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Comparison of Ganglion Cell Complex in Glaucoma Patients and Non-Glaucomatous Healthy Volunteers

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ABSTRACT

Background: Glaucoma is the leading cause of irreversible blindness globally. In developing nations like India, the loss of vision or visual handicap due to glaucoma is substantial. The best strategy is early diagnosis and treatment of glaucoma. The Fourier Domain OCT(FD-OCT) is a useful tool in the pre-perimetric or early diagnosis and follow up of glaucoma. The measurement of the Ganglion Cell Complex (GCC) parameters is valuable in glaucoma. **Methods:** We undertook the present study on a FD-OCT to compare the Ganglion cell complex in 50 eyes each of established primary open angle glaucoma patients (Group A) and non-glaucomatous healthy volunteers (Group B). In all the candidates, the Ganglion Cell Complex evaluation was done by Fourier- Domain Optical Coherence Tomography. Only images with Signal Strength Index of more than 45 were used. All the subjects included in the study were >40 years of age. **Results:** Using independent t-test the difference between both the glaucoma and non-glaucomatous groups was found to be highly significant for all the GCC parameters. The focal loss of volume (FLV) %was 3.692±3.533 in the glaucoma eyes and 0.856±1.211 in the non-glaucomatous eyes, p<0.0001. The global loss of volume (GLV)% or diffuse loss of volume was 13.849±8.485 for the glaucoma group and 2.031±1.681for the healthy eyes (p<0.0001). **Conclusion:** This clearly demonstrates that the GCC plays a vital role in the diagnosis and follow-up of all cases of glaucoma and cases suspected of having glaucoma

Keywords: FD-OCT, GCC, GLV, FLV, VHS.

INTRODUCTION

In India, an estimated 12 million people suffer from glaucoma, while 1.5 million are blind due to it. More than 75% of glaucoma are undiagnosed.[1] Glaucoma is the leading cause of irreversible blindness in the world.[2]

The role of FD-OCT for the early diagnosis and follow-up of glaucoma is well established. The Ganglion Cell Complex can give additional and valuable information in patients of glaucoma. Perimacular GCC parameters could be useful and added to peripapillary retinal fibre layer thickness (RNFL) measurements for diagnosis in patients of normal tension glaucoma.[3]

The advantage of Optical coherence tomography (OCT) is that it gives objective, quantitative, and reproducible measurements of the ganglion cell complex (GCC) and retinal nerve fiber layer (RNFL) thickness.[4] Fourier-domain (FD)-OCT has resolution power up to 5 µ in measuring the average RNFL thickness, offering a marked advantage in the early detection of glaucoma and in the objective Assessment of progression of glaucomatous damage.[5]

We conducted the first study of its kind in our tertiary care institute on the comparison of Ganglion Cell Complex (GCC) in glaucoma patients and non-glaucomatous healthy volunteers.

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MATERIALS AND METHODS

The present study was conducted using the Fourier-Domain Optic Coherence Tomography (RTVue-100).

A total of 100 consecutive eyes were assigned into two groups:

Group A: 50 eyes of 33 patients of Primary Open Angle Glaucoma randomly selected from patients visiting the Glaucoma Unit of the Regional Institute of Ophthalmology, Pandit Bhagwat Dayal Sharma, Post Graduate Institute of Medical Sciences, Rohtak.

Group B: 50 eyes of 35 non-glaucomatous age and sex-matched healthy volunteers were also enrolled in the study.

Informed consent was taken from all candidates enrolled in the study.

Inclusion Criteria:

1. **Group A:-** Established cases of Primary Open Angle Glaucoma fulfilling the following criteria: Open anterior chamber angle, glaucomatous Visual Field loss (defined as a Pattern Standard Deviation [P<0.05] or Glaucoma Hemi field Test result [P<0.01] outside the normal limits in a consistent

pattern on three qualifying Visual Fields, optic nerve head changes such as diffuse or localized rim thinning, disc (splinter hemorrhage), notch in the rim, vertical cup disc ratio more than fellow eye by more than .2 or previous photographic documentation of progressive excavation of the disc, progressive thinning of neuroretinal rim or Nerve Fibre Layer defects visible on slit-lamp bio microscopy, or progressive loss of Nerve Fibre Layer, corrected intraocular pressure >21 at presentation.

