Original Article

Diurnal variation of central corneal thickness and intraocular pressure in eyes with pseudoexfoliation

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Purpose: Pseudoexfoliation syndrome (PXS) is an age related microfibrillopathy characterized by deposition of whitish flaky material over various ocular tissues. PXS eyes are known to have thinner corneas and thus can lead to an underestimation in intraocular pressure measurement. The purpose of this study was to find if there is any variation in central corneal thickness and intraocular pressure in PXS eyes and if there was any relationship between them. **Methods:** A prospective observational study was done on 141 eyes of 85 patients with PXS without glaucoma between November 2015 to April 2017 in the department of Ophthalmology in a tertiary hospital. CCT and IOP were measured by a handheld ultrasonic pachymeter (DGH Technology INC. Pachette 2, USA) and Goldmann applanation tonometer respectively at 4 different times during office hours. **Results:** A significant reduction of about 10 μm in mean CCT and 1.4 mmHg in mean IOP was noted over the 4 sessions which was statistically significant ($P < 0.001$). A significant correlation exists between IOP and CCT in PXS eyes at all times during the day ($P < 0.001$). **Conclusion:** The CCT measurements show significant thinning throughout the day, similar drop in IOP was also noted. Our study shows that there is a significant correlation between diurnal variation of CCT and IOP. Hence, it is prudent to measure CCT along with IOP at all times.

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Pseudoexfoliation syndrome (PXS) is an age-related systemic condition characterized by deposition of grey and white material over various tissues.[1] It is the most common identifiable cause of open-angle glaucoma throughout the world.[1] The probability of developing glaucomatous optic neuropathy at similar intraocular pressure (IOP) levels is greater in eyes with PXG than in other forms of glaucoma.[2] Various studies have shown that eyes with PXS display thinner central corneal thickness as compared to normal eyes[3,4] and thin corneas are now considered as a significant risk factor for glaucoma independent of IOP.[5] A thin cornea is an independent risk factor for glaucoma progression due to underestimation of intraocular pressure.[5]

Diurnal variation in central corneal thickness (CCT) exists in eyes with no pathology[6] and Keel *et al*. showed this variation was higher in PXS eyes.[7] Studies report that CCT is thickest in the morning upon awakening an decreases as the day progresses.[6,8] To date, no study is reported to find the diurnal variation of CCT and IOP in PXS eyes without glaucoma in India. Assessing this variation in CCT would help in earlier detection of individuals at risk of developing pseudoexfoliation glaucoma (PXG) as a variation in CCT during the day would cause a false IOP reading. We have therefore investigated whether there is a significant CCT fluctuation among PXS eyes without evidence of glaucoma and whether this CCT fluctuation has a linear relationship with variations in IOP. This study could suggest the correct timing of IOP and CCT measurement in diagnosis of PXG and the need for a regular CCT measurement in an outpatient setting while screening PXS.

Methods

A prospective observational study was done on 141 eyes of 85 subjects selected randomly with pseudoexfoliation syndrome without glaucoma which was conducted in the department of Ophthalmology in a tertiary care center. The Institutional Medical Ethics Committee approved this study. All patients above the age of 40 years were screened in the department of Ophthalmology between September 2015 to April 2017. A complete ophthalmic examination including best corrected visual acuity, intraocular pressure, ophthalmic history, slit lamp examination and fundus examination using 90D lens was done. A case of PXS was defined as an eye with PXS material present on the pupillary margin or on anterior lens capsule or on gonioscopy. A complete glaucomatous investigation (Optic nerve head exam, IOP and reliable visual fields) was done by the examiner and was ruled out. Patients presenting

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with pseudoexfoliation syndrome but with no evidence of glaucoma were included in the study. Patients with diabetes mellitus, corneal injuries, corneal ectasia, severe dry eye and post keratorefractive surgeries were excluded from the study as they may independently influence CCT readings.[6] A written informed consent was obtained from subjects which matched the inclusion criteria.

Subjects underwent four measurements of intraocular pressure and central corneal thickness during office hours on a single day at 4 different sessions 8 AM, 11 AM, 2 PM and 5 PM. The times were chosen in accordance with similar studies in this area of research.[9] All the measurements were done by a single examiner to avoid any interexaminer variability. IOP was measured using a Goldmann applanation tonometer. Central corneal thickness was measured using ultrasound pachymetry (DGH technology, Inc, Pachette 2, USA). 25 readings were obtained and averaged. Values with Standard Deviation (SD) of 5 µm or less were considered suitable for inclusion.

Statistical analysis was carried out using SPSS version 19.0 (IBM SPSS, US) software with Regression Modules installed. Descriptive analyses were reported as mean and standard deviation of the variables with 95% confidence intervals. A Simple Correlation was used to find out if there was an association between IOP and CCT at 4 different times and were plotted on a scatter diagram. *P* value < 0.05 was considered statistically significant.

