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Original Article

Ophthalmology Section

Comparison of Central Corneal Thickness Measurement using Optical and Ultrasound Pachymetry in Primary Open Angle Glaucoma Patients

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ABSTRACT

Introduction: A thinner Central Corneal Thickness (CCT) is an important criterion in determining the probability of progression from Ocular Hypertension (OHT) to Primary Open Angle Glaucoma (POAG). The most common devices for measuring CCT are ultrasound and optical pachymeters. Ultrasound pachymetry is a quick and precise approach to quantify corneal thickness that is also portable and inexpensive. The advantages of optical method include operator independency and non invasiveness.

Aim: To compare central corneal thickness using optical and ultrasound pachymetry in patients with POAG.

Materials and Methods: This cross-sectional study was conducted at the Department of Opthalmology, ESI Post Graduate Institute of Medical Sciences and Research, Basaidarapur, Delhi, India, from October 2020 to April 2022. There were 105 POAG patients (210 eyes), divided into three subgroups of 35 subjects each (70 eyes each), based on the number of antiglaucoma medications being instilled, topically (one/two/three drugs), and 35 healthy antiglaucoma controls (70 eyes). Central corneal thickness measurements were taken by Ultrasonic Pachymeter (USP) TOMEY SP-100, and by CEM-530 Non Contact Specular Microscope (NCSM) (optical). Statistical analysis was performed by the Statistical Package for Social Sciences (SPSS) program for Windows, version 17.0 (SPSS, Chicago, Illinois).

Results: The mean CCT taken with NCSM and USP was 540.83±35.51 µm and 538.74±36.22 µm, respectively, in Right Eyes (RE) of 35 glaucoma patients on one drug, (p-value=0.80). Similarly, Left Eyes (LE), mean CCT with NCSM was 544.17±33.98 µm, and with USP was 541.69±36.6 µm (p-value=0.76). Mean CCT taken with NCSM and USP was 539.83±30,85 µm and 537.66±30.5 µm, respectively in RT eyes of 35 glaucoma patients on two drugs (p-value=0.76). Left eyes, mean CCT was 541.91±29.79 µm with NCSM as compared to USP which was 540.11±29.89 µm (p-value=0.80). On comparing the mean CCT values of RE in glaucoma subjects who were controlled on three antiglaucoma drugs it was found to be 528.37±26.44 µm using NCSM and 527.09±26.17 µm using USP (p-value=0.84). The mean values of CCT for LE was 521.94±26.53 µm with NCSM and with USP was 520±26.52 µm, respectively (p-value=0.81). Comparison of mean CCT measurements using NCSM and USP in 35 age-matched controls RE eye was found to be 517.83±21.27 µm and 515.97±20.91 µm, respectively (p-value=0.71). Similarly, for LE mean CCT values were 518.8±24.21 µm and 516.8±24.37 µm, respectively (p-value=0.73).

Conclusion: The CCT measured using NCSM was found to be higher than that measured using USP in POAG subgroups patients as well as healthy age-matched controls, however the difference was not statistically significant. There was highly significant linear correlation between the CCT measured using NCSM and USP in all POAG subgroups as well as healthy controls. This suggests that the devices could be used interchangeably in glaucoma patients as well as healthy subjects of similar age group.

Keywords: Antiglaucoma drugs, Corneal biomechanical properties, Intraocular pressure

INTRODUCTION

Primary Open Angle Glaucoma (POAG) is progressive optic nerve head neuropathy that can be prevented or stabilised by early diagnosis and treatment [1]. Glaucoma is one of the leading cause of irreversible blindness in the adult population [2]. Intraocular Pressure (IOP) elevation is a well-known primary risk factor for POAG [3]. A thinner Central Corneal Thickness (CCT) is an important criterion in glaucoma therapy to determine the likelihood of progression from Ocular Hypertension (OHT) to Primary Open-Angle Glaucoma (POAG) as well as previously treated glaucoma [4].

An Ultrasonic Pachymeter (USP), Specular Microscopy (SM), Corneal topography screening, Confocal microscopy, Optical coherence tomography, and the Scheimpflug imaging method, all can be used to quantify Central Corneal Thickness (CCT) [5]. Many modern contact and non contact pachymetry measurement methods have been published; however, the methods most typically employed in clinical practices are USP and Non Contact Specular Microscopy (NCSM) [6,7].

