IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 7 Ver. II (July. 2015), PP 21-24
www.iosrjournals.org

Role of Optical Coherence Tomography in Glaucoma Suspects

Dr. Misba Shams

I. Introduction

Glaucoma is a leading cause of irreversible blindness throughout the world. A 1996 study estimated the prevalence of glaucoma in the world by the year 2000 to be 66.8 million, with 6.7 million suffering from bilateral blindness.[1] Glaucoma is characterized by loss of retinal ganglion cells (RGCs) and their respective axons, which comprise the retinal nerve fibre layer (NFL), on pathologic examination. [2, 3, 4, 5, 6]

Injury prevention before Optic nerve head changes occur is the prime strategy to detect the early losses. Significant axonal loss may precede the development of visual field defects and identifiable cupping[7, 8, 9] and subjective assessments of optic nerve head cupping are not sufficiently sensitive enough to detect the subtle changes especially notches, thus are liable to varied interpretation and resultant missing of early cases.

Current diagnostic techniques such as retinal, optic nerve head (ONH) analysis instruments and stereo-fundus photography lack sensitivity and reproducibility. It can assess nerve head rim area and other indices of ONH structure but cannot reliably differentiate between glaucomatous and normal and are unable to pick up progression.

Secondly, it may take years to show a definitive progression on the basis of WOW perimetric changes. Early detection of disease process is essential for diagnosis to be made before appearance of any irreversible loss. The newer diagnostic modalities may enable us to make a pre-perimetric diagnosis of glaucoma and pre-empting the progression of the disease such as Optical Coherence Tomography (OCT), Confocal scanning laser (HRT), Scanning laser polarimetry (GDxVCC). They provide quantitative, reproducible, and objective measurements of ONH and RNFL thickness.

II. Optical Coherence Tomography

OCT is a non-invasive, non contact, transpupillary, in vivo imaging system, using a super luminescent diode light source to create high resolution, real time, cross sectional tomographic images of retina. OCT is an interferometric imaging technique offering millimetre penetration depths of a sample under test with 10 micrometer axial and lateral resolution.

In our study we aimed to assess RNFL thickness, optic nerve head changes (ONH) clinically and by OCT and correlate RNFL Thickness by OCT with visual fields by standard automated perimetry (SAP) in glaucoma suspects, highlighting the usefulness of OCT in glaucoma suspect patients where diagnosis by standard means are not confirmatory.

III. Materials And Method

A total of 64 eyes of 32 patients attending the OPD, were included in this study conducted in our institute over a period of 20 months from January 2013 to August 2014.

The procedures followed were in accordance with the ethical standards committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 2000. Patients included were above 18 years of age and had suspected glaucomatous changes such as asymmetrical cupping of optic disc between fellow eyes with the difference of >0.2, or Cup\disk ratio >0 .6 in one eye. Patients were excluded on basis of media clarity grade III Or IV, nonreacting pupil due to other optic neuropathies, angle closure glaucoma, any inflammation like uveitis, advanced glaucoma, refractive error >4D. Patients with any previous intraocular surgery, ocular trauma, and secondary glaucoma were excluded along with patients with diabetes, pathological changes in the posterior segment. Demographic details along with detailed history regarding headache, frequent change of glasses, myopia, steroid intake, and family history of glaucoma was elicited from the patients in the OPD.

A complete ophthalmic examination including careful Slit lamp biomicroscopy, gonioscopy was performed. IOP was measured by indentation tonometer to have baseline documentation at least at 3 visits one month apart. Fundus examination using 78 D\90D was with drawings of optic nerve head and RNFL was noted in red free\ green light.

Visual fields using 30-2 SITA standard full threshold programme on Humphrey Field analyser perimeter (Carl Zeiss Meditec, Inc, Dublin,CA) were recorded as baseline. Patients already exhibiting Glaucomatous visual field loss. Only patients who had more than two reliable consistent visual field results were included. Colour vision(CV) ,Contrast sensitivity(CS) using Pelli Robson chart were recorded finally Spectral OCT using Optovue(45531 Northport Loop Wess Frengrit, CA 94531 USA) was done.