Results

Out of the 85 subjects, 62 (73%) subjects were males and 23 (27%) were females. Mean age of the patients was 62.51 ± 8.9 years. About 52% presented with unilateral presentation of PXS. All the subjects belonged to the South Indian region (Asian).

There was a drop in mean IOP from 14.68 mmHg to 13.26 mmHg in the right eye and from 14.56 mmHg to 13.18 mmHg in the left eye [Table 1]. Mean CCT also decreased from 514.95 µm to 505.84 µm in the right eye and from 513.47 µm to 504.30 µm in the left eye [Table 2]. The change in both was found to be statistically significant ($P < 0.001$). The change in mean IOP exhibited a statistically significant ($P < 0.001$) positive correlation with change in mean CCT [Fig. 1]. By applying linear regression, on every 6.7 µm reduction in central corneal thickness there was a 1 mmHg decrease in intraocular pressure.

Discussion

The landmark study "The ocular hypertension treatment study" observed the impact of CCT on applanation tonometer and showed the measurement of IOP by Goldmann applanation tonometer was influenced by central corneal

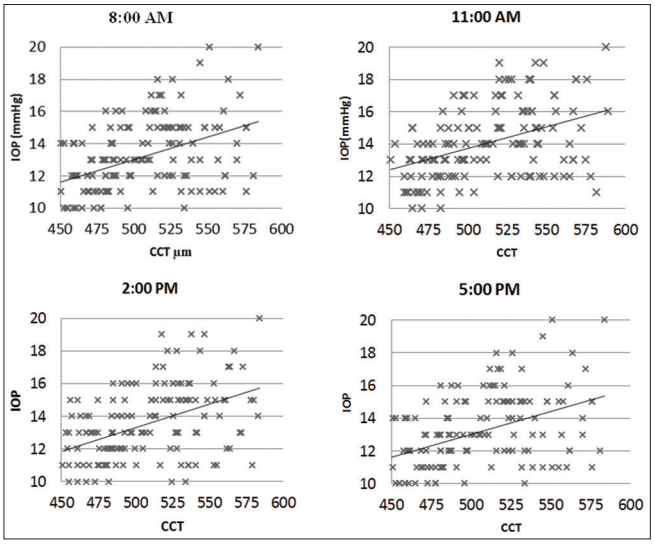

Figure 1: Scatter plot showing a positive correlation between IOP and CCT during the 4 sessions

Table 1: Diurnal variation of IOP and CCT in right eye of study group

Right eye	IOP (mmHg)				*P*	CCT (µm)				*P*
	Mean	Standard deviation	95% confidence interval			Mean	Standard deviation	95% confidence interval		
			Lower bound	Upper bound				Lower bound	Upper bound	
8AM	14.68	2.458	14.091	15.272	<0.001	514.95	34.208	505.87	524.02	<0.001
11 AM	14.17	2.203	13.645	14.703		511.68	34.080	502.64	520.73	
2 PM	13.71	2.276	13.163	14.257		508.30	34.980	499.02	517.58	
5 PM	13.26	2.356	12.695	13.827		505.84	34.896	496.58	515.10	

Table 2: Diurnal variation of IOP and CCT in left eye of study group

Left eye	IOP (mmHg)				*P*	CCT (µm)				*P*
	Mean	Standard deviation	95% confidence interval			Mean	Standard deviation	95% confidence interval		
			Lower bound	Upper bound				Lower bound	Upper bound	
8 AM	14.56	2.543	13.89	15.24	<0.001	513.47	34.204	504.40	522.55	<0.001
11 AM	13.96	2.383	13.33	14.60		509.77	34.692	500.57	518.98	
2 PM	13.37	2.512	12.70	14.03		506.89	35.210	497.55	516.24	
5 PM	13.18	2.529	12.50	13.85		504.30	35.306	494.93	513.67	

thickness and hence IOP could be either underestimated or overestimated.[10]

Studies have shown that CCT decreases over a day in normal eyes.[6] The clinical significance of this observation has not been yet conclusively established. However this suggests that true IOP may be over or underestimated depending on the patient's scheduled appointment time.

PXS eyes have been shown to have a thin cornea,[3] and a thin cornea is an added risk factor for progression of glaucoma. Previous researchers have shown a diurnal variation in CCT exists with CCT thickest in the morning and thinnest in the evening although it is still not known if this variation is clinically significant.[6,8,11] A similar study done on Australian population comparing PXS eyes to normal eyes showed a greater variation of CCT in PXS eyes. However, they had studied only 14 eyes of 7 patients.[7] Our study concluded that there was a significant variation in CCT during office hours with a mean value of around 10 μm, during office hours which is slightly higher as compared to Keel *et al*. which showed a variation of about 6.45 μm.[7] In our study, the maximum fluctuation in CCT seen was around 27 μm.