2. **Group B:-** Both eyes had corrected intraocular pressure of less than 21 mm of Hg, normal visual fields as obtained using Humphrey Swedish Interactive Thresholding Algorithm 30-2 [Defined as having a Mean Deviation and Pattern Standard Deviation within 95% limits of normal reference and glaucoma hemi field test results within 97% limits], an open anterior chamber angle, a normal appearing optic nerve head, a normal nerve fibre layer and no history of ocular disease, surgery or systemic corticosteroid use. .

Exclusion Criteria:

Following patients were excluded from present study

- History of any ocular disease or intraocular surgery.
- Coexisting retinal disease or non-glaucomatous optic atrophy.
- Corneal abnormalities.
- Myopia of > -6D or Hypermetropia of >3D.
- Age less than 40 or more than 79 years.
- Cataractous Lens.
- Diabetes mellitus.

❖ The work-up of the candidates included detailed history taking and clinical examination, visual acuity, CCT, tonometry, gonioscopy, automated perimetry, direct ophthalmoscopic examination and Ganglion Cell Complex evaluation by Fourier- Domain Optical Coherence Tomography.

In the current study, only images with Signal Strength Index of more than 45 were used.

Ganglion Cell Complex:

It was evaluated using software version 4.0. We devised 3-dimensional scans of the macular region called the Ganglion Cell Complex scan that samples the macula with 14,928 a-scans over a 7-mm square area in 0.6 seconds. We chose to limit the scan time to 0.6 second to reduce the problems of eye movement and corneal drying associated with long scan time. The scan pattern consisted of 1 horizontal line and 15 vertical lines at 0.5-mm intervals. The center of the Ganglion Cell Complex scan was shifted 0.75 mm temporally to improve sampling of the temporal periphery.

The results within both the groups were analyzed using Graph pad prism version 5 and SPSS 17.

RESULTS

In the present study, mean age of the patients in Group A was 51.78 ± 1.36 years (range 40-71 years), mean age of patients in Group B was 50.86 ±1.199 years (range 40-72 years).

There were 46% males and 54% females in Group A and 54% males and 46% females in Group B.

Signal Strength Index of Retinal Nerve Fibre Layer of Group A and Group B was 53.56 ± 10.137 and 61.838 ± 11.436 respectively.

[Table 1] shows comparison between GCC parameters of Group A and Group B. Using independent t-test the difference between both the groups was found to be very highly significant for all the parameters except for SD.

Table 1: Comparison of Ganglion Cell Complex (GCC) Parameters between Group A and Group B

Parameters	Group A (Mean ± SD)	Group B (Mean ± SD)	p-Value
Average (µm)	85.36 ±9.385	103.2±5.420	<0.0001 (VHS)
Superior (µm)	85.32±10.170	102.7±5.590	<0.0001 (VHS)
Inferior (µm)	85.37±10.198	103.8±6.145	<0.0001 (VHS)
FLV %	3.692±3.533	0.856±1.211	<0.0001 (VHS)
GLV %	13.849±8.485	2.031±1.681	<0.0001 (VHS)
SD	5.210 ± 5.899	3.285± 3.959	0.058 (NS)

Table 2: Area Under Receiver Operating Characteristic Curve (AROC) of Ganglion Cell Complex (GCC)

Parameters	AROC Area	Standard Error	p-Value	Sensitivity	
				Specificity >85%	Specificity >95%
GCC Average	0.9822 (0.958-1)	0.01019	<0.0001 (VHS)	96	94
GCC Superior	0.966 (0.936-0.996)	0.01519	<0.0001 (VHS)	92	86
GCC Inferior	0.9704 (0.943-0.998)	0.01415	<0.0001 (VHS)	96	86
FLV	0.813 (0.728-0.899)	0.044	<0.0001 (VHS)	62%	46%
GLV	0.986 (0-1)	0.009	<0.0001 (VHS)	98%	96%
SD	0.588 (0.475-0.701)	0.058	0.129 (NS)	30%	6%

[Table 2] shows AROC of GCC parameters in Group A and Group B. Among AROC of GCC parameters, average, superior and inferior GCC were very highly significant. FLV and GLV were also very highly significant. AROC of GLV was highest.

