International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 10, October 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.10.2024.81

ORIGINAL RESEARCH

Study of macular ganglion cell layer changes in Ocular hypertension by swept-source optical coherence tomography

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Received Date: 25 August, 2024 Accepted Date: 28 September, 2024

ABSTRACT

Background: Ocular Hypertension (OHT) poses a risk for developing Primary Open-Angle Glaucoma (POAG), which is a leading cause of irreversible blindness. Early detection of retinal ganglion cell (RGC) thinning may help identify OHT patients who require closer monitoring. **Methods:** This hospital-based, cross-sectional case-control observational study was conducted from February 2021 to January 2022. We included patients aged 40 years and older with Best Corrected Visual Acuity (BCVA) of 6/12 or better, diagnosed with OHT, and age-matched normal controls. Swept-source optical Coherence Tomography (SS-OCT) was used for macular ganglion cell layer (GCC) analysis, and visual field assessment was done using Humphrey Field Analyzer 10-2 and 24-2. **Results:** A significant thinning of the macular ganglion cell layer was observed in the inferior and inferonasal sectors in the OHT group (68.75±3.67 µm and 69.71±3.33 µm, respectively), compared to the normal group (69.88±4.34 µm and 71.83±2.64 µm, respectively). This thinning may be an indicator of early RGC loss in OHT patients. **Conclusion:** Macular ganglion cell layer thinning, particularly in the inferior and inferonasal sectors, may serve as an early marker for identifying OHT patients at higher risk of glaucoma progression, requiring more vigilant follow-up.

INTRODUCTION

Ocular hypertension is defined as elevated intra-ocular pressure of more than 21mmHg on two or more occasions along with normal open anterior chamber angle, absence of glaucomatous optic nerve changes or retinal nerve fibre layer defects and the absence of visual field abnormalities.[1][2][3] The worldwide prevalence of ocular hypertension varies between 0.32-12.2% in those older than 40 years of age. [4][5][6][7][8][9][10] Over 10% of these patients would develop glaucoma without any intervention in the following 5 to 10 years. [11] As glaucoma is a major cause of irreversible blindness and is the second most common cause of blindness in the world therefore it is essential to identify patients of OHT who are at high risk of conversion to primary open-angle glaucoma.[13][14]

Despite the known risk factor model of the Ocular hypertension treatment study, it is often challenging for ophthalmologists to decide on a follow-up schedule for these patients based on these risk factors.[3][15][16][17] Reduction of intraocular pressure has proven to be beneficial in delaying POAG onset and progression, however, treatment of all OHT patients is not justified because of its high prevalence, low conversion rate to glaucoma; cost and possible adverse effects of the treatment. Therefore, it is important to identify predictive factors for its conversion to POAG so that we can identify those OHT patients who might benefit from close observation and early treatment.[3][18][19][20][21]

Various changes in glaucoma occur secondary to the loss in the ganglion cells and their respective axons, which comprise the retinal nerve fibre layer (RNFL).[12] Visual field evaluation is dependent on subjective responses and patient cooperation and gives positive results only when 30% or more optic nerve fibres are damaged in glaucoma. [22][23]. As the highest concentration of retinal ganglion cells i.e., more than 30 %, are in the macula, for early detection, this area seems to be most appropriate to be investigated.[24] SS-OCT may help detect early ganglion cell loss in OHT by measuring ganglion cell layer thickness (GCC parameter at macula) to predict patients who may need close follow-up in future.

DOI: 10.69605/ijlbpr_13.10.2024.X

MATERIAL AND METHODS

It is a Tertiary eye care hospital-based cross-section, case-control observational study conducted from 01 February 2021 to 31 January 2022,to study retinal ganglion cell (RGC) layer thickness at the macula in Ocular Hypertension and normal patient.