Method

Each eye was dilated with tropicamide 1% and scans were performed with a minimum pupillary diameter of 5 mm. The internal fixation target was used owing to its higher reproducibility.

The fast retinal nerve fibre layer thickness protocol was used for assessment of RNFL thickness. It has better reproducibility than a single scan. Mean RNFL thickness was calculated with the inbuilt RNFL thickness average analysis protocol.

Various machine-generated parameters were used for evaluation of RNFL thickness, including RNFL average thickness over the entire cylindrical section and average RNFL thickness in each quadrant (superior, nasal, temporal, and inferior).

Fast Optical disc scan was used for ONH scan which compresses six optical disc scan into one scan and acquire scan in short time of 1.92 seconds.

Optic nerve head (ONH) analysis and various ONH parameters including optic disc tomography included average disc area, cup area, rim area (disc area minus the cup area), vertical integrated rim area (VIRA), horizontal integrated rim width (HIRW), cup volume, average cup disc ratio and horizontal and vertical cup-disc ratios were calculated using the inbuilt ONH analysis protocol.

Scan quality was considered satisfactory if signal strength > 7, a clear fundus image allowing optic disc and scan circle visibility prior to and during image acquisition, even and dense colour saturation throughout all retinal layers with red colour visible in the retinal pigment epithelium and RNFL and a continuous scan pattern without missing or blank areas (i.e. no algorithm failure)

Following the OCT scan the patients were categorised into two groups according to study conducted by **Dr. R. Sihota et al.** [10] evaluating the diagnostic capability of OCT in glaucoma

GROUP 1-Avg RNFL Thickness <0.111mm, and
GROUP 2-Avg RNFL Thickness >0.111mm

Group 1 and 2 with 32 and 30 eyes respectively were analysed on the basis of mean IOP, mean CDR. They were also compared for Inferior and superior quadrant RNFL thickness along with ONH Parameters.

Statistics

Statistical analysis was performed using SPSS software version 15 (SPSS Inc, Chicago, IL). Z test was used to evaluate differences between Group 1 and Group 2 eyes. Receiver operating characteristic (ROC) curves were used to describe the ability of spectral OCT to differentiate early glaucoma from healthy eyes in both groups for ONH (Rim area and C/D area ratio) parameter.

The ROC curve shows the trade-off between sensitivity and 1-specificity. An area under ROC (AROC) of 1.0 represents perfect discrimination, whereas an area of 0.5 represents chance discrimination.

IV. Results

64 eyes of 32 patients were studied and the age group included in the study was between 25-55years, majority of the patients i.e.: 19 (62.62%) were above the age 45 years. All the patients had IOP within normal limits and majority(71.87%) had IOP in the range of 13- 18 mm Hg, all the eyes had Mean Deviation (MD) within normal limits <-6.dB8. I.e. all cases were perimetrically normal.

Cup: disc ratio is assessed clinically by using 78D condensing lens and 31 eyes (48.43%) had CDR in range of 0.50 to 0.60 in the study group. Additionally 21 subjects (65.62%) had asymmetry of CDR of >0.2 between the two eyes.

Cases were divided into two groups following OCT scans according to study conducted by **Dr. R. Sihota et al. (2006)** [10] evaluating the diagnostic capability of optical coherence tomography in glaucoma

GROUP 1-Avg RNFL Thickness <0.111mm, and
GROUP 2-Avg RNFL Thickness >0.111mm

Group 1 and Group 2 with 32 and 30 eyes respectively were analysed

On basis of mean IOP where group1 &2 had mean IOP of 14.56 and 15.00 mmHg respectively, p value was 0.51 indicating no statistical significance between two groups. A major drawback of our study was that the IOP was recorded with Schiotz indentation method rather than Goldman applanation tonometry central corneal thickness of the subjects was not measured due to lack of equipment and financial constraints of our subjects. Hence the IOP was not adjusted for central corneal thickness which could have lead to false values.

