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Evaluation of corneal biomechanical properties using an ocular response analyser to examine aphakic and pseudophakic patients after congenital cataract surgery

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ABSTRACT.

Purpose: **We evaluated corneal biomechanical properties in aphakic and pseudophakic patients after congenital cataract surgery and compared the data with those of age-matched normal subjects.**

Methods: **We included 43 eyes of 43 aphakic or pseudophakic patients treated via congenital cataract surgery. As controls, 42 healthy age- and sex-matched subjects were enrolled. After a complete ophthalmic examination, central corneal thickness (CCT) and intraocular pressure (IOP) were determined. Corneal hysteresis (CH), corneal resistance factor (CRF), corneal-compensated IOP (IOPcc) and Goldmann-correlated IOP (IOPg) were recorded using an ocular response analyser.**

Results: **In the study group, 18 eyes were aphakic and 25 eyes pseudophakic. We found a significant difference in CCT between the aphakic, pseudophakic and control groups ($p < 0.001$). No significant among-group differences were detected in CH or CRF ($p > 0.05$). We found significant differences in IOPcc, IOPg and IOP measured with Goldmann applanation tonometry (IOP_{GAT}) between the study and control groups ($p < 0.001$). In contrast, we found no significant differences within the two study groups in terms of these three IOP values ($p > 0.05$).**

Conclusion: **Although CCT increased after congenital cataract surgery, corneal biomechanical parameters, including CH and the CRF, were not affected by such surgery. Determination of the IOPcc did not provide any additional information on true IOP, which was independent of CCT in both aphakic and pseudophakic patients after congenital cataract surgery.**

Key words: central corneal thickness – congenital cataract – corneal biomechanics – ocular response analyser

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Introduction

Aphakic glaucoma is one of the most important vision-threatening complications of congenital cataract surgery. Despite advances in modern surgical methods, the prevalence of glaucoma following successful cataract removal remains between 6% and 58% (Papadopoulos & Khaw 2003; Chen et al. 2004). Diagnosis of paediatric aphakic glaucoma is challenging problem because of difficulties associated with determination of intraocular pressure (IOP) and in performance of gonioscopy, fundus examination, and visual field and other diagnostic testing, because of young age, a poor fundoscopic appearance or nystagmus. As IOP is the key parameter used to diagnose glaucoma, any variable affecting IOP determination could lead to a false diagnosis (Simsek et al. 2006).

Determination of IOP is influenced by several corneal properties, including curvature, elasticity, rigidity and central thickness (Kniestedt et al. 2008). Any surgical intervention on corneal tissue induces substantial tissue structural changes and can thus alter the corneal biomechanical properties. It has been shown that central corneal thickness (CCT) increased after congenital cataract surgery (Simon et al. 2005; Simsek et al. 2006; Faramarzi et al. 2010). In contrast, limited information is available on corneal biomechanical properties of aphakic glaucoma patients following congenital

cataract surgery. The ocular response analyser (ORA) determines biomechanical properties of the cornea *in vivo*, including corneal hysteresis (CH) and the corneal resistance factor (CRF), which reflect the viscous and elastic properties of the cornea, respectively (Luce 2005). In the present study, we investigated the biomechanical properties of the cornea using the ORA to examine aphakic and pseudophakic patients who had undergone congenital cataract surgery and compared the data with those of age-matched normal subjects.

Methods

A total of 43 aphakic or pseudophakic patients were enrolled in a prospective, comparative clinical study. Patients with a history of ocular trauma, chronic uveitis, contact lens use, glaucoma drainage device surgery, central corneal opacity or scarring, corneal oedema, refractive surgery, or penetrating keratoplasty were excluded from the study. As a control group, 42 age- and sex-matched healthy volunteers were recruited. The control subjects were examined carefully and were found to yield normal ophthalmic findings in all clinical respects, including retinoscopy, anterior segment examination and dilated fundus examination.