Ocular hypertension was diagnosed as a patient having anIOP of more than 21mmHg on two or more occasions and the control group having a normal IOP of less than 20mmHg, with an absence of optic disc or visual field changes in both the groups. Patientswere included from OHT and normal groups based on the following inclusion and exclusion criteria. Patients included of age 40 years and above, withbest corrected visual acuity (BCVA) 6/12 or better who were willing forparticipate. This study excluded participants with ocular pathologies such as close angles on gonioscopy, history of any intra-ocular surgery, refractive error > +/-5.0D,and media opacities, that might bias retinal ganglion cell thickness or visual field assessment.Informed written consent was taken in each case regarding the purpose of the study and for the publication of data thereafter, as per Helsinki guidelines

A complete ophthalmic glaucoma workup including:

- Humphrey visual field analyzer (SITA 24-2 and 10-2)
- Swept-source OCT (DRI OCT 1 Std. version 9.3) for macular ganglion cell layer assessment was done.

RESULTS

A totalof96 eyes of 48 patients were included in the study and classified into two groups, 48 eyes each with ocular hypertension (group 1) and normal patients (group 2) respectively.

Table 1: number of eyes in each sector with macular ganglion cell layer thinning (group 1)

Sectoral distribution of macular ganglion cell layer thickness	Number of eyes with MGC layer thinning noted in each sector
Supero-temporal	1
Superior	2
Supero-nasal	3
Inferotemporal	6
Inferior	6
Infero-nasal	5

Table 2a: sector wise distribution of GCC layer thinning noted in 8 eyes of patient of group1(OHT) using SS-OCT

8 eyes of the patient with GCC layer thinning noted	Sector-wise distribution of GCC layer thinning present (+)					
	ST	S	SN	IT	I	IN
1	-	-	-	+	+	-
2	-	-	-	+	+	+
3	-	-	-	+	+	+
4	-	-	-	+	+	+
5	-	-	+	-	+	+
6	-	-	-	-	+	+
7	+	+	+	+	-	-
8	-	+	+	+	-	-

Table 2b: Total number of sectors per eye of OHT patient thinning noted in GCC thickness map

Total Number of sectors per patient thinning noted in the GCC thickness map	Number of eyes
0	**40**
1	**0**
2	**2**
3	**5**
4	**1**
5	**0**
6	**0**

(Tables 1 and 2): 8 out of 48 eyes of ocular hypertensive patients had thinning in their SS-OCT GCC layer thickness scan, i.e., 16.67% of eyes had abnormal thinning present whereas 40 eyes had normal macular GCC thickness scan (83.3%). As shown in Tables1 and2a in most of the eyes retinal ganglion cell layer thinning was

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noted in the inferotemporal, inferior and inferonasal sectors (6, 6 and 5 eyes respectively) and as shown in Table 2b out of the 8 eyes with thinning noted 5 eyes had 3 sectors involved in GCC layer thickness map.

Table 3: Intergroup comparison of mean Ganglion layer thickness in different sectors

SN	Sectors	Group 1		Group 2		ANOVA	
		Mean	SD	Mean	SD	F	P
1	Supero-temporal	71.23	3.48	70.52	2.10	0.819	0.443
2	Superior	71.00	3.66	70.56	2.33	1.855	0.160
3	Supro-nasal	71.06	3.97	71.56	2.26	0.551	0.577
4	Inferotemporal	70.56	4.20	70.56	2.04	0.026	0.975
5	**Inferior**	68.75	3.67	69.88	4.34	3.158	0.046
6	**Infero-nasal**	69.71	3.33	71.83	2.64	20.877	<0.001

(Table 3) Statistically, there was no significant difference present in the mean retinal ganglion cell layer thickness in the supro-temporal, superior, superonasal, and inferotemporal sectors between the two groups (OHT and normal), however, a statistically significant thinning was noted in the inferior (68.75±3.67 u) andinferonasal (69.71±3.33 u) sector in group 1when compared to group 2(normal) (69.88±4.34 u) (71.83±2.64 u) with P value <0.05 and 0.001 respectively.

