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Case Study

Comparative evaluation of Optical Coherence Tomography (OCT) with Pattern Reversal Visual Evoked Potential (PRVEP) in early primary open angle glaucoma

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Abstract: Present study is to correlate the average retinal nerve fiber layer (RNFL) thickness and the visual function evaluated by electrophysiologic retinal and cortical responses assessed in primary open-angle glaucoma (POAG) eyes by a Case-control study. One hundred and sixty-one control and glaucoma patients (mean age, 55.18±5.19 years for study group and 54.45±4.81 years for control group) were selected in the study**.** Average Retinal Nerve fiber layer thickness was measured by optical coherence tomography. Retinal and visual pathway function was assessed by simultaneously recording pattern reversal visual evoked potentials (PRVEPs) Linear regression analyses were adopted to establish the correlation between average RNFL thickness and PRVEP parameters. Average Retinal Nerve fiber layer thickness were taken. PRVEP, P100 latency and N75-P100 amplitude were also measured. In POAG eyes, we found a significant ($P< 0.01$) reduction in average RNFL thickness with respect to the values observed in control eyes. PRVEP parameters showed a significant ($p< 0.01$) delay in p100 latency and reduced N75 p100 amplitude. Positive correlations between average RNFL values and PRVEP parameters were found. There is a positive correlation between PRVEP changes and average RNFL thickness, in POAG patients.

Key words: Pattern Reversal Visual Evoked Potential; Optical Coherence Tomography; Primary Open Angle Glaucoma

Introduction

Glaucoma is fast emerging as a major cause of blindness in India second only to cataract [1]. 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 characteristic subjective visual field abnormalities and manifests by cupping and atrophy of the optic disc [2]. The damage results either from the direct mechanical effects of high intra – ocular pressure (IOP), from compromises to the vascular supply or from a combination of these and other factors.(3) Anatomical studies have documented that visual field defects usually develop only after the loss of 30% - 50% of ganglion cells. (4)

Optical coherence tomography (OCT) is a noninvasive technique that allows cross – sectional imaging of the retina and quantifies the thickness of the retinal nerve fiber layer (RNFL) around the optic nerve head. The degree of RNFL thickness reduction has been shown to correlate with visual field defects(5). OCT has been used successfully to capture retinal ganglion cell axon loss in early glaucoma and in other forms of anterior visual pathway disease, including traumatic optic neuropathy, chiasmal lesion, and acute optic neuritis. (6)

Recording the spontaneous electrical activity of the brain from electrodes placed on the scalp has been a clinical practice for many years now. The visual evoked potential (VEP) is one of several evoked potentials that can be recorded from scalp electrodes. It is well acknowledged that VEPs are useful for investigating the physiology and pathophysiology of the human visual system, including the visual pathways and visual cortex [7].

The pattern visual evoked potential (VEP) has been shown to be sensitive to optic nerve lesions caused by demyelinization, ischemia, and compression of the anterior visual pathway. Glaucoma has also been reported to affect the VEP by causing both reductions in amplitude and increases in latency. Increased pattern VEP latency has been associated with optic disc cupping and the presence of visual field loss [8].

Electrophysiological methods may also be used to identify early structural and functional damage in

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glaucoma. Over the past few years patients with early – stage glaucoma have been evaluated for abnormalities using electrophysiological tests, including different form of electroretinography (ERG) and visual evoked potential (VEP). [4]

Pattern reversal visual evoked potential provides an objective and sensitive readout of the function of retinal ganglion cells (RGCs), and the latency of P100 can be used as a measure of early glaucomatous damage before RGCs death. [9]. The purpose of this study is to compare the Optical Coherence Tomography and Pattern Reversal Visual Evoked Potential in the detection of early changes in optic nerve fiber in a patient with early cases of primary open angle glaucoma. To prevent irreversible structural and physiological damage in patient of glaucoma by detecting as early as possible.

Objective

- To assess the changes of P100 latency and amplitude in primary open angle glaucoma (POAG).
- To assess the changes in the thickness of RNFL.
- To compare the findings of OCT & PRVEP.

Materials and Methods

This study was conducted on early cases of Primary Open Angle Glaucoma patients attending the Ophthalmology OPD of Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha. Detailed history and eye examination was done by expert Ophthalmologist. Total 161 subjects were selected for the study and both OCT and PRVEP test was performed after consent of the patient was obtained.