All subjects underwent routine ophthalmic examinations, including ORA analysis (Reichert Ophthalmic Instruments, Buffalo, NY, USA), IOP determination via Goldmann applanation tonometry (GAT), CCT determination, and biomicroscopic and dilated fundus examinations. Visual field and gonioscopic examinations were performed only on co-operative children aged at least 7 years old. IOP measurement was performed between 9 and 11 am by the same clinician (TS). Ocular response analyser measurements were performed a minimum of 30 min before GAT measurements by the same examiner (DS). Four consecutive ORA determinations were obtained per eye and that with the highest waveform score was selected for analysis. The ORA analysed all measurements and yielded four variables: CH, CRF, Goldmann-correlated IOP (IOPg) and corneal-compensated IOP (IOPcc).

After application of topical proparacaine hydrochloride 0.5% eye drops (Alcon Laboratories Inc., Fort Worth, TX, USA), a fluorescein strip was applied to the inferior conjunctival fornix for a few seconds and the IOP was determined by the same clinician using a calibrated GAT. At least two values were recorded, and the mean IOP was defined as the mean of two or three IOP values. In patients taking antiglaucomatous medication, the drops were discontinued and the IOP determined a minimum of 1 week after the washout period. CCT was determined using an ultrasonic pachymeter attached to the ORA, prior to applanation tonometry.

Glaucoma was defined as the presence of optic nerve damage with an IOP > 22 mmHg. Patients with an IOP > 22 mmHg but without any optic nerve damage were defined as having ocular hypertension.

The present study followed the tenets of the Declaration of Helsinki. Written informed consent was obtained from a parent of all participating children and directly from adult subjects. The study protocol was approved by Institutional Ethics Committee.

Statistical analysis was performed using SPSS 16.0 software (SPSS Inc., Chicago, IL, USA). The normality of data distribution was evaluated using the Shapiro–Wilk and Kolmogorov–Smirnov tests. As the IOP cc, IOPg, IOP_{GAT} and CCT values were not distributed normally, the nonparametric Mann–Whitney *U*-test and the Kruskal–Wallis test were used to compare data. The distributions of CH and CRF values were normal, and thus, ANOVA testing was used for comparisons. Two-tailed Spearman's correlation analysis was performed to explore the relationships between parameters. A value of $p < 0.05$ was taken to indicate significant difference. Bland–Altman analysis was performed to determine the extent of agreement between GAT and ORA values.

Results

Study was performed between January 2010 and March 2013 in a tertiary hospital setting. In total, 43 aphakic or pseudophakic patients were enrolled in the study. We previously demonstrated a difference in CCT between aphakic and pseudophakic eyes. Therefore, the study group was subdivided into two groups, aphakic and pseudophakic. The clinical and demographic characteristics of the study and control groups are presented in Table 1. Because CCT, IOPg, IOPcc and IOP_{GAT} values were not disturbed normally, median (min–max) values were given for these parameters. The median CCT, IOPg, IOPcc and IOP_{GAT} values, and the mean CRF and CH values, are presented in Figs 1 and 2, respectively. The median CCT values were significantly greater in the aphakic and pseudophakic eyes compared to control eyes ($p < 0.001$). In addition, we found significant differences in the IOPcc, IOPg and IOP_{GAT} between the study and control groups (all p values < 0.001) (Table 2).

We compared the IOP values (IOPcc, IOPg and IOP_{GAT}) within groups. In the aphakic and pseudophakic groups, we found no significant differences ($p = 0.826$). In the control group, the IOP_{GAT} was significantly lower than the IOPcc and IOPg values ($p = 0.003$). No significant differences were found in terms of CH ($p = 0.066$) or CRF ($p = 0.163$) among the groups. The mean CH and CRF values and the median CCT and IOP values obtained via GAT and the ORA are presented in Table 3.

Spearman's correlation analysis was performed on the CCT, IOPg, IOPcc, IOP_{GAT}, CH and CRF values. Table 4 shows significant correlations between parameters in study and control groups.

In pseudophakic eyes, intraocular lens (IOL) implantation was performed at the time of congenital cataract

Table 1. Demographic characteristics of the study and control groups.