The ultrasonic approach is currently the gold standard for pachymetry [8]. Ultrasound pachymetry is a quick and precise approach to quantify corneal thickness. It is also portable and inexpensive. However, this device has limitations, which include measurements that require corneal contact and thus instillation of topical anaesthetic drop, chances of incorrect and unrepeatable probe placement, the lack of a fixation light for gaze control, ill-defined points of ultrasound reflection within the cornea, and the variability of sound speed in wet and dry tissues [6,7]. Changes in the tear film that may occur during measurement, pressure on the cornea, failure to measure from the exact center of the cornea, and positioning the probe at an oblique angle to the cornea, all can create measurement mistakes [9-12]. Some degree of experience regarding probe placement may be required for accurate measurement. Corneal tissue hydration also influences measurements [6,13].

Specular microscope is a non contact optical instruments. Its measurements depend on the reflection of light waves from the anterior and posterior corneal surfaces. Non contact specular microscopes also provide pachymetry measurements along

with specular microscopy findings. The advantages of Specular microscopy include operator independency and non invasiveness [4]. However, due to the operating principle of specular microscopy, clear reflections of the epithelial and endothelial surfaces are required to obtain reliable thickness measurements; thus, its limited clinical use [13].

Many studies been done on healthy and young individuals to compare both devices [7,14,15]. However, there are just a few studies that compare CCT measurements in POAG patients. The purpose of the current study was to compare central corneal thickness using optical and ultrasound pachymetry in patients with POAG, who were further divided into three subgroups on the basis of number of topical antiglaucoma eye drops instilled and between healthy controls in Indian population. Secondary objective was to determine correlation (r^2) between the CCT measurements acquired through these two techniques, also to investigate whether the devices can be used interchangeably.

MATERIALS AND METHODS

This cross-sectional study was conducted at the Department of Opthalmology, ESI Post Graduate Institute of Medical Sciences and Research, Basaidarapur, Delhi, India, from October 2020 to April 2022. The Ethical Review Committee of the hospital had approved the study {DM(A)H-19/14/17/IEC/2012-PGIMSR(part-II)}. Informed and written consent was obtained from each subject before enrollment.

Sample size calculation: To calculate the number of participants needed for the present study, the significance level was set at 95% (α=0.05), and the power of the test was set at 80% with a type II error (β) of 0.20. The minimum participants required for this study were 140 (280 eyes). All patients were recruited by non randomised convenience sampling method.

Inclusion criteria: Cases group: Patients age between 40-70 years,of either gender and diagnosed case of POAG. POAG patients were recruited from glaucoma clinic. POAG was defined as-a normal anterior chamber with an open-angle on gonioscopy, damage to the inner layers of the retina, an optic nerve head with typical glaucomatous appearance and corresponding nerve fibre layer and/or visual field defects [3].

Controls group: Age matched patients who did not have POAG, who visited to Department Ophthalmology Outpatient Department for refractive corrections.

Exclusion criteria: Presence of past intraocular surgery, corneal disease or any signs of previous corneal disease, ocular inflammation or trauma, refractive error more than +6D, contact lens wear, secondary glaucoma, angle closure glaucoma, diabetic patients were excluded from the study.

Cases: There were 105 POAG patients (210 eyes), divided into three subgroups of 35 subjects each (70 eyes each), based on the number of antiglaucoma medications being instilled, topically. The antiglaucoma drugs were-topical β-blocker (timolol) (0.5%), α2-agonist (brimonidine) (0.2%), carbonic anhydrase inhibitor (dorzolamide) (2%), prostaglandin analogue (latanoprost) (0.005%).

- Glaucoma patients on one drug
- Glaucoma patients on two drug
- Glaucoma patients on three drug

Controls: There were 35 healthy age-matched controls (70 eyes).

Study Procedure

Age and gender, duration and treatment of glaucoma, current medical treatment, history of medical illness. All subjects were underwent following complete ophthalmic examination: visual acuity assessment, refraction, intraocular pressure measurement using applanation tonometer, slit-lamp biomicroscopy and fundus examination by 90D lens. The CCT was measured by SP-100 USP and CEM-530 NCSM.