In Group A mean ± SD of average, superior and inferior Ganglion Cell Complex thickness were 85.36±9.385 µm, 85.32±10.17 µm, 85.37±10.198 µm respectively and in Group B mean average, superior and inferior Ganglion Cell Complex thickness were

103.2±5.42 µm, 102.7±5.59 µm, 103.8±6.145 µm respectively.

Comparison of Ganglion Cell Complex thickness in Group A (POAG) and Group B (Control) shows a very highly significant p-Value (<0.0001). The results were consistent for average, superior, & inferior Ganglion Cell Complex thickness.

Area Under Receiver Operating Characteristic Curve ± standard error of average, superior and inferior Ganglion Cell Complex were 0.982±0.01, 0.966±0.015, 0.97±0.014 respectively.

In Group A mean ± SD of Focal Loss Volume, Global Loss Volume and Standard Deviation were 3.692±3.533, 13.849±8.485, 5.210 ± 5.899 respectively and in Group B mean ± SD of Focal Loss Volume, Global Loss Volume and Standard Deviation were 0.856±1.211, 2.031±1.68, 3.285 ± 3.959 respectively.

Comparison of Focal Loss Volume and Global Loss Volume in Group A and Group B shows a very highly significant difference (p-Value <0.0001).

Comparison of Standard Deviation between both the groups shows no significant difference.

Area Under Receiver Operating Characteristic Curve ± standard error of Focal Loss Volume, Global Loss Volume and Standard Deviation were 0.813 (0.728-0.899), 0.986 (0-1), 0.588 (0.475-0.701) respectively. The Area Under Receiver Operating Characteristic Curve of Standard Deviation was not significant.

In the present study among the Area Under Receiver Operating Characteristic Curve of Retinal Nerve Fibre Layer thickness parameters, Optic Nerve Head parameters and Ganglion Cell Complex parameters, Global Loss Volume had the greatest Area Under Receiver Operating Characteristic Curve. This is in accordance with the study done by Tan O et al and Kim NR et al which signifies the importance of measuring Ganglion Cell Complex in POAG patients.[6,7]

Study done by Rao H et al Seong M et al and Mori S et al shows Area Under Receiver Operating Characteristic Curve of Ganglion Cell Complex parameters equal to or little lower than Area Under Receiver Operating Characteristic Curve of Retinal Nerve Fibre Layer thickness.[8-10]

The higher value of Area Under Receiver Operating Characteristic Curve of Ganglion Cell Complex parameter in the present study can be contributed to use of more advanced software version in the present study (previous studies were conducted using software version 1 to 3 in which photographers did not look for signal strength or segmentation error because the processing software was not available at that time).

In the current study we used software version 4 which has automated segmentation and we have only taken Signal Strength Index of >45.

DISCUSSION

This study was designed with the major objective of evaluating the association between Ganglion Cell Complex (GCC) of patients with Primary Open Angle Glaucoma (POAG) and a healthy Control Group. We found this association to be significant, emphasizing the role and significance of GCC in cases of glaucoma.

Ganglion cell damage occurring in glaucoma leads to thinning of Ganglion Cell Complex. With the help of Fourier-Domain Optical Coherence Tomography it possible to measure Ganglion Cell Complex, which shows a racial variation and various values may be specific to the population under study. Ganglion Cell Complex is also affected by age. Fourier-domain Optical Coherence Tomography gives age and race adjusted value.

Among the Ganglion Cell Complex parameters Global Loss Volume (GLV) had highest Area Under Receiver Operating Characteristic Curve. This is in accordance with the study done by Tan O et al and Kim NR et al,[6,7] which signifies the importance of measuring Ganglion Cell Complex in POAG patients.

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The higher value of Area Under Receiver Operating Characteristic Curve of Ganglion Cell Complex parameter in the present study can be contributed to use of more advanced software version in the present study.

CONCLUSION

FD-OCT has proved to be a useful tool in the early diagnosis of glaucoma to prevent blindness. Thus Ganglion Cell Complex parameters are a very good tool for the diagnosis of glaucoma. We evaluated the association between Ganglion Cell Complex (GCC) of patients with Primary Open Angle Glaucoma (POAG) and a healthy Control Group. We found this association to be significant, emphasizing the role and significance of GCC in cases of glaucoma.

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