Characteristics	Study group	Control group	p Value
Median age (years) (range)	13.0 (6–39)	13.5 (10–20)	0.783
Sex, *n* (%)			0.056
Male	18 (41.8)	25 (59.5)	
Female	25 (58.2)	17 (40.5)	
Aphakia, *n* (%)	18 (41.9)	–	
Pseudophakia, *n* (%)	25 (58.1)	–	

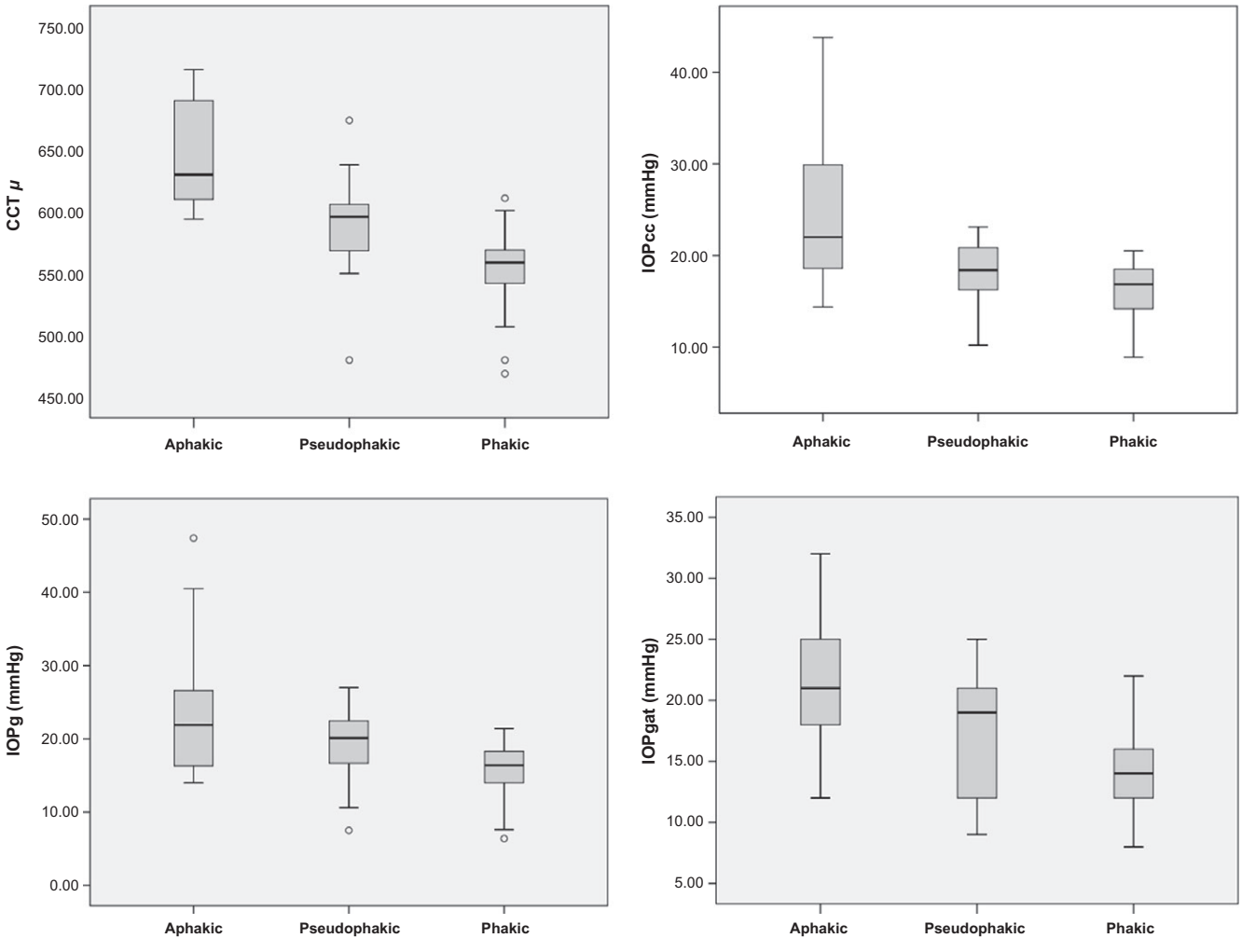


Fig. 1. Box-and-whisker plots of IOPcc, IOPg, IOP_{GAT} and CCT values of the groups. The middle line in each box indicates the median value. The height of the box indicates the upper and lower quartiles. IOPg, Goldmann-correlated intraocular pressure; IOPcc, corneal-compensated intraocular pressure; IOP_{GAT}, Goldmann applanation tonometric intraocular pressure; CCT, central corneal thickness.

