Diurnal Variation of Central Corneal Thickness (CCT) and Intraocular Pressure (IOP) in Subjects with Pseudoexfoliation Glaucoma, Pseudoexfoliation Syndrome and in Normal Subjects

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ABSTRACT

BACKGROUND

Pseudoexfoliation syndrome (PXF) is an age-related systemic disease characterized by synthesis and accumulation of abnormal fibrillar material throughout anterior segment of eyes. PXF along with raised IOP and optic nerve head changes leads to pseudoexfoliation glaucoma (PXFG). PXF and PXFG are characterized by thinner corneas with large 24-h IOP fluctuations. We wanted to evaluate if any variation occurs in diurnal central corneal thickness (CCT) and intraocular pressure (IOP) between eyes with pseudoexfoliation syndrome (PXF), pseudoexfoliation glaucoma (PXFG) and in normal subjects.

METHODS

This is a prospective study conducted among 104 subjects (M=54, F=50). Amongst those, 30 patients had PXF in one eye, 3 patients in both the eyes and 24 patients had PXFG in one eye. Remaining 47 were taken as controls for the study. Testing included CCT and IOP measurement at four different times of the day (8.00 am; 11 am; 2 pm; 5 pm).

RESULTS

PXFG eyes showed a significantly thinner overall mean CCT (497 µm) followed by PXF eyes (518 µm) as compared to controls with a mean CCT of 527 µm. The mean overall IOP in PXFG (23.6 mmHg) was significantly higher as compared to PXF (14.6 mmHg) and the control group (14.2 mmHg). Furthermore, a significant reduction in CCT and IOP occurred in PXFG group from 8.00 am to 5.00 pm. A significant association between IOP and CCT was found in PXFG eyes.

CONCLUSIONS

A significantly thinner mean CCT shows the importance of measuring CCT on a regular basis having such clinical setup in order to avoid falsely low IOP measurement in a high-risk glaucoma population. Moreover, a significant correlation between IOP and CCT in PXFG eyes suggests that the decrease in mean CCT that occurred from 8 am to 5 pm may partly be responsible for the similar pattern of decrease in IOP from 8 am to 5 pm with mean CCT and IOP being highest in the morning within three hours of waking up and thereafter decreasing during the day.

KEYWORDS

Diurnal Variation, Central Corneal Thickness, Intra-Ocular Pressure, Pseudoexfoliation Syndrome

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DOI: 10.18410/jebmh/2020/2

Financial or Other Competing Interests: None.

How to Cite This Article:
Kumar Nanda P, Bishnupriya K, Shradha P. Diurnal variation of central corneal thickness (CCT) and intraocular pressure (IOP) in subjects with pseudoexfoliation glaucoma, pseudoexfoliation syndrome and in normal subjects. J. Evid. Based Med. Healthc. 2020; 7(1), 6-9. DOI: 10.18410/jebmh/2020/2

Submission 08-12-2019,
Peer Review 12-12-2019,
Acceptance 29-12-2019,
Published 01-01-2020.

BACKGROUND

Pseudoexfoliation syndrome is characterized by systemic synthesis and deposition of grey-white fibrillary amyloid like material throughout the anterior segment of the eye. Mutations in a single gene, LOX1, seem to be present in nearly all cases of pseudoexfoliation syndrome (PXF) and pseudoexfoliation glaucoma (PXFG). It can present unilaterally or bilaterally. Often, this disorder presents unilaterally, and the uninvolved eye manifests signs of the disease at a later time. This syndrome is strongly age related, mostly occurring in individuals older than 70 years. The classic characteristic of pseudoexfoliation syndrome is the deposition of fibrillar deposits in a "bulls-eye" pattern on the anterior lens capsule best seen after pupillary dilatation. This pattern has a clear intermediate area in between a central and peripheral zone of the material. Pseudoexfoliative material blocks spaces in trabecular meshwork, promoting the accumulation of pigment and cellular debris. This causes obstruction of channels through which aqueous humour normally outflows into Schlemm's canal. This is believed to be the causative factor for chronic elevations of IOP and the development of pseudoexfoliative glaucoma.

Many studies have been done in the past to determine the effect of PXF on central corneal thickness (CCT).[1,3,4,5] In one study done by Inoue et al in 2003, they reported that in PXF eyes irrespective of presence of glaucoma in the patients, the central cornea is thin and endothelial cell density is decreased.[3] In another study done by Brandt et al in 2004, they found that thinner cornea in itself is considered to be significant risk factor in the development of glaucoma due to underestimation of IOP readings.[6] Hence assessment of 24-h variation in CCT could also help in earlier detection of those subjects who are at risk of developing glaucoma as variation of CCT all through the day would simultaneously cause a different IOP measurement. A lot of research has been done in literature regarding significant diurnal fluctuation in CCT occurring in normal subjects over a 12-48 hr period.[7,8,9] It has been demonstrated by Read et al in 2009 is that CCT is highest in the morning upon waking up and gradually CCT decreases as the day progresses, with the maximum degree of variation taking place in the 3 hr after waking up.[10] In another study done by Syed et al in 2019, they concluded that CCT measurements show significant thinning throughout the day with corresponding drop in IOP.[2] This might be due to increase in corneal hydration because of reduced evaporation of tear film which occurs during sleep. Hence during first 2 hrs of waking, IOP increases because of increased corneal thickness.