Type of study: Case-Control Study Design.
Inclusion criteria:

A. Age 40 to 60 years and both genders.
B. Suspected cases of glaucoma patients present with
   1. Maximum Intra Occular Pressure(IOP)> 21 mmHg
   2. Suspected glaucomatous disc changes (Neuro-retinal rim damage)
   3. Glaucomatous early field defect
   4. Open angle at Gonioscopy

Exclusion criteria: Exclusion criteria for participation in this study includes

1. Secondary or angle closure glaucoma
2. Hazy media (corneal or lenticular opacities)
3. Optic neuritis
4. Disease involving macula or retina
5. High myopia
6. Diabetes mellitus
7. Previous intraocular surgery
8. Multiple sclerosis and parkinsonism disease
9. Neuromuscular transmission disorders, Nystagmus

Sample Size Estimation

Sample size was calculated on the basis of P100 latency correlation factor in the study of Kothari R, Bokaria P, Sing R, Sing S, Narang P (r = 0.187)" [10]

$N = [Z\alpha + Z\beta / C]2 + 3$
$C = 0.5 \log [C1 + r / 1\text{-}r]$
$= 0.5 .\log [1+ 0.187 / 1- 0.187]$
$= 0.31$
$N = [0.84 + 1.96 / 0.31]^2 + 3$
$N = 84.54 \sim 85$

Optical Coherence Tomography (OCT)

RNFL thickness in Primary Open Angle Glaucoma (POAG) was calculated by HD-CIRRUS-SD-OCT 500, Software version -3.0, Carl Zeiss Meditec, Dublin, CA.

Procedure for OCT

Patient needs to be in sitting position with chin kept on chin rest. Patient asked to focus on green light inside machine. Each eye is tested individually. Atleast 3 scans were taken for each eye and best of 3 scans was taken as reading or scan with score >7 out of 10 will be considered.

Procedure for pattern reverse VEP recording

1. The patient was seated comfortably at a distance of 1 meter away from the screen of the VEP monitor so that accommodation of eye is relaxed.
2. The source of light was stimulus. Standard disc EEG electrodes will be placed on the scalp areas after preparing the skin by spirit with a conducting jelly or electrode paste rubbed lightly into the area with a cotton swab.
3. As per 10-20 International System of EEG placements, the reference electrode (Fz) was placed 12 cm above the nasion, the ground electrode (Cz) at the vertex and the active electrode (Oz) at approximately 2 cm above the inion.
4. After controlling all factors that influence the VEP pattern, the subject was instructed to close one eye with his hand without any pressure on the eye and to fixate his other eye on a small red dot at the centre of the screen of the VEP monitor, on which black and white checker board pattern is generated full field and reversed at a rate of 1/sec.
5. The recording was done monocularly for the left and right eyes separately.
6. At the viewing distance of 100 cm the check edges subtended 15 degree of visual angle.
7. Low frequency cut-off filter set was at 1-3 Hertz and the high frequency cut-off filter set at 100- 300 Hertz.
8. The sensitivity was kept at 2μV. The luminance of the white areas was 80 cd /m2 with a contrast of at least 75% compared to black squares.

9. The sweep duration was maintained between 250 ms to 500 ms. Responses to 200 stimuli were amplified and averaged for each eye, which were then analyzed by inline computer having automatic artifact rejection mechanism.
10. At least two trials for each eye were obtained and superimposed on one another to ensure replicability of the VEP pattern.
11. The absolute latencies of the peaks of positive wave P100 and the negative waves N75 and N145 was recorded.
12. The amplitude of P100 was measured from the preceding negative peak N75 to the peak of P100 and the latency is the time from stimulus onset to the peak of each component were considered in the test.
13. The electrode impedance was kept below 5KΩ.
14. The test was recorded in air conditioned, sound proof and dark room in Central Electrophysiology Laboratory, Acharya Vinoba Bhave Rural Hospital (AVBRH) Sawangi (M) Wardha.
15. Visual evoked potential study was performed by using the Neuron Spectrum 5 machine

Statistical analysis

Statistical Analysis was done by using descriptive and inferential statistics using chisquare test, students unpaired t test and Pearsons' correlation coefficient and software used in the analysis were SPSS 20.0 version and GraphPad Prism 6.0 version and $p<0.05$ is considered as level of significance.

Risk factor: As it is non- invasive study there was no harm to the patients.

Results

The main demographic, clinical, and electrophysiologic data pertaining to control participants and POAG patients are reported in table 1, 2 and 3.