Mean CDR [figure1] was 0.591 for group1 and 0.473 for group2 with a p value 0.001[figure 2] which was statistically highly significant.

Further specific RNFL and ONH parameters were analysed.

Average RNFL Thickness [figure 3] group1 mean was computed to be 0.0827mm± 0.017 and group2 mean was 0.1215mm±0.007. The p value was 0.001 which is highly significant. Inferior quadrant thickness for group 1&2 was 0.0871mm± 0.027 & 0.1279mm ± 0.033 respectively. Difference between the two was highly significant (p value 0.001). Superior quadrant RNFL thickness group1 mean was 0.099 ± 0.035mm group2 mean was 0.139± 0.080mm with a p value of 0.1 which is statistically significant. [Figure 4]

Mean CD area ratio [Figure 5] was o.6377± 0.145, 0.5263± 0.1423 for group1 and 2 respectively. The p value was 0.007 (highly significant) and AUC 0.715. [Figure 6] In case of rim area, 17 eyes had Rim area >1.20 which is within normal limits and 47 (73.43%) eyes had rim area outside normal limits. This parameter showed a p value of 0.003 between the two groups which is statistically significant along with AUC of 0.703. [Figure 7]

V. Discussion

Majority of the patients in our study were found to be above the age of 45 yrs.

It is consistent with the study of **Gordon, Mae O., et al.(2002)** "The Ocular Hypertension Treatment Study [11] found the mean age to be 55.8 years.

In our study the two groups GROUP1- Avg. RNFL Thickness <0.111mm ,and GROUP2- Avg. RNFL Thickness >0.111mm with 34 and 30 eyes respectively were analysed on the basis of mean IOP, mean CDR, ,in which difference between mean CDR comes out to be statistically significant (p value <0.001), and IOP value was statistically insignificant (p value 0.51)

Further Group1 and group2 were compared in relation to average inferior quadrant thickness and average superior quadrant thickness. Difference between Average inferior quadrant RNFL thickness between group1 mean of 0.8721 ± 0.27 mm and group 2 mean 0.1279 ± 0.33mm was statistically highly significant. (p value 0.001). Superior quadrant RNFL thickness difference between group1 mean was 0.099 ± 0.035mm group2 mean was 0.139± 0.080mm was statistically significant (p value of 0.1) . Average RNFL Thickness group1 mean was computed to be 0.0827mm ± 0.017 and group2 mean was 0.1215mm ± 0.007 which is highly significant (p value was 0.001) showing significant differences in the RNFL thickness parameters among normal eyes and glaucoma suspects

Previous studies have shown that OCT-generated RNFL thickness is reliable for differentiating eyes with early glaucoma from normal eyes.

Sihota et al. (2006) [10] compared normal and glaucoma sub groups for RNFL thickness parameters and found a significant difference in all parameters between the two sub groups(P < 0.001) with average and inferior RNFL thicknesses showing the largest area under the ROC curve (0.905 and 0.862 for normal and early glaucoma subjects respectively)

Mannasakon A et al (2006) [12] found highest area under the receiver operating characteristic curves (0.93 ± 0.02, 0.92 ± 0.03, and 0.90 ± 0.03, for RNFL thickness at the 7 o'clock sector, inferior quadrant, and the vertical C/D ratio respectively in a study to compare the outcome of RNFL thickness and Optic disk algorithm to detect glaucoma.

Chen et al. (2005)[13]showed for differentiating early glaucoma from normal eyes that average RNFL thickness was the most effective parameter (AROC 0.793).**Kanamori et al. (2001)** [14] demonstrated inferior RNFL (AROC of 0.93) as the best parameter for differentiating normal from early glaucomatous eyes.