surgery in 16 eyes and secondarily in 9 eyes. We found significant differences between pseudophakic eyes in which an IOL was implanted at the time of cataract surgery and, secondarily, in all of the CCT ($p < 0.001$), IOP_{GAT} ($p < 0.001$), IOPcc ($p = 0.02$), IOPg ($p = 0.01$) and CRF ($p = 0.05$) values.

Discussion

In the present study, we found no differences between the IOPcc, IOPg and IOP_{GAT} within the two study groups. The IOPcc, which is thought to be unaffected by corneal thickness, was expected to be lower than other IOP values in thicker corneas. Therefore, determination of the IOPcc did not provide any additional information on the true IOP, which is less effected by CCT, in aphakic and pseudophakic patients following congenital cataract surgery. The results of the study on IOPcc are inconsistent. One study shows promising results that the ORA is able to provide an IOP reading that independent of corneal factors (Medeiros & Weinreb 2006). It was found that IOPcc values were higher than IOP_{GAT} values (Hirneiß et al. 2011). Kotecha et al. (2006, 2010) demonstrated that IOP_{GAT}–IOPcc differences were not significantly associated with CCT, suggesting that the corneal biomechanical effect is not completely eliminated from the IOPcc measurement. Razeghinejad et al. (2014) compared three different tonometers (Tono-Pen XL, ORA and GAT) in children with aphakic glaucoma. In this study, IOPcc and IOPg measurements obtained by the ORA were higher than those obtained by the GAT in both aphakic and healthy eyes. They also concluded that relying on the result of the ORA measurement, which is considered to be independent of corneal biomechanical characteristics, may be misleading in aphakic glaucoma following congenital cataract surgery. Based on these data, we need to make *in vivo* manometric studies to confirm the relations between corneal biomechanic factors, CCT, measured IOP and actual IOP. These studies will reveal whether the ORA give a true measurement of IOP.

In the present study, the mean CH value, which represents the ability of the cornea to absorb energy and the mean CRF value, which indicates the total resistance of the cornea to applanating force, did not different among aphakic, pseudophakic and healthy subjects. CH and especially CRF which reflects the ocular rigidity can influence the IOP measurement. But exact relationships between these parameters are

