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Original Research Article

Retinal nerve fiber layer thickness analysis in normal, ocular hypertensive, and primary open angle glaucoma: an optical coherence tomography study

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ABSTRACT

Background: To correlate the findings of optical coherence tomography (OCT) evaluation of retinal nerve fiber layer (RNFL) thickness in primary open angle glaucoma, ocular hypertensive and normal eyes.
Methods: A 34 consecutive normal, 26 consecutive ocular hypertensives and 40 consecutive glaucomatous eyes underwent a complete ophthalmic examination, including applanation tonometry, disc evaluation, gonioscopy and perimetry. Thickness of the RNFL around the optic disc was determined with 3.4 mm diameter-wide 3D 2000 TOPCON OCT. Average and segmental RNFL thickness values were compared among all groups.
Results: Of the 100 eyes enrolled, the mean RNFL thickness was significantly less in glaucomatous eyes (83.165±15.938) than in normal's (102.42±15.2) and ocular hypertensive's (100.45±7.38). RNFL, average thicknesses in all four quadrants in POAG patients were significantly decreased compared with the OHT and the control groups.
Conclusions: RNFL measurement with SD-OCT could provide important information for detection of early stages of glaucoma. (pre-perimetric glaucoma) as well as help in evaluating progression of glaucoma.

Keywords: Ocular hypertension, Optical coherence tomography, Primary open angle glaucoma

INTRODUCTION

Glaucoma is the second leading cause of blindness in the world (surpassed only by cataracts, a reversible condition). More than 3 million people are bilaterally blind from Primary Open Angle Glaucoma (POAG) worldwide, and more than 2 million people will develop POAG each year. Over a 5-year period, several studies have shown the incidence of new onset of glaucomatous damage in previously unaffected patients to be about 2.6-3% for IOPs 21-25mmHg, 12-26% incidence for IOPs 26-30mmHg, and approximately 42% for those higher than 30mmHg. Prevalence of POAG is 3-4 times higher in blacks than in Caucasians; in addition, blacks are up to 6 times more susceptible to optic disc nerve damage than Caucasians. Population based studies have estimated the prevalence of glaucoma in India to be 11.9 million. A higher prevalence of larger cup-to-disc ratios exists in the normal black population as compared with white controls. Age older than 40 years is a risk factor for the development of POAG, with up to 15% of people affected by the seventh decade of life. Ocular hypertension has a 10-15 times greater prevalence than POAG. Ocular Hypertension Treatment Study (OHTS) states that over a 5-year-period, patients with ocular hypertension and IOP levels of 24 mm Hg or more have a 10% overall risk of developing glaucoma.[1-3]

Primary open-angle glaucoma is described distinctly as a "multifactorial optic neuropathy that is chronic and progressive, with a characteristic acquired loss of optic nerve fibers. Such loss develops in the presence of open anterior chamber angles, characteristic visual field abnormalities, and intraocular pressure that is too high for the continued health of the eye " Many risk factors have been identified, to include the following: elevated IOP, thin central corneal thickness, hypertension, diabetes, myopia, thyrotoxicosis, family history, race, age older than 40 years. Ocular hypertension simply means a raised intraocular pressure of more than 22mmHg in one or both eyes, as measured by applanation tonometry on 2 or more occasions without any optic disc changes and any visual field changes. Risk factors for conversion of OHT to glaucoma: higher IOP, greater age, lower central corneal thickness, larger C/D ratio, higher pattern standard deviation on perimetry and family history.

The retinal nerve fiber layer (RNFL) is formed by the expansion of the fibers of the optic nerve. The nerve fiber layer is thickest at the nasal edge of the disc, where it measures 20-30μm. The temporal part of the optic disc receives nerve fiber only from a small part of the retina because of which the thickness of the nerve fiber layer is reduced to 10μ here. Certain processes can excite its natural apoptosis. Factors such as age, gender, axial length, size of the optic disc, refractive status of the eye, ethnicity/race are shown to affect the RNFL thickness, as well as situations such as raised intra ocular pressure (IOP), intraocular inflammation, vascular diseases and any kind of hypoxia can lead to changes in the RNFL thickness which can in future leads to glaucomatous changes.

Although RNFL can be directly visualized and imaged *in vivo*, using red free fundus ophthalmoscopy and photography, these techniques allow, so far, subjective and qualitative evaluation of the RNFL but not quantitative thickness measurement, also these measurements are variably reproducible. There is wide inter-observer and sometimes, intra-observer variability in between different examinations. With the introduction of the optical coherence tomography (OCT) objective measurement of the RFNL thickness may be indirectly estimated.

OCT is a non-invasive, non-contact imaging technique which produces cross-sectional images with millimeters penetration (approximately 2-3mm in tissue) and micrometer scale axial and transverse resolution of not only the retina and optic nerve, but also the anterior segment of the eye. The high resolution of OCT allows precise measurement of retinal thickness as well-visualization of intraretinal layers, particularly the RNFL. The technique was first demonstrated in 1991 with ~30μm axial resolution. With advancement in technology, today we have the conventional OCT with an axial resolution of ≤10μm.

The principle of OCT involves a low coherence infrared (843nm) diode light source which is divided into reference and sample paths. Reflected sample light from the subject's eye creates an interference signal with the reference beam, which is detected by fiberoptic interferometer.[4]

Our study aims to measure the RNFL thickness by OCT in eyes with primary open angle glaucoma (POAG) and in ocular hypertensives (OHT) and to compare the results with that of age-matched normal eyes.