In order to avoid the potential effect of epithelial compression on consecutive measurements at the same location, CCT measurements were taken first via non contact specular microscope CEM 530 (NIDEK). At the second stage of the study, i.e., after about 10 minutes, CCT measurement were performed using an ultrasound pachymeter SP-100 (Tomey, Nagoya, Japan), after putting one drop of topical anaesthetic eye drop (proparacaine hydrochloride, 0.5%).

STATISTICAL ANALYSIS

Statistical analysis was performed by the Statistical Package for Social Sciences (SPSS) program for Windows, version 17.0 (SPSS, Chicago, Illinois). Continuous variables were presented as mean±SD, and categorical variables were presented as absolute numbers and percentage. Data was checked for normality before statistical analysis. Normally distributed continuous variables were compared using the unpaired t-test, whereas the Mann-Whitney U-test was used for those variables that were not normally distributed. Categorical variables were analysed using either the Chi-square test or Fisher's-exact test. A p-value <0.05 was considered statistically significant.

RESULTS

[Table/Fig-1] shows the demographic characteristics of each POAG subgroups and control groups. There were no significant differences in the age (p-value=0.69) or gender (p-value=0.53) of the patients between the groups.

Variables	Glaucoma patients on one drug (n, %)	Glaucoma patients on two drugs (n, %)	Glaucoma patients on three drug (n, %)	Control (n, %)	p-value
Age group (years)					
40-49 years	11 (31.43%)	14 (40%)	11 (31.43%)	16 (45.71%)	0.69
50-59 years	13 (37.14%)	12 (34.29%)	14 (40%)	11 (31.43%)	
60-69 years	11 (31.43%)	9 (25.71%)	10 (28.57%)	8 (22.86%)	
Mean±SD	54.00±8.377	52.77±8.412	53.62±7.757	51.74±9.284	
Gender					
Male	16 (45.71)	22 (62.86)	20 (57.14)	20 (57.14)	0.53
Female	19 (54.29)	13 (37.14)	15 (42.86)	15 (42.86)	

[Table/Fig-1]: Distribution of POAG patients and controls into different age groups and sex.

Mean IOP within POAG Subjects and Controls

[Table/Fig-2] shows the mean intraocular pressure in primary open angle glaucoma subjects controlled on one drug, on two drugs, on three drugs and control group-all of them are within the normal range of intraocular pressure. [Table/Fig-3] the NCSM showed a higher reading compared to USP, in Right Eye (RE) of all three subgroups as well in control group. [Table/Fig-4] the NCSM giving a higher reading compared to USP, in Left Eye (RE) of all three subgroups as well in control group.[Table/Fig-5] the NCSM the significant correlation between the CCT, RE and LE measured using NCSM and USP in POAG subjects on one drug. [Table/Fig-6] shows the significant correlation between the CCT, RE and LE measured using NCSM and USP in POAG patients on two drugs. [Table/Fig-7] shows the significant correlation between the CCT, RE and LE measured using NCSM and USP in POAG patients on three drugs.

Intraocular pressure	Glaucoma patients on one drug	Glaucoma patients on two drugs	Glaucoma patients on three drugs	Control
IOP right eye (mmHg) (Mean±SD)	13.51±1.85	12.8±1.86	13.23±2.45	14±2.39
p-value (each group against the control)	0.345	0.022	0.187	
IOP left eye (mmHg) (Mean±SD)	13.94±1.91	13.29±1.79	13.11±2.11	13.8±2.45
p-value	0.786	0.319	0.214	

[Table/Fig-2]: Mean intraocular pressure in the POAG subjects and the controls.
*IOP: Intraocular pressure

[Table/Fig-8] shows the significant correlation between the CCT, RE and LE measured using NCSM and USP in control patients.

Central corneal thickness right eye (µm)	Glaucoma patients on one drug	Glaucoma patients on two drugs	Glaucoma patients on three drugs	Control
NCSM	540.83±35.51	539.83±30.85	528.37±26.44	517.83±21.27
USP	538.74±36.22	537.66±30.5	527.09±26.17	515.97±20.91
p-value	0.80	0.76	0.84	0.71
Difference (µm)	2.09±1.98	2.17±1.87	1.29±1.72	1.86±1.91

[Table/Fig-3]: Comparison of mean Central Corneal Thickness (CCT) right eye values, by Non Contact Specular Microscope (NCSM) and Ultrasonic Pachymeter (USP), in different POAG subgroups and controls.