We wanted to ascertain if any difference exists in diurnal CCT and IOP between eyes with pseudoexfoliation glaucoma, pseudoexfoliation syndrome and in normal subjects.

METHODS

This is a prospective study conducted among 104 subjects (Males- 54, Females- 55) from February 2019 to September 2019 in the Department of Ophthalmology. Among 104 patients, 30 patients were diagnosed as having unilateral PXF and 3 had bilateral PXF, 24 were diagnosed as having PXFG and remaining 47 were normal subjects with no ocular pathology.

Inclusion Criteria

- Age group-50-70 yrs.
- PXF Group- Presence of characteristic granular deposits on the anterior segment structures of the eye on slit lamp and by gonioscopic examination with IOP <21 mmHg and normal appearing optic disc(cup-disc ratio of ≤0.5, asymmetry ≤0.2)
- PXFG Group- Presence of characteristic granular deposits on the anterior segment structures of the eye on slit lamp and by gonioscopy along with raised IOP (>21 mmHg) or optic nerve head changes (cup-disc ratio ≥0.5, or asymmetry of 0.2 or more) and visual field changes in perimetry. Presence of pseudoexfoliative material was reassured after full mydriasis. All these patients were on topical anti-glaucoma medications i.e. both latanoprost 0.005% once daily at bed time and timolol 0.5% twice daily.
- Normal subjects- Those with no ocular pathology with normal anterior and posterior segment findings except for the decrease in visual acuity either due to refractive error or due to cataract.
- Those giving consent for the study.

Exclusion Criteria

- Subjects with systemic diseases like Diabetes mellitus and Hypertension.
- H/O Ocular trauma
- Severe dry eye
- Scarred or hazy corneas
- Contact lens users, Surgery (LASIK)
- Pseudophakia
- Nystagmus
- Keratoconus
- Any current conjunctival or corneal infections
- Subjects with myopia or hypermetropia >3D or astigmatism >1D.

Keeping in accordance with the inclusion and exclusion criteria, the subjects were tested during 4 separate times of the day from 8 A.M. to 5 pm i.e. 8.00 A.M., 11 A.M., 2 P.M. and 5 P.M. The times chosen are in accordance with similar studies in this area of research and were selected as they are within routine ophthalmic consulting hours and if diagnoses or treatment is prescribed or carried out, it is customarily based on the clinical measures taken during this time frame. IOP was measured by Goldman applanation tonometer in sitting position after instillation of proparacaine and staining cornea with fluorescein before each measurement at 4 times of the day. CCT was recorded after IOP readings were taken with the help of Optical tonopachymeter (Topcon CT-1P) at 4 times of the day. No dilatation or gonioscopy was used at that time in order to avoid any corneal surface damage or distortion. All the

measurements were taken by a single observer at 4 different times of the day.

RESULTS

There were 24 cases of PXFG, 33 cases of PXF and 47 normal persons enrolled in the study. The male to female ratio was 13:11 in PXFG group, 18:15 in PXF group and 23:24 in normal subjects. Of 33 subjects with PXF 30 were unilateral cases and remaining 3 were bilateral PXF. The mean age was 63.36±5.562 years in normal subjects, 64.03±5.247 years in PXF group and 67.29±2.773 years in PXFG group. All the three groups were similar with regards to age and sex.

Groups	8 A.M. (Mean± SD)	11 A.M. (Mean ± SD)	2 P.M. (Mean ± SD)	5 P.M. (Mean ± SD)
Normal	15.17±1.833	14.47±1.755	13.85±2.417	13.55±1.691
PXF	16.15±2.167	14.73±1.957	14.09±2.150	13.64±1.949
PXFG	25.12±2.401	23.67±2.777	23.38±2.667	23.12±2.802

Table 1. Mean IOP in mmHg Recorded at 4 Different Times of the Day in Normal, PXF and PXFG Groups

Groups	8 A.M. (Mean ± SD)	11 A.M. (Mean ± SD)	2 P.M. (Mean ± SD)	5 P.M. (Mean ± SD)
Normal	530.79±11.022	527.36±10.503	526.06±10.109	525.45±10.004
PXF	521.09±9.511	519.24±9.22	518.24±9.206	517.15±9.213
PXFG	500.08±10.553	497.38±10.332	496.54±10.516	495.67±10.696