METHODS

Prospective, comparative study was done on 34 consecutive normal, 26 consecutive ocular hypertensives and 40 consecutive glaucomatous eyes. Each subject underwent a complete ophthalmological examination including best corrected visual acuity, IOP measurements with Goldmann applanation tonometer (taking central corneal thickness into account), normal diurnal variation, slit lamp biomicroscopy, gonioscopy and fundus evaluation after pupil dilatation on the slit lamp using 90D lens. Detailed history including family history and history pertaining to risk factors were recorded. Optic disc of all the patients and control were evaluated and were classified accordingly. All subjects underwent standard automated perimetry on Humphrey’s field analyzer using 30-2 testing protocol by SITA FAST strategy. Visual field reliability criteria included fixation loss of less than 20% and false positive and negative rates of less than 33%. Patients with no reliable fields at three separate times were excluded. Gonioscopy was done for all patients and control. Patients and controls with open angles were only included in the study.

All included subjects were scanned with the 3D 2000 TOPCON OCT by single operator. Scans with minimum signal strength >7 were included in the study. One of the two scan, obtained on the same day, with maximum signal strength was included. For this study we analyzed the global average RNFL thickness, average RNFL thickness in the superior, inferior, nasal, temporal quadrant.

The results were analyzed, p value was calculated for each parameter and relationships were considered significant if $P < 0.05$. Data were reported as arithmetic mean±SD.

RESULTS

A 100 Participants were included in the study with mean age of 57 years. On comparison of average global RNFL thickness lowest was found to be in POAG patients (83.165±15.938) and highest in normal patients (102.42±15.2) with p value < 0.05. RNFL thickness was lowest in nasal quadrant followed by temporal, superior and highest in inferior quadrant (Table 1).

Comparison done by Bonferroni method in Table 2 shows that there was a significant difference seen RNFL values of all groups in all quadrants as the p value was <0.05.

Table 1: RNFL thickness value in all parameters measured by OCT.

OCT parameter	POAG	OHT	Control
Avg. global	83.165±15.938	100.45±7.38	102.42±15.2
Superior	98.90±5.61	125.04±3.76	128.94±4.16
Inferior	106.32±4.79	128.75±2.60	129.45±6.87
Nasal	60.64±5.10	76.02±1.85	78.69±9.86
Temporal	66.80±3.26	72.01±2.25	72.62±6.50

Table 2: Comparison between different groups of participants oct values by p value.

Quadrants	Participants		Std. error	P value
Superior	1	2	1.177	0.006
		3	1.054	0.000
	2	1	1.177	0.006
		3	1.138	0.000
	3	1	1.054	0.000
		2	1.138	0.000
Inferior OD	1	2	1.171	0.744
		3	1.048	0.000
	2	1	1.171	0.744
		3	1.132	0.000
	3	1	1.048	0.000
		2	1.132	0.000
Nasal	1	2	1.080	0.040
		3	0.967	0.000
	2	1	1.080	0.040
		3	1.044	0.000
	3	1	0.967	0.000
		2	1.044	0.000
Temporal	1	2	0.815	1.00
		3	0.730	0.000
	2	1	0.815	1.00
		3	0.788	0.000
	3	1	0.730	0.000
		2	0.788	0.000

DISCUSSION

Glaucoma is the second leading cause of blindness in the world so the main goal of glaucoma management is to diagnose this disease when it is asymptomatic. Visual field testing is essential in the diagnosis and monitoring of glaucoma. However, it is known that standard perimetry cannot detect VF defects until 20-40% of ganglion cells have been lost.[5,6] Nowadays RNFL defects have been objectively demonstrated earlier than VF defects with new investigative technologies. Measuring RNFL thickness by OCT enables an objective and quantitative assessment of glaucomatous structural loss. It has been shown that all generations of OCT provide reproducible measurements of RNFL thickness in many previous studies.[7-12]

Analysis of the pattern of RNFL defects with SD-OCT imaging demonstrated that the most frequently RNFL defects have been at the inferotemporal meridian followed by the superotemporal meridian.[13]

Yalvac et al, suggested that the best parameters for distinguishing the high risk OHT group from the moderate and low risk groups, defined according to Scoring Tool for assessing risk (STAR) score, were inferior average and 6 o'clock area in Stratus OCT RNFL thickness parameters.[14]

Mwanza et al reported that, in the mild POAG patients, focal RNFL thickness loss was found in the inferior area.[15] In the moderately advanced disease subgroups, RNFL defects were in sectors 1, 6, and 7. RNFL defect extended through almost all sectors in the advanced disease subgroups.[16]

CONCLUSION

In this study we found that RNFL global average thickness, average thickness in superior and inferior quadrant was significantly lower in POAG patients. The best parameter to differentiate ocular hypertensive at risk from normal eyes was found to be RNFL thickness in superior quadrant. Our results suggest that the RNFL thickness in the inferior quadrant and global average RNFL thickness were other useful parameter for detecting changes in RNFL thickness in POAG and ocular hypertensive patients.

We suggest initiating an early treatment for the patients who show structural change in OCT in one or more quadrant so as to prevent the likely damage to optic nerve head in future. Treatment may also be initiated in the patients without structural changes in OCT in presence of risk factor. OCT can be used as a helpful tool in POAG and ocular hypertensive patients for measurement of structural loss which precedes functional loss alerting ophthalmologist to start early treatment especially in presence of risk factor and contributes to quality of life.

SD-OCT could catch significant differences between POAG, ocular hypertensive patients and healthy subjects in RNFL thickness measurement. OCT thus is helpful in early detection of glaucoma as well as in keeping an eye on progression of glaucoma.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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