Central corneal thickness left eye (µm)	Glaucoma patients on one drug	Glaucoma patients on two drugs	Glaucoma patients on three drugs	Control
NCSM	544.17±33.98	541.91±29.79	521.94±26.53	518.8±24.21
USP	541.69±36.6	540.11±29.89	520.4±26.52	516.8±24.37
p-value	0.76	0.80	0.81	0.73
Difference (µm)	2.49±6.97	1.8±2.19	1.54±1.99	2±0.69

[Table/Fig-4]: Comparison of mean Central Corneal Thickness (CCT) left eye values in different POAG subgroups and controls.

Central corneal thickness		CCT NCSM (RE)	CCT UPS (RE)	CCT NCSM (LE)	CCT USP (LE)
NCSM	Pearson correlation	1	0.999**	1	0.983**
	Sig. (2-tailed)		0.0001		0.0001
USP	Pearson correlation	0.999**	1	0.983**	1
	Sig. (2-tailed)	0.0001		0.0001	

[Table/Fig-5]: Correlation between variables in Glaucoma patients on one drug Right Eye (RE) and Left Eye (LE).
**Correlation was significant at the 0.01 level (2-tailed)

Central corneal thickness		CCT NCSM (RE)	CCT USP (RE)	CCT NCSM (LE)	CCT USP (LE)
NCSM	Pearson correlation	1	0.998**	1	0.997**
	Sig. (2-tailed)		0.0001		0.0001
USP	Pearson correlation	0.998**	1	0.997**	1
	Sig. (2-tailed)	0.0001		0.0001	

[Table/Fig-6]: Correlation between variables in Glaucoma patients on two drug Right Eye (RE) and Left Eye (LE).
**Correlation was significant at the 0.01 level (2-tailed)

Central corneal thickness		CCT NCSM (RE)	CCT USP (RE)	CCT NCSM (LE)	CCT USP (LE)
NCSM	Pearson correlation	1	0.998**	1	0.997**
	Sig. (2-tailed)		0.0001		0.0001
USP	Pearson correlation	0.998**	1	0.997**	1
	Sig. (2-tailed)	0.0001		0.0001	

[Table/Fig-7]: Correlation between variables in Glaucoma patients on three drug Right Eye (RE) and Left Eye (LE).
**Correlation was significant at the 0.01 level (2-tailed)

Central corneal thickness		CCT NCSM (RE)	CCT USP (RE)	CCT NCSM (LE)	CCT USP (LE)
NCSM	Pearson correlation	1	0.996**	1	1.000**
	Sig. (2-tailed)		0.0001		0.0001
USP	Pearson correlation	0.996**	1	1.000**	1
	Sig. (2-tailed)	0.0001		0.0001	

[Table/Fig-8]: Correlation between variables in control group Right Eye (RE) and Left Eye (LE).
**Correlation was significant at the 0.01 level (2-tailed)

DISCUSSION

Central corneal thickness has an important role in the measurement of intraocular pressure assessment using Goldmann Applanation Tonometry especially in cases of glaucoma. Measurement of accurate CCT and hence the accurate IOP helps in maintaining the intraocular pressure using antiglaucoma medications with in required range to avoid further damage to the optic nerve and thus vision. Measurement of CCT should provide rapid, objective and accurate results [14]. It should be convenient for examiner and patient both. Since, NCSP and USP are the two widely used devices for the measurement of central corneal thickness, their agreeability in giving CCT measurements is of particular importance.

The present study compared the CCT measurements using the CEM 530 NIDEK Specular microscope and the SP 200 Tomey Ultrsound pachymeter in 35 POAG patients each controlled on one drug, two drugs and three drugs against 35 age-matched healthy controls. The CCT measured using NCSM was found to be higher than the one measured using USP among all POAG subgroups. Normal aging process results in remodelling of the extra cellular matrix and collagen molecules. In glaucoma patients the remodelling is even accelerated [15]. Thus, the speed of ultrasound increases and hence USP readings are lower compared to NCSM readings. A cross-sectional observational study conducted by Pillunatetal (2019) [14], found a significant difference between the CCT measurements between the two devices in healthy young subjects, USP measurements were higher than NCSM, but in healthy elderly and glaucoma subjects there was no significant difference, also in glaucoma subjects the values were reversed with the NCSM giving higher values. They hypothesised that the increased ultrasound speed due to biomechanical changes in the cornea with age and glaucoma may be responsible for the observation. They concluded that the devices could be used interchangeably in elderly and glaucoma patients but not in young subjects. The present study also showed similar results in patients of mean age (54.00±8.377 years) that the CCT measured using NCSM was slightly higher but statistically non significant than that measured using USP. The two devices could be used interchangeably in glaucoma subjects.