Table 2. Mean CCT in µm Recorded at 4 Different Times of the Day in Normal, PXF and in PXFG Groups

Groups	IOP (Mean ± SD)	CCT (Mean ± SD)
Normal	14.26±1.73	518.93±9.263
PXF	14.644±1.98	527.42±10.347
p-value	0.187	0.000082

Table 3. Mean IOP and CCT in Normal vs PXF Group (Mean of IOP and CCT Each at 4 Times of the Day)

Groups	IOP (Mean ± SD)	CCT (Mean ± SD)
Normal	14.26±1.73	518.93±9.263
PXFG	23.82±2.63	497.42±10.505
p-value	0.0001	0.00001

Table 4. Mean IOP and CCT in Normal vs. PXFG Group (Mean of IOP and CCT Each at 4 Times of the Day)

In Table 1- Mean± SD of IOP of PXFG group was significantly higher as compared to PXF and normal groups at each of the four times of the day. At 8 A.M. in the morning the Mean± SD of intraocular pressures in each of the 3 groups is highest and thereafter decreases with more or less remaining the same from 11 A.M. to 5 P.M. In Table 2- Mean ± SD of CCT in PXFG groups was significantly thinner as compared to normal group at each of the four times of the day. Similarly Mean± SD of PXF group was also thinner as compared to normal subjects at each of the 4 times chosen. At 8 A.M. in the morning the Mean± SD of central corneal thickness in each of the three groups is highest and thereafter decreases attaining a plateau from 11 A.M. to 5 P.M. In Table 3- There was a significant difference in CCT between normal and PXF groups i.e. p=0.000082 (p<0.05 considered statistically significant), but there was no significant difference in IOP between normal and PXF groups i.e. p=0.187 (p>0.05). In Table 4- There was a statistically significant difference in IOP between normal and PXFG groups (p=0.0001, i.e. p<0.05) and also in CCT between normal and PXFG groups (p=0.00001, i.e. p<0.05).

DISCUSSION

The study "The ocular hypertension treatment study" observed the influence of CCT on applanation tonometer and found out that the measurement of IOP by Goldmann applanation tonometer was affected by central corneal thickness and hence IOP could either be underestimated or over-estimated.[11] Studies have shown that CCT decreases over a day in normal eyes.[7] The clinical significance of this finding has not been yet established. However, this suggests that the patients true IOP may be overestimated or underestimated depending on the time of the day IOP is measured.

In another study corneal biomechanical features of subjects with PXF were found to be changed as compared to healthy controls. In these patients corneal hysteresis (CH), corneal resistance factor (CRF) and CCT were found to be lower which was more obvious in patients with PXFG in comparison to PXF patients.[12] Previous research suggests that displaying a thin cornea is considered a risk factor for glaucoma.[13,14] The findings of PXF group in our study displaying a statistically significant (p<0.000082) thin mean CCT of 518 µm as compared with the control group having mean CCT of 527 µm is consistent with previous studies.[3,5] This highlights the importance of measuring CCT in all PXF individuals without glaucoma to avoid falsely underestimated IOP measurements i.e. 14.64 mmHg in PXF group vs 14.26 mmHg in control group caused by a thin CCT (p value=0.187).

Similar to previous studies that have assessed the diurnal variation of IOP in PXF individuals,[15] this study found that the IOP variation was higher in PXF group as compared to controls. The difference between the mean IOP at 8 A.M. and the mean IOP at 5 P.M. in PXF eyes in this study was 2.51 mmHg as compared to 1.62 mmHg in control group. This variation in IOP being higher in the morning and reduced later in the afternoon is noteworthy as a wide diurnal fluctuation in IOP is believed to be a major risk factor for glaucoma development. Previous studies in literature have shown that diurnal variation in CCT exists, with CCT being thickest in the morning and thinnest in the evening although still not proven if this variation is clinically significant.[7,9,10] Our study concluded that there was no significant variation in CCT during office hours i.e. from 8 A.M.. to 5 P.M. with a mean value of 3.94 µm in PXF group as compared to 5.34 µm in the control group. In our study we also found a statistically significant correlation between mean IOP in PXFG group vs controls (p<0.0001) and also between mean CCT in PXFG group vs controls (p<0.00001). Correlation between IOP and CCT has been done widely with few studies showing positive correlation and some others with no significant relationship between them.[1,16,17,18] The results of this study showed a positive correlation between IOP and CCT in PXF eyes and its variation at all the four

times of the day. This is in accordance to the findings of Fogagnolo et al in 2006 in patients with primary open angle glaucoma suggesting that a correlation does exist between IOP and CCT.[18] That is a decrease in CCT that occurred in PXF eyes between 8 A.M. to 5 P.M. may be responsible for the reduction in IOP measurements.