Nouri-Mahdavi et al. (2004) [15] showed that OCT had better capability to differentiate early glaucomatous changes as demonstrated by disc and field changes as compared to that of glaucoma suspects demonstrated by disc changes with normal visual fields. The best combination for sensitivity and specificity was the 7-o'clock parameter (85/88). The parameter for highest AUROC was 11-o'clock (0.93; 95% CI, 0.91– 0.96). On the whole, they demonstrated inferior quadrant and average RNFL thickness had the greatest combination of sensitivity and specificity individually.

Our study results revealed average, inferior average followed by superior average RNFL thickness to be the best criteria for differentiating normal eyes from eyes with early glaucomatous changes.

Ganglion cell axons, neuroglia and the astrocytes together make up a healthy nerve fiber layer. The glaucomatous process results in a loss of retinal ganglion cells.[16] **Quigley et al. (1996)** [17] showed that even in the absence of a visual field defect up to 40%-50% nerve fibres could be lost. Later a study revealed that when statistical abnormalities appear on automated perimetry at least 25% to 35% reduction in the retinal ganglion cell population has taken place.

Group1 and group 2 were also analysed on basis of ONH parameter of CD area ratio and rim area we found nine eyes had a C/D Area Ratio between 0.2- 0.4 which is within the normal range while fifty five eyes had C/D Area ratio outside normal limits. [18] Mean CD area ratio was o.6377± 0.145, 0.5263± 0.1423 for group1 and 2 respectively. The p value was 0.007 (highly significant) and AUC 0.715

In case of rim area, 17 eyes had Rim area >1.20which is within normal limits and 47 eyes had rim area outside normal limits. This parameter showed a p value of 0.003 between the two groups which is statistically significant along with AUC of 0.703.

This was consistent with the findings of **Mannasakorn A. et al. (2006)** [18] who found rim area as one of the better parameters to differentiate normal eyes from glaucomatous eyes. (AUC of 0.86± 0.04 for rim area and C/D area ratio AUC of 0.88± 0.03)

Medeiros et al. (2005) [19] found no statistically significant difference (P value 0 .28) between the areas under the ROC curves (AUC) for the RNFL thickness parameter and the ONH parameter (the largest AUC inferior thickness, AUC 0.91 in RNFL thickness, largest AUC cup/disk area ratio, AUC =0.88 in ONH parameters). The inferior thickness RNFL parameter had a considerably bigger AUC than the macular thickness parameter with highest AUC which was the inferior outer macular thickness, AUC =0.81 (P 0.004). It demonstrated that when applied to the independent sample an amalgamation of selected ONH and RNFL parameters led to the most excellent classification function for glaucoma detection (AUC of 0.97).

Our study suggests that certain OCT-generated measurements such as average and inferior RNFL thickness can help in providing valuable information regarding degree of glaucomatous damage. When both RNFL and Optic disc parameters are combined they can aid in better discrimination and detection of glaucoma in its earlier stages when significant visual morbidity has yet not taken place, these measurements can complement the results of perimetry and clinical observation in providing more objective and quantitative information regarding the degree of glaucomatous damage.

However, further larger studies with longitudinal follow-up are needed, to substantiate these findings as we understand that our finding may have a lesser significance due to a small sample size and IOP unadjusted for CCT and discrepancies arising from manual error during tonometry.

References

[1]. Quigley HA. Number of people with glaucoma worldwide. British Journal of ophthalmology. 1996; 80:389.

[2]. Quigley HA, Miller NR, George T. Clinical evaluation of nerve fiber layer atrophy as an indicator of glaucomatous optic nerve damage. Archives of Ophthalmology. 1980; 98:1564–1571.

[3]. Sommer A, Miller NR, Pollack I. The nerve fiber layer in the diagnosis of glaucoma. Archives of Ophthalmology. 1977; 95: 2149–2156.

