender, and Goldman IOP, in order to understand the differences between CCT and corneal biomechanical properties, including CH and Corneal Resistance Factor (CRF). This research was performed as previous studies have reported different results on the comparison of CCT between normal and congenital glaucoma, especially in the Iranian population [9-11]. This study compared CCT between children in these two groups and attempted to determine the effect of CCT and biomechanical properties (CH, CRF) on IOP measurements in these two groups.

MATERIALS and METHODS

This was a retrospective study that was done at a tertiary eye care center, under the supervision of Shiraz University of Medical Sciences. The study protocol was approved by the Ethics Committee of Shiraz University of Medical Sciences and was in accordance with the Declaration of Helsinki. Written informed consent was obtained from the parents/guardians of all participants. In light of their ophthalmological status and history, two groups of patients were recruited, including normal controls and those with Primary Congenital Glaucoma (PCG). Normal control subjects were children and there was no medical history of refractive or cataract surgery. Children with corneal disease, clinical proof of eye disease, glaucoma, cataract, eyelid abnormalities, elevated Goldman intraocular pressure (measured by ORA; IOPg > 21 mmHg) or abnormal cup to disc ratio, and a history of intraocular surgery were excluded from participation. Syndromic children were also excluded. All patients underwent a complete eye examination, including medical history assessment, slit lamp bio-microscopy, and fundoscopic examination. Patients with Primary Congenital Glaucomatous (PCG) were followed by the tertiary eye care center. Inclusion criteria in PCG included patients with PCG, who were cooperative. Exclusion criteria included lack of cooperation, presence of corneal pathology (corneal edema, corneal scar, or band keratopathy), secondary glaucoma, and congenital optic neuropathies. The participants had undergone trabeculectomy as the first surgical procedure for glaucoma treatment. If patients had uncontrolled IOP after the surgery, they were given medication or received shunt surgery. Complete eye examinations were performed for all patients. These examinations included slit lamp biomicroscopy and gonioscopy with a Sussman goniolens (if patients did not have the necessary cooperation for gonioscopy, their gonioscopy records were used throughout surgical procedures or examinations under anesthesia). Fundus slit lamp biomicroscopy was done using a Volk Superfield lens. Ocular Response Analyzer (ORA) measurements were performed for all patients during the medical ophthalmological examination. Atypical signals were excluded. An experienced operator took about four measurements from every subject by an ORA and the results with highest wave score were used for recording CH, CRF, Goldman intraocular pressure (measured by ORA; IOPg), and corneal compensated intraocular pressure (IOPcc) values [12]. Because of the potential confounding effect of diurnal IOP variation, all IOP measurements were obtained between 9:00 and 11:00 AM. The average of the two GAT measurements were used for statistical analysis. The pachymetries were performed on the central cornea using an ultrasound pachymeter (Paxis, Biovision Inc., Clermont-Ferrand, France) All pachymetry was performed on the central cornea with an ultrasound pachymeter (Paxis, Biovision Inc., Clermont-Ferrand, France). About ten measurements were obtained at the center of the cornea and the outliers were excluded, and the average value was noted as CCT [13]. One eye of each subject (case and control) In two was selected randomly for statistical analysis. The Student's t-test ($P<0.05$) was used to search for significant differences between the two groups.

RESULTS

Table 1 summarizes baseline characteristics, GIOP, CCT, CRF, CH, IOPcc, and IOPG in in case and control groups .

This research included a total of 95 eyes of 95 patients, of whom 48 subjects served as normal controls and 47 had congenital glaucoma. The two groups were matched for age ($P = 0.34$) and gender ($P = 0.47$), and GAT ($P = 0.17$). Mean CH values in control and PCG cases were 11.87 ± 2.05 mmHg and 8.68 ± 3.20 mm Hg, respectively. Mean CCT values were 536.5 ± 33.16 µm and 594.5 ± 64.3 µm, respectively. Corneal hysteresis and CRF were significantly lower in PCG than in normal eyes ($P < 0.0001$), yet CCT was significantly thicker in PCG than in normal eyes ($P < 0.0001$). There were no significant differences in GIOP and IOPg between the two groups (P