Strengths of our study included an age-matched control group and a single examiner was involved in measuring IOP and CCT in order to avoid any inter-examiner variability. Limitations of this study included a small sample size and uneven number of participants in study vs control group.

CONCLUSIONS

Both PXFG and PXF eyes have significantly thinner CCT as compared to controls. A small but significant reduction in IOP and CCT was seen both in PXFG and PXF groups from 8 A.M. to 5 P.M. The mean overall CCT in PXF eyes was significantly lower than the control group. A significant association between IOP and CCT was found in PXF and PXFG eyes. Thus, measurement of CCT is necessary in all patients with glaucoma and especially in those with PXF and PXFG eyes due to thinner cornea and risk of underestimating IOP. This study shows the importance of measuring CCT in all established glaucoma and glaucoma suspect cases in tertiary care hospital setups and wherever available in order to avoid falsely underestimated IOP readings in thin susceptible corneas and overestimating IOP readings in thick corneas thus prompting early treatment in order to avoid further damage and progression.

ACKNOWLEDGEMENT

We thank Prof Dr. Sumita Mohapatra for her support. Special thanks to Dr. Sambit Kumar Mohanty and Dr. Jayaram Meher for helping with the data collection and patient management.

REFERENCES

[1] 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(11):1072-1076.
[2] Syed Z, Srikanth K, Nagarajan S. Diurnal variation of central corneal thickness and intraocular pressure in eyes with pseudoexfoliation. Indian J Ophthalmol 2019;67(10):1607-1609.
[3] Inoue K, Okugawa K, Oshika T, et al. Morphological study of corneal endothelium and corneal thickness in pseudoexfoliation syndrome. Jpn J Ophthalmol 2003;47(3):235-239.
[4] Shah S, Chatterjee A, Mathai M, et al. Relationship between corneal thickness and measured intraocular pressure in a general ophthalmology clinic. Ophthalmology 1999;106(11):2154-2160.
[5] Detorakis ET, Koukoula S, Chrisohoou F, et al. Central corneal mechanical sensitivity in pseudoexfoliation syndrome. Cornea 2005;24(6):688-691.
[6] Brandt JD. Corneal thickness in glaucoma screening, diagnosis and management. Curr Opin Ophthalmol 2004;15(2):85-89.
[7] Harper CL, Boulton ME, Bennett D, et al. Diurnal variation in human corneal thickness. Br J Ophthalmol 1996;80(12):1068-1072.
[8] Kiely PM, Carney LG, Smith G. Diurnal variations of corneal topography and thickness. Am J Optom Physiol Opt 1982;59(12):976-982.
[9] du Toit R, Vega JA, Fonn D, et al. Diurnal variation of corneal sensitivity and thickness. Cornea 2003;22(3):205-209.
[10] Read SA, Collins MJ. Diurnal variation of corneal shape and thickness. Optom Vis Sci 2009;86(3):170-180.
[11] Gordon MO, Beiser JA, Brandt JD, et al. The ocular hypertension treatment study: baseline factors that predict the onset of primary open-angle glaucoma. Arch Ophthalmol 2002;120(6):714-720.
[12] Yazgan S, Celik U, Alagoz N, et al. Corneal biomechanical comparison of pseudoexfoliation syndrome, pseudoexfoliation glaucoma and healthy subjects. Curr Eye Res 2015;40(5):470-475.
[13] Herndon LW, Weizer JS, Stinnett SS. Central corneal thickness as a risk factor for advanced glaucoma damage. Arch Ophthalmol 2004;122(1):17-21.
[14] Congdon NG, Broman AT, Bandeen-Roche K, et al. Central corneal thickness and corneal hysteresis associated with glaucoma damage. Am J Ophthalmol 2006;141(5):868-875.
[15] Altintas O, Yuksel N, Karabas VL, et al. Diurnal intraocular pressure variation in pseudoexfoliation syndrome. Eur J Ophthalmol 2004;14(6):495-500.
[16] Laiquzzaman M, Bhojwani R, Cunliffe I, et al. Diurnal variation of ocular hysteresis in normal subjects: relevance in clinical context. Clin Exp Ophthalmol 2006;34(2):114-118.
[17] Shen M, Wang J, Qu J, et al. Diurnal variation of ocular hysteresis, corneal thickness and intraocular pressure. Optom Vis Sci 2008;85(12):1185-1192.
[18] Fogagnolo P, Rossetti L, Mazzolani F, et al. Circadian variations in central corneal thickness and intraocular pressure in patients with glaucoma. Br J Ophthalmol 2006;90(1):24-28.