STUDY OF PATTERN REVERSAL VISUAL EVOKED POTENTIAL (PR-VEP) IN PRIMARY OPEN ANGLE GLAUCOMA

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Abstracts: **Background & Objectives**: Glaucoma is characterized by an optic neuropathy, often associated with elevated intra occular pressure (IOP) leading to characteristic visual field defects and optic nerve head damage. Elevation of intraocular IOP is believed to cause pressure on the retinal nerve fibers bundles as they course into the optic nerve which alters the VEP waveforms. Pattern VEP has been shown to be sensitive to glaucomatous optic neuropathy since they are compatible with the functions of retinal ganglion cells. Aim of study is to compare pattern VEP in patients with POAG and in healthy controls to assess the utility of VEP in detecting cases of glaucoma. **Methods:** Study was done in 60 subjects (120 eyes). Group1: POAG (30 patients) & Group2: Controls (30 subjects). All underwent PR VEP investigation in the Dept. of Physiology, Govt.medical college,Bhavnagar. Latency and amplitude of N75, P100, N145 were recorded. Visual fields were assessed at Ophthalmology dept. Sir T hospital, Bhavnagar. The differences of PRVEP parameters among POAG and control groups were compared. **Results:** N75, P100, N145 latency was prolonged in all 60 eyes(100%) and P100-N75 amplitude was reduced in 56 eyes (93.33%) in group1. The Mean Deviation (MD) values and sLV in the POAG patients were negatively correlated with the latency time of P100. POAG has been found to affect the PR-VEP by causing both the reductions in P100 amplitude and increments in all latencies when compared with that of the control group. **Interpretation and Conclusion:** Our study advocates the use of PRVEP as an objective electrophysiological tool for detecting optic nerve pathology in POAG, because increase in latency times are significantly associated with optic nerve damage.

Key Words: primary open angle glaucoma, pattern reversal visual evoked potential, P100-N75 Amplitude, Latency.

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Introduction:

Primary open angle glaucoma is a widely prevalent eye disease affects more than 67 million people in the world and is the leading cause of irreversible blindness in the world.[1] It is the major cause of blindness second to cataract in India .[2] It is characterized by an optic neuropathy, often associated with elevated intra occular pressure (IOP) leading to characteristic visual field defects and optic nerve head damage.

Perimetry is the routine test used to see field defects in glaucoma patients and is most disliked by them because lot of concentration is needed and there are arrays of buttons to click upon and the results may be unreliable and contradictory.

VEP used primarily to measure the functional integrity of the visual pathway from retina via the optic nerves to the visual cortex. Pattern VEP has been shown to be sensitive to glaucomatous optic neuropathy since they are compatible with the functions of retinal ganglion cells. The elevation of Intra ocular pressure is believed to cause pressure on retinal nerve fibre bundles as they course into the optic nerve and cause damage to retinal ganglion cells/ axons and is associated with the loss of visual function, which alters VEP waveforms. [3] VEP techniques has potential to be a useful tool in the early detection of functional deficits in glaucoma and its longitudinal assessment.[4] As compared to perimetry, VEP can measure patient's ability to see accurately and objectively and correlate well with the structural changes in the retina and optic nerve head and it takes only 5-6 minutes.

Present study is conducted to compare pattern VEP in patients with Primary open angle glaucoma and in healthy controls to assess the utility of VEP in detecting and cases of glaucoma.

Material and Methods:

Participants :

After obtaining Ethical clearance from Institutional Review Board, study was carried out in 60 subjects. Participants was divided into 2 groups. Group1 :POAG patients (30 patients) & Group2: Controls (30 subjects). Subjects were recruited from Out patient department of Ophthalmology department, Sir T hospital, Bhavnagar. All participants were informed verbally about the nature of the study & written informed consent were taken before the study.

Inclusion Criteria:Group1 : POAG Patients exhibited Best corrected visual acuity <6/9, Maximum IOP >21 mmHg using Goldmann applanation tonometer, Open angle at gonioscopy, Glaucomatous optic nerve changes including diffuse or focal neural rim thinning & Enlarged cupping on fundus examination, Nerve fibre layer defects with corresponding glaucomatous visual field loss on automated perimetry.