= 0.173, P = 0.764) yet IOPcc in the PCG group was significantly higher than normal subjects (P = 0.005). Significant correlations were found between CCT, CRF and CCT, CH in the control group (r = 0.552, p < 0.001) (r = 0.406, p < 0.01) yet there were no significant correlations between CCT, CRF and CCT, CH in the PCG group (P = 0.114, P = 0.895). In normal subjects, a significant negative correlation was found between IOPcc and CH (P < 0.0001) and there was a significant positive correlation between IOPg, CRF (P < 0.0001). In the PCG group, a significant negative correlation was found between IOPcc and CH (P < 0.0001) and there was a significant correlation between IOPg, CRF (P < 0.0001) and IOPg, CCT (P = 0.036). In the study of the regression equation (Table 2) on the effect of CH, CRF, and CCT on GIOP in the normal group, it was shown that the CH and CRF (P-value = 0.004, P-value = 0.003) had a significant effect yet CCT did not have any significant effect (P-value = 0.601). The regression equation on the effect of CH, CRF, and CCT on GIOP in the PCG group showed that the CH and CRF (P-value = 0.001, P-value < 0.0001) also had a significant effect yet CCT had no significant effect (P-value = 0.691).

Table 1: Baseline Characteristics, CCT, CH, CRF, GIOP, and IOP measured with the ORA (IOPG and IOPcc) in Normal Controls (n = 48) and Patients with PCG (n = 47), values are Means ± Standard Deviation (SD).

	Normal (mean± SD)	PCG (mean± SD)	t-test P-value
Age, years	8.98 ± 1.62	9.59 ± 3.57	0.34
GIOP, mmHg	16.17 ± 0.97	17.05 ± 3.9	0.17
CCT, µm	536.5 ± 33.16	594.5 ± 64.3	< 0.0001*
CH, mmHg	11.87 ±2.05	8.68 ± 3.2	< 0.0001*
CRF, mmHg	12.90 ± 2.13	10.28 ± 3.3	< 0.0001*
IOPg, mmHg	19.59±2.82	19.96 ± 7.2	0.764
IOPcc, mmHg	17.92 ± 2.84	21.68 ± 7.5	0.005*

ORA: Ocular Response Analyzer; PCG: Primary Congenital Glaucoma; IOPg: Goldman Intraocular Pressure measured by ORA; IOPcc: Corneal Compensated Intraocular Pressure; mmHg: Millimeter of Mercury; µm: Micrometer. CCT: Central Corneal Thickness; CH: Corneal Hysteresis; CRF: Corneal Resistance Factor; GIOP: Goldman Applanation Tonometry.

*** P Values less than 0.05.**

Table 2: The Effect of CH, CRF, and CCT on GIOP, IOPg and IOPcc in the Regression Equation

Groups	Normal			PCG		
	CH	CRF	CCT	CH	CRF	CCT
GIOP	-1.06	1.2	0.083	-0.761	1.01	-0.06
	P=0.004*	P=0.003*	P=0.601	P=0.001*	P<0.0001*	P=0.691*
IOPg	-2.04	2.49	0.002	-1.17	1.45	-0.07
	P<0.0001*	P<0.0001*	P=0.84	P<0.0001*	P<0.0001	P=0.036*
IOPcc	-2.54	2.15	-0.12	-1.43	1.23	-0.007
	P<0.0001*	P<0.0001*	P=0.186	P<0.0001*	P<0.0001*	P=0.037*

PCG: Primary Congenital Glaucoma; GIOP: Goldman Applanation Tonometry; IOPg: Goldman Intraocular Pressure measured by ORA; IOPcc: Corneal Compensated Intraocular Pressure by ORA; ORA: Ocular Response Analyzer; mmHg: Millimeter of Mercury; µm: Micrometer. CCT: Central Corneal Thickness; CH: Corneal Hysteresis; CRF: Corneal Resistance Factor; GIOP: Goldman Applanation Tonometry; R^2: R-Squared.