On comparing with both devices, CCT is lower in glaucoma patients than in the elderly. One of the causes could be that glaucoma patients were given different IOP-lowering drugs. Various studies have found a reduction of CCT after IOP lowering medications as these drugs may possibly decrease corneal hydration, which further decreases CCT. Prostaglandins also alters matrix metalloproteinases and remodelling of extracellular matrix [16]. Prostaglandin analogue Latanoprost (0.005%) used as antiglaucoma medication in current study.

In a study conducted in healthy subjects by Suzuki S et al., CCT measured using specular microscopy was found to be smaller than the CCT measured using USP [7]. However, in the present study, in glaucoma patients the CCT measured using NCSM was slightly higher than that measured using USP but the difference was statistically insignificant. There was also significant linear correlation between the CCT measurements of the two devices.

In the study conducted by Kwana K et al., where they compared the CCT measurements in post LASIK patients using four devices, the NCSM and USP gave similar results with significant linear correlation between the two devices [17]. In the present study also there was similar result with significant linear correlation between the two devices.

In the study conducted by Ucakhan OO et al., CCT measurements were taken in keratoconus eyes and found that NCSM findings were significantly smaller compared to USP findings and they concluded that both the devices should be used in caution in keratoconus eyes [18]. In present study, in glaucoma patients the CCT measured using NCSM was slightly higher but statistically insignificant. There was significant linear correlation between the measurements indicating they could be used interchangeably among glaucoma patients and elderly healthy patients.

Zhao MH et al., conducted a study on refractive surgery patients where they compared CCT measurements taken by using NCSM and USP before and after refractive surgery and concluded that there was no significant difference, seen between the measurements of

CCT taken by both instruments, before and after refractive surgery [19]. The present study also proved that there is no significant difference between the CCT measurements of the two devices in glaucoma patients as well as healthy age-matched controls. The study also showed significant linear correlation between the CCT measurements.

Tai LY et al., compared CCT measurements using various imaging devices including NCSM and USSP in healthy subjects and found that the CCT measured using NCSM was 20-30 µm thinner than that measured using other devices [14]. Cevik SG et al., found that the CCT measurement using NCSM was a significantly 35 µm lower than that measured using USP, and had a significant linear correlation between the CCT measurements [15]. In the present study, there was no significant difference between the CCT measurements of the two devices, the CCT measured using NCSM was slightly higher compared to that measured using USP but was statistically non significant. Ucak T et al., conducted a study on healthy subjects in which they measured the CCT using different imaging devices and compare that to USP and found that the imaging devices including NCSM showed agreement with USP [20]. Scotto R et al., also found that the CCT measured using NCSM was significantly higher compared to that measured using USP. Based on their findings they concluded that these devices cannot be used interchangeably [21].

Results of this study provide a greater insight into the understanding of the measurement of CCT by different devices in POAG patients on various drugs.

Limitation(s)

In current study, the influence of topical anaesthetic drops in ultrasonic pachymetry could not be commented. Furthermore, the exact corneal location in each repetitive readings could not be assessed for ultrasonic pachymetry, while taking measurements on the anterior surface of cornea.

CONCLUSION(S)

The CCT measured using NCSM was higher than that measured using USP in POAG patients on one drug, two drugs, three drugs as well as healthy age-matched controls, however the difference was not statistically significant. This may be due to the increase in ultrasound speed due to structural and biochemical changes in cornea with glaucoma and aging. These findings provide indirect evidence that corneal biomechanical characteristics changes with aging and glaucomatous disease process. There was highly significant linear correlation between the CCT measured using NCSM and USP in all POAG subgroups on one drug, two drugs, three drugs as well as healthy controls. This suggests that the devices could be used interchangeably in glaucoma patients as well as healthy subjects of similar age group.

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