Group2: Control subjects defined as having Best corrected visual acuity 6/6, Normal IOP <21 mmHg, Open angle at gonioscopy, Normal visual field with standard automated perimetry, Normal optic nerve head and retinal nerve fibre layer on clinical examination, Negative family history for glaucoma.

Exclusion Criteria: Secondary or angle closure glaucoma, Hazy media (corneal or lenticular opacities), Optic neuritis, Diseases involving macula or retina, High myopia (>6 diopters), Diabetes mellitus, Previous intra occular surgery ,Multiple sclerosis, Parkinson's disease.

Procedure:

Study was carried out by RMS EMG EP MK II computerized software, 4 channel instrument at neurophysiology lab, dept of Physiology, govt. medical college, Bhavnagar, manufactured by Recorders & Medicare Systems (P) Ltd. Each subject was briefed previously about the procedure to alleviate apprehension and assure full relaxation during the test. The subject was seated comfortably at a distance of 1 meter away from the screen of the VEP monitor, so that accomodation of eye is relaxed and ask them to wear optical corrections as necessary. Electrodes were placed on the scalp after preparing the skin by degreasing and a suitable conducting gel applied to ensure good, stable conduction. The scalp electrodes are placed in midline between the nasion and the inion and over the vertex as per 10-20 International system of electrode placement. Active electrode placed on the scalp over the visual cortex at Oz : approximately 2cm above the inion. Reference electrode : at Fz: 5-7 cm above the nasion & Ground electrode: at the scalp or wrist. After the preparation subject is instructed to close one eye with hand without any pressure on the eye and to fix another eye on a small red dot that appears at centre of the screen of the VEP monitor, on which black and white checker board pattern is generated full field at a reversal rate of 1.71/second. Size of checks :8 x 8, Luminance : 59 cd/sqm, Contrast level : 80%. The subject is instructed to avoid blinking as it produces muscle artefacts or any mental activity such as counting or thinking as these are found to decrease the latencies and increases the amplitude of waveform of VEP. The recording is done monocularly for the left and right eye separately. 2 recordings for each eye obtained to ensure replicability of the VEP pattern.

The Waveforms of VEPs: VEPs consists of a series of waveforms of opposite polarity. N75, P100, N145. The N denotation stands for a negative waveform, and the P denotation stands for a positive waveform. The number following the letter is the time in milliseconds of the average occurrence of the peak. Latency is the time it takes for the signal to travel to the visual cortex from the retina. Amplitude of P100 from the preceding N75 peak is measured. The amplitude or difference from the trough of N75 to the peak of P100 represents the strength of the signal reaching the visual cortex in relation to how many functional retinal ganglion cells are present. The difference in the right eye and left eye stimulation (inter-occular difference) is determined. N75 results from foveal stimulation and originates in Area 17. P100 originates in area 19. N145 reflects the activity of area 18.

Normal Values of parameters of P100 are: Latency (ms) :100, Amplitude (μv) :11, Duration (ms) :60

Visual fields of all POAG patients were assessed using the Octopus 900 field analyzer program. All patients had experienced the standard automated perimetry (SAP) examination at least two times and

the second SAP visual fields were chosen for the present study.

The standard indices Mean deviation (MD) i.e. index of global visual field damage and sLV i.e. index of localized visual field damage were considered in the study.

Statistical Analysis:

The data was transferred on Excel spreadsheet and descriptive analysis was expressed as mean ± standard deviation. All calculations were accomplished by using GraphPad InStat3 software (demo version). The comparison of mean differences was done by student's t test. Difference was considered statistically significant with P value <0.05.

Result:

Table 1: Characteristics of study groups

Characteristics	POAG patients	Controls
Age (Years)	62.16 ±9.266	62.26 ± 10.255
Gender(M/F)	24(80%)/6(20%)	24(80%)/6(20%)
IOP (mmHg)	26.05±3.654	16.26±2.365
Occipito-frontal circumference (cm)	55.12 ± 1.32	55.34 ±1.57

The general characteristics indicating age, gender, Intraoccular pressure **and occipito