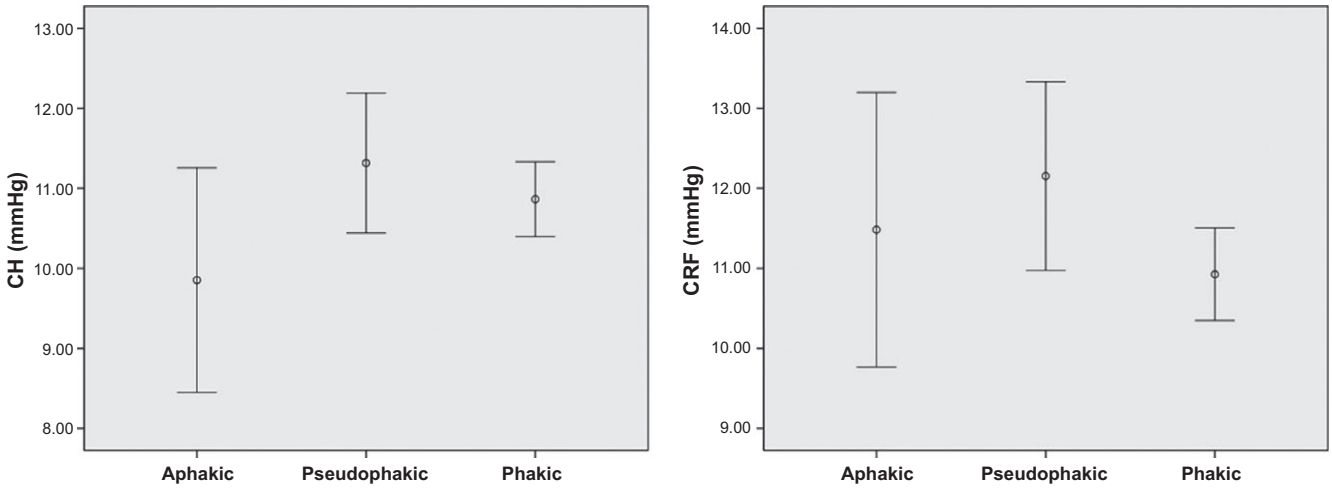


Fig. 2. Mean corneal hysteresis and corneal resistance factor values of the groups.

still under investigation. It is known that CH and the CRF are decreased in patients with myopia, keratoconus, Fuchs' endothelial dystrophy, primary open angle glaucoma, pseudoexfoliative glaucoma, normal tension glaucoma, primary congenital glaucoma, and after LASEK and LASIK surgery (Shah et al. 2007; Kirwan & O'Keefe 2008; del Buey et al. 2009; Chang et al. 2010; Cankaya et al. 2012; Grise-Dulac et al. 2012; Gatzioufas et al. 2013). In contrast, the CH and CRF are elevated in patients with nanophthalmos and acromegaly (Altan et al. 2012; Ozkok et al. 2014). The CCT was found to be greater in patients with nanophthalmos than a control group, but was normal in acromegaly patients. Ozkok et al. (2014) suggested that the higher CH and CRF values in acromegaly patients were possibly associated with structural changes to the cornea, caused by hormonal factors rather than CCT. We similarly propose that CH is not associated with CCT. Although CCT values were elevated in our study groups, neither the CH nor the CRF differed from those of the control group.

In population studies, CH values varied over a wide range and were weakly correlated with CCT. Laiquzzaman et al. (2010) found no correlation between CCT, CH or the CRF in postkeratoplasty eyes. They concluded that an elevated CCT was not associated with higher levels of rigidity or elasticity. Mangouritsas et al. (2009) found a stronger correlation between CH and CCT in healthy eyes in contrast to glaucomatous eyes. In the present study, we found a positive correlation between CCT, CH and CRF in the control group. However, in aphakic and pseudophakic eyes, the correlations between these parameters were not significant. It might be result from chronically increased IOP, antiglaucomatous medications or various structural changes apart from CCT.

Table 2. p Values between the three groups.

	Aphakic eyes–control eyes	Pseudophakic eyes–control eyes	Aphakic eyes–pseudophakic eyes
IOP_{GAT}	$p < 0.001$*	$p < 0.001$*	$p > 0.05$
CCT	$p < 0.001$*	$p < 0.001$*	$p < 0.001$*
IOPcc	$p < 0.001$*	$p > 0.05$	$p > 0.05$
IOPg	$p < 0.01$*	$p < 0.01$*	$p > 0.05$
CH	$p > 0.05$	$p > 0.05$	$p > 0.05$
CRF	$p > 0.05$	$p > 0.05$	$p > 0.05$

CH = corneal hysteresis, CRF = corneal resistance factor, IOPg = Goldmann-correlated intraocular pressure, IOPcc = corneal-compensated intraocular pressure, GAT = Goldmann applanation tonometric intraocular pressure, CCT = central corneal thickness.
* Indicates significant difference.

Table 3. CCT, CH, CRF and IOP values obtained with ORA and GAT.

	Aphakic	Pseudophakic	Control	p
CH mmHg, mean ± SD	10.3 ± 3.2	11.2 ± 2.0	10.8 ± 1.5	0.066
CRF mmHg, mean ± SD	10.9 ± 3.8	11.8 ± 3.1	10.9 ± 1.8	0.163
IOPg mmHg, median (range)	23.1 (14.0–62.9)	21.0 (7.5–27.1)	16.4 (6.4–21.4)	<0.001
IOPcc mmHg, median (range)	22.7 (14.0–65.3)	18.4 (9.2–23.1)	16.8 (8.9–20.5)	<0.001
IOP_{GAT} mmHg, median (range)	22.5 (9.0–30.0)	19.0 (9.0–27.0)	14.0 (8.0–22.0)	<0.001
CCT μm, median (range)	660 (583–715)	597 (480–674)	559 (469–611)	<0.001

CH = corneal hysteresis, CRF = corneal resistance factor, IOPg = Goldmann-correlated intraocular pressure, IOPcc = corneal-compensated intraocular pressure, IOP_{GAT} = Goldmann applanation tonometric intraocular pressure, CCT = central corneal thickness.