Table 1: Demographic Characteristics

	Study Group	Control Group	ϰ2-value
Age Group (yrs)			
40-49 yrs	10(12.35%)	13(16.25%)	
50-59 yrs	52(64.20%)	51(63.75%)	
60-69 yrs	18(22.22%)	16(20%)	1.51
≥70 yrs	1(1.23%)	0(0%)	P=0.67, NS
Total	81(100%)	80(100%)	
Mean±SD	55.18±5.19	54.45±4.81	
Gender			
Male	60(74.07%)	66(82.50%)	1.68
Female	21(25.93%)	14(17.50%)	P=0.19, NS

Maximum 64.20% of the patients in study group and 63.75% in control group were in the age group of 50-59 years and 22.22% in study group and 20% in control s group were in the age group of 60-69 years which is statistically not significant ($ϰ^2$-value=1.51, p-value=0.67) and 74.07% of the patients in study group and 82.50% in control group were males ($ϰ^2$-value=1.68, p-value=0.19).

Table 2: Mean Values and Standard Deviation of Electrophysiologic Parameters in Control Subjects and in Patients Affected by Primary Open-angle Glaucoma; Student's unpaired t test)

Group	NFL Thickness	p100 Latency	N75 p100 Amplitude
Study Group	63.90±10.70	108.39±3.66	3.33±1.13
Control Group	87.25±6.92	101.05±1.29	5.65±0.62
t-value	16.41	16.90	16.07
p-value	0.0001, S	0.0001, S	0.0001, S

In POAG eyes, we observed mean RNFL overall thickness of 63.90±10.70 and in control group it was 87.25±6.92 and this was significantly reduced when compared with those of controls (*t-value=16.41, p=0.0001*), mean p100 latency of 108.39±3.66 and in control group it was 101.05±1.29 which was significantly prolonged when compared with those of controls (*t-value=16.90, p=0.0001*) and mean N75 p100 amplitude of 3.33±1.13 and in control group it was 5.65±0.62 which was significantly reduced when compared with those of controls (*t-value=16.07, p=0.0001*).

Table 3: Linear Regression and Correlation between Electrophysiologic and Perimetric Parameters and average Retinal Nerve Fiber Layer in POAG

	Mean	Std. Deviation	N	Correlation 'r'	p-value
RNFL	63.90	10.70	81	-	-
P100 Latency	108.39	3.66	81	0.172	0.125, NS
N75 p100 Amplitude	3.33	1.13	81	0.031	0.783, NS

The correlation between average RNFL thickness and PRVEP parameters is shown in Table 3. In POAG eyes, the average RNFL thickness and p100 latency (r=0.172, p-value=0.125) and N75 p100 amplitude (r=0.031, p-value=0.783) values were positively correlated.

Discussion

In present study, we found that the latency of P100 was delayed and the amplitude of P100 was reduced in POAG patients when compared with that of control subjects, which is consistent with previous investigations reported in glaucoma patients in the past by Parisi *et al.,* [11], Bach [12],

Horn [13], Grippo *et al.,* [14], Tong [15], Vaegan and Hollows [16]. Previous electrophysiologic evidence [17,18,19] indicated that the impaired PRVEP responses observed in POAG patients could be ascribed to impaired neural conduction in the optic nerve and in the whole post retinal visual pathways as a consequence of the dysfunction of the innermost retinal layers.

The OCT readings are comparable to those previously observed in normal and glaucomatous eyes by several authors. [20] In our Primary open angle glaucoma patients, we observed a significant reduction in average NFL thickness and observed positive correlation between average RNFL values and PRVEP responses did not reach statistical significance.

The lack of correlation between average RNFL thickness and PRVEP responses could also be explained by considering that PRVEP responses depend on the magnitude and timing of afferent inputs to the visual cortex and result from both retinal activity and neural conduction along the post retinal visual pathways. [20]

Farzad Fatehi *et al.,* study shows that PRVEP sensitivity was superior at 81% and RNFL (75%) was thinner with severe onset and disease recurrence. In our study P100 latency sensitivity is 98.40% and RNFL sensitivity is 44%.

Conclusion

- Our results indicate that there is a positive correlation between PRVEP changes and average RNFL thickness in POAG
- This study concluded that PRVEP parameter, such as P100 latency is a better predictor of primary open angle glaucoma than average RNFL parameter of OCT.

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