DISCUSSION

Macular-ganglion cell complex and ocular hypertension

The present cross-sectional study was conductedto study retinal ganglion cell (RGC) layer thickness at the macula in Ocular Hypertension and normal patient. Zimmer et al [25] were the first to suggest imaging of the macula as a potential location for glaucoma evaluation. Mwanza JCet al [26] conducted a study to analyze the diagnostic efficacy of macular ganglion cell-inner plexiform layer (GCIPL) thickness to discriminate normal eyes and eyes with early glaucoma. They observed that the ability of macular GCIPL parameters to discriminate normal eyes and eyes with early glaucoma is high and is comparable to that of the best peripapillary RNFL and ONH parameters.

In the present study, there was a statistically significant thinning ofthe RGC layer in theinferior and inferonasal sectorsin patients of OHT as compared to normal patients (*68.*75±3.67u*vs.* 67.71±4.60 u) (69.71±3.33u*vs.* 67.92±2.91 u, respectively). RGC layer thinning was found in 8 out of 48 eyes of ocular hypertensive patientsin various sectorsi.e., 16.67% of eyes had abnormal thinning present. Jung *et al.*[27]in their study also noted significant thinning in inferonasal inferotemporal ganglion cell–inner plexiform layer (GCIPL). Zhang *et al.*[28] studied the relationship between macular ganglion cells and inner plexiform layer thickness and estimated macular retinal ganglion cell (RGC) counts in glaucoma. It was reported the average estimated macular RGC count in glaucomatous eyes was significantly lower as compared to healthy eyes. Glaucomatous eyes had 41% fewer estimated macular RGCs than healthy eyes and suspect 21% fewer. There was a strong correlation between estimated macular RGC counts and mGCIPL thickness.

Donald C. Hood et al [29] stated glaucomatous damage to the macula is common and can occur early in the disease.Macular damage is typically arcuate and often associated with local RNFL thinning in a narrow disc region, which we call the macular vulnerability zone (MVZ). According to their schematic model of macular damage, most of the inferior region of the macula projects to the MVZ, which is located largely in the inferior quadrant of the disc, a region that is particularly susceptible to glaucomatous damage.

Visual field 10-2, 24-2 and macular ganglion cell thickness

The visual field 10-2 and 24-2 in all the patients included in our study were normal. This study does notattempt to correlate VF and macular ganglion cell layer changes however following studies found a correlation between the two in early glaucoma. Ji-Woong Lee et al [30] studied the relationship between central visual field sensitivity and macular ganglion cell/inner plexiform layer thickness in glaucoma. In their study, 10-2 VF test points demonstrated correlations with GC/IPL thickness in localized arcuate patterns mostly limited within the central 4.8×4.0 mm measurement ellipse. They concluded macular OCT/VF relationships have localized arcuate characteristics in the central region of the macula. Grillo et al [31] in 2016 determined that the 24-2 visual field test misses central macular damage confirmed by the 10-2 visual field test and optical coherence tomography. The study concluded that eyes with macular glaucomatous damage may be classified as normal based on the 24-2 VF alone.Behzad Fallahi, Motlagh; Ali Sadeghi [32]in their study found a correlation between macular thickness and visual field in early open-angle glaucoma. Seeing the results of these studies we may presume that our patients who had significant ganglion cell layer thinning present may progress to having glaucomatousfield changes inthe near future.

CONCLUSION

In this study,8 out of 48 eyes of ocular hypertensive patients had thinning in their SS-OCT GCC layer thickness scan (16.67%). A statistically significant thinning was seen in the inferior and infero-nasal

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sectors. Based on the above discussion we feel that ganglion cell layer thinning may form a criterion to identify patients of OHT who are at risk of conversion to glaucoma and therefore require a more vigilant follow-up.

Financial Support
No financial support was provided for this study.

Abbreviations Used
RGC – Retinal Ganglion Cells
OHT – Ocular Hypertension
SS-OCT – Swept-Source Optical Coherence Tomography
BCVA – Best Corrected Visual Acuity
HFA – Humphrey Field Analyzer
GCC – Ganglion Cell Complex
VF – Visual Field
RNFL – Retinal Nerve Fiber Layer
POAG – Primary Open-Angle Glaucoma
GCIPL – Ganglion Cell-Inner Plexiform Layer
ONH – Optic Nerve Head
MVZ – Macular Vulnerability Zone

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