A large fluctuation in IOP is a risk factor for optic nerve head damage. PXS eyes have shown to have a larger fluctuation of IOP as compared to normal eyes.[12] Our study revealed there was a drop of about 1.4 mmHg which also followed in all cases, with a few eyes where IOP was high in the evenings as compared to mornings. The variation of IOP that was observed was lesser than what has been established by literature.[7] A simultaneous observation of reduction in CCT over time points to probable errors if all IOP's were corrected to a single CCT. We therefore propose that IOP should be corrected to CCT measured at that particular time if such a correction is applied in practice. Due to lack of normal age matched control eyes, our study couldn't compare this fluctuation between PXS eyes and normal eyes.

Relationship between IOP and CCT has been studied widely and there is no consensus over its relationship. Our study shows there is a positive correlation between IOP and CCT in PXS eyes and its diurnal variation at all times. Keel *et al*. also concluded that there was a correlation between IOP and CCT.[7] This is also in accordance with Fogagnolo *et al*. which showed a correlation between IOP and CCT exists in POAG.[13]

Our study had a few limitations like lack of age matched controls to compare the fluctuation of IOP and CCT with PXS eyes, gender imbalance – which is expected as gender bias exists in this condition.[14]

Strengths of the study include a fairly large sample size, all the readings were done by a single examiner to avoid any interexaminer variability. To our knowledge, this is the first study in India and second worldwide in assessing the diurnal variation in CCT and IOP in PXS eyes without glaucoma.

Conclusion

The CCT measurements show significant thinning throughout the day, similar drop in IOP was also noted. Our study shows that there is a significant correlation between diurnal variation of CCT and IOP. Hence, it is prudent to measure CCT along with IOP at all times to avoid false IOP readings in patients with PXS with no evidence of glaucoma.

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Conflicts of interest

There are no conflicts of interest.

References

1. Ritch R. Exfoliation syndrome. Curr Opin Ophthalmol 2001;12:124-30.
2. Allingham RR, Damji KF, Shields MB. Shields Textbook of Glaucoma. 6th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2011. p. 610.
3. Inoue K, Okugawa K, Oshika T, Amano S. Morphological study of corneal endothelium and corneal thickness in pseudoexfoliation syndrome. Jpn J Ophthalmol 2003;47:235-9.
4. Puska P, Vasara K, Harju M, Setälä K. Corneal thickness and corneal endothelium in normotensive subjects with unilateral exfoliation syndrome. Graefes Arch Clin Exp Ophthalmol 2000;238:659-63.
5. Asrani S, Zeimer R, Wilensky J, Gieser D, Vitale S, Lindenmuth K. Large diurnal fluctuations in intraocular pressure are an independent risk factor in patients with glaucoma. J Glaucoma 2000;9:134-42.
6. Harper CL, Boulton ME, Bennett D, Marcyniuk B, Jarvis-Evans JH, Tullo AB, *et al*. Diurnal variations in human corneal thickness. Br J Ophthalmol 1996;80:1068-72.
7. Keel S, Malesic L, Chan SP. Diurnal variation in central corneal thickness and intraocular pressure in eyes with pseudoexfoliation syndrome without glaucoma. Indian J Ophthalmol 2014;62:1072-6.
8. du Toit R, Vega JA, Fonn D, Simpson T. Diurnal variation of corneal sensitivity and thickness. Cornea 2003;22:205-9.
9. Shen M, Wang J, Qu J, Xu S, Wang X, Fang H, *et al*. Diurnal variation of ocular hysteresis, corneal thickness, and intraocular pressure. Optom Vis Sci 2008;85:1185-92.
10. Gordon MO, Beiser JA, Brandt JD, Heuer DK, Higginbotham EJ, Johnson CA, *et al*. The ocular hypertension treatment study: Baseline factors that predict the onset of primary open-angle glaucoma. Arch Ophthalmol 2002;120:714-20; discussion 829-30.
11. Read SA, Collins MJ. Diurnal variation of corneal shape and thickness. Optom Vis Sci 2009;86:170-80.
12. Altintaş O, Yüksel N, Karabaş VL, Qağlar Y. Diurnal intraocular pressure variation in pseudoexfoliation syndrome. Eur J Ophthalmol 2004;14:495-500.
13. Fogagnolo P, Rossetti L, Mazzolani F, Orzalesi N. Circadian variations in central corneal thickness and intraocular pressure in patients with glaucoma. Br J Ophthalmol 2006;90:24-8.
14. Thomas R, Nirmalan PK, Krishnaiah S. Pseudoexfoliation in southern India: The Andhra Pradesh eye disease study. Invest Ophthalmol Vis Sci 2005;46:1170-6.