[4]. Sommer A, Quigley HA, Robin AL. Evaluation of nerve fiber layer assessment. Archives of Ophthalmology. 1984; 102:1766–1771.

[5]. Pederson JE, Anderson DR. The mode of progressive disc cupping in ocular hypertension and glaucoma. Archives of Ophthalmology. 1980;98:490–495.

[6]. Sommer A, Katz J, Quigley HA. Clinically detectable nerve fiber atrophy precedes the onset of glaucomatous field loss. Archives of Ophthalmology. 1991; 109:77–83.

[7]. Quigley HA, Katz J, Derick RJ, Gilbert D, Sommer A. An evaluation of optic disc and nerve fiber layer examinations in monitoring progression of early glaucoma damage. Ophthalmology. 1992; 99:19–28.

[8]. Airaksinen, P Juhani, S M Drance, G R Douglas, D K Mawson, and H Nieminen. Diffuse and localized nerve fiber loss in glaucoma. American journal of ophthalmology, 98(5), 566-571.

[9]. Harwerth RS, Carter-Dawson L, Shen F, Smith EL 3rd, Crawford ML. Ganglion cell losses underlying visual field defects from experimental glaucoma. Investigative Ophthalmology & Visual Science. 1999; 40:2242–2250.

[10]. Sihota R, Sony P, Gupta V, Dada T, Singh R. Diagnostic Capability of Optical Coherence Tomography in Evaluating the Degree of Glaucomatous Retinal Nerve Fiber Damage. Investigative Ophthalmology & Visual Science. 2006 May; 47(5):2006-10.

[11]. Gordon, Mae O, Julia A Beiser, James D Brandt, Dale K Heuer, Eve J Higginbotham et al. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. Archives of ophthalmology 120, no. 6 (2002): 714-720.

[12]. Manassakorn, Anita, Kouros Nouri-Mahdavi, and Joseph Caprioli. Comparison of retinal nerve fiber layer thickness and optic disk algorithms with optical coherence tomography to detect glaucoma. American journal of ophthalmology. 141, no. 1 (2006): 105-115.

[13]. Chen, H. Y., & Huang, M. L. (2005). Discrimination between normal and glaucomatous eyes using Stratus optical coherence tomography in Taiwan Chinese subjects. Graefe's Archive for Clinical and Experimental Ophthalmology. 243(9), 894-902.

[14]. Zangwill LM, Bowd C, Berry CC, Williams J, Blumenthal EZ, Sánchez-Galeana CA et al. Discriminating between normal and glaucomatous eyes using the Heidelberg retina tomograph, GDx nerve fiber analyzer and optical coherence tomograph. Archives of Ophthalmology. 2001;119:985-993.

[15]. Nouri-Mahdavi K, Hoffman D, Tannenbaum DP, Law SK, Caprioli J. Identifying early glaucoma with optical coherence tomography. American Journal of Ophthalmology. 2004; 137: 228-235.

[16]. Hee MR, Izatt JA, Swanson EA, Huang D, Schuman JS, Lin CP, Fujimoto JG Puliafito,. Optical coherence tomography of the human retina. Archives of Ophthalmology. 1995 Mar;113(3):325-32.

[17]. Quigley, Harry A, Gregory R, Dunkelberger, and W. Richard Green. Retinal ganglion cell atrophy correlated with automated perimetry in human eyes with glaucoma. American Journal of Ophthalmology 107.5 1989: 453-464.

[18]. Manassakorn, Anita, Kouros Nouri-Mahdavi, and Joseph Caprioli. Comparison of retinal nerve fiber layer thickness and optic disk algorithms with optical coherence tomography to detect glaucoma. American journal of ophthalmology 141.1 2006: 105-115.

[19]. Medeiros, Felipe A. Evaluation of retinal nerve fiber layer, optic nerve head, and macular thickness measurements for glaucoma detection using optical coherence tomography. American journal of ophthalmology 139.1 2005: 44-55 **.**