*** P Values less than 0.05.**

DISCUSSION

Kirwan et al. concluded that CH in children is like that found in adults [14]. Kotecha et al. found that the effect of age on biomechanical properties of the cornea decreased with older age [15]. In the current study age was matched (Table 1). In the study of CCT in the congenital glaucomatous group, it was shown that CCT in glaucomatous eyes was significantly lower than normal fellow eyes [10] yet when congenital glaucomatous eyes were compared with normal eyes in the Persian race, there was either no significant differences between them [11] or subjects with congenital glaucoma had thicker CCT than normal controls [9]. Distributed data were ambiguous with regards to CCT in PCG cases with both thicker [16] and thinner CCT [17]. In the current study, corneal edema was considered as an exclusion criterion. In the current study, a significantly higher CCT in PCG cases was found compared with normal controls (P < 0.0001). Since studies on Iranian PCG patients showed

similar results, these differences may be attributed to racial differences. Of course, when comparing two eyes in unilateral PCG, it could be predictable to reduce the CCT in the glaucomatous eyes than the normal fellow one, as the IOP has risen unilaterally and there is corneal stretching. The current research found a significant decrease in CH ($P < 0.0001$) and CRF ($P<0.0001$) in the PCG group compared with the normal group, which is similar to the information obtained from previous studies [11, 18]. Intraocular pressure and CCT are among factors affecting CH. In the normal group, a significant relationship was found between CCT, CH ($r = 0.41$, $P=0.004$) and CCT, CRF ($r = 0.55$, $P < 0.0001$) and these results were also obtained in similar studies in the normal control group [19, 20]. In the PCG group, a significant relationship was not found between CCT, CH ($P = 0.895$) and CCT, CRF ($P = 0.114$). Different results have been reported regarding the relationship between CCT and CH in glaucomatous patients [19, 21, 22] and this is probably due to the effect of IOP on CH. In the regression equation, the effect of each of the CH, CRF and CCT values on GIOP were assessed in two groups (Table 2). As shown in Table 2, the effect of CH and CRF on GIOP was significant yet CCT did not have any significant effect on GIOP in the two groups. Although CCT was significantly different in the two groups, corneal biomechanical properties (CH and CRF) were more effective than CCT in determining the ultimate GIOP. In this equation, there was a negative coefficient for CH effect and a positive coefficient for the CRF effect in both groups. In other words, by reducing CH and increasing the CRF, the amount of IOP obtained from GAT was increased. Dascalescu et al. [8] also concluded that corneal biomechanical properties (CH and CRF) that affect IOP measurements are the most important factors in the investigation and follow-up of glaucoma patients. Kaushik et al. [22] investigated the relationship between biomechanical properties (CH and CRF), CCT, and IOP in a range of patients with glaucoma and concluded that CH and CRF was an important risk factor for glaucoma patients and GIOP was more significantly affected by the CRF than the CCT. However, the coefficient of CRF was greater in the regression equation of the PCG, and this may be due to the significant increase in CCT in the PCG group than the normal controls. Dey et al. [23] investigated the difference between GIOP and IOPcc and implied that CH and CRF better explained variability in IOP measurements, which is similar to the current results. In a comprehensive meta-analysis on IOP and CCT in healthy children by Farvardin et al. [24], it was concluded that there was a significant correlation between GIOP and CCT in normal children. Nejabat et al. [25] also found a positive correlation between CCT and GIOP in healthy Persian children. They found that CCT in Persian children was less than most other racial groups [25]. In previous studies, it has commonly been stated that biomechanical properties influence IOP measurements, regardless of CCT, especially in glaucomatous patients [8]. The current analysis was done at a single time-point. These values can change over time. It would be interesting to analyze the variation of CH, CRF, and CCT during longer follow-ups at two or more time intervals. Changes in these variables can be reviewed over time.

CONCLUSIONS

In this study, researchers investigated the biomechanical properties and CCT of normal and primary congenital glaucomatous children and compared these variables in the two groups. In the PCG group, CCT was greater than normal. A significant decrease in CH and CRF was found in the PCG group compared to normal controls. These results showed the usefulness of biomechanical properties (CH and CRF) in order to interpret IOP measurements correctly. Certainly, further studies in the future will need to extend this information.

DISCLOSURE

Ethical issues have been completely observed by the authors. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published. No conflict of interest has been presented.

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