Table 4. Significant correlations between parameters in groups (Spearman's correlation analysis).

Correlations (r, p)	Aphakic	Pseudophakic	Control
IOP_{GAT}-CCT	$r = 552$, $p = 0.018$		
IOPcc-IOPg	$r = 934$, $p < 0.001$		
IOP_{GAT}-IOPcc		$r = 726$, $p < 0.001$	
IOP_{GAT}-IOPg		$r = 783$, $p < 0.001$	
IOPcc-IOPg		$r = 894$, $p < 0.001$	
IOPg-CRF		$r = 587$, $p = 0.002$	
CCT-IOP_{GAT}			$r = 494$, $p = 0.001$
CCT-IOPg			$r = 386$, $p = 0.012$
CCT-CH			$r = 558$, $p < 0.001$
CCT-CRF			$r = 738$, $p < 0.001$

IOPg = Goldmann-correlated intraocular pressure, IOPcc = corneal-compensated intraocular pressure, IOP_{GAT} = Goldmann applanation tonometric intraocular pressure, CCT = central corneal thickness, CH = corneal hysteresis, CRF = corneal resistance factor.

Different surgical procedures can create a variety of influences on the biomechanical properties of the cornea. Recently, it has been shown that CH fell significantly after cataract surgery and pars plana vitrectomy (PPV), but returned to preoperative levels after a few months (Kucumen et al. 2008; Seymenoğlu et al. 2013). Corneal hysteresis significantly reduced after clear corneal cataract surgery, and it was returned preoperative level approximately 14 days later in a study (Kandarakis et al. 2012). Unlike what was noted after cataract surgery or PPV, CH fell permanently after keratoplasty, and after LASIK and LASEK surgery, both of which feature tissue ablation and development of permanent structural changes in the cornea (Kirwan & O'Keefe 2008; Laiquzzaman et al. 2010). It may be that surgical procedures that permanently alter corneal structure may also change corneal biomechanical behaviour in the long term.

Faramarzi et al. (2010) demonstrated that CCT was normal before congenital cataract surgery but increased after lens removal. Apart from CCT, it is impossible to evaluate corneal biomechanics in small children using current technologies. ORA values can be obtained only in the sitting position and require patient co-operation. Corneal biomechanics, like other surgical variables, probably change after congenital cataract surgery. However, the values may ultimately return to preoperative levels, because, in the present study, we found no differences in corneal biomechanical parameters between the groups. It is interesting congenital cataract surgery exerted a permanent effect on CCT, but temporary effects on corneal biomechanical parameters. Further studies are needed to clarify this issue.

We postulate that certain relationships exist between CH, the CRF and CCT in diseases that originate primarily from the cornea (e.g. keratoconus, Fuchs' dystrophy) and in diseases exerting lifelong impacts on the cornea (e.g. acromegaly, nanophthalmos). In contrast, under transient conditions, including surgical trauma, no relationship may exist between corneal biomechanical factors and CCT. Surgery induces temporary alterations in corneal biomechanical factors. As the changes in CH, the CRF and CCT were not correlated, concomitant evaluation of these parameters in the context of IOP is of limited value in the clinical determination of IOP in aphakic and pseudophakic eyes. A further limitation of the ORA in our patient group was evaluation difficulties caused by nystagmus, because ORA measurement requires a steady fixation during the examination. Although the ORA is valuable in some instances, ORA is clearly of minimal use in determining IOP in aphakic and pseudophakic patients after congenital cataract surgery. Undefined factors (thus other than CCT and corneal biomechanical parameters) might affect IOP determination. Further experimental and clinical studies are required to define the factors affecting IOP evaluation in aphakic and pseudophakic patients following congenital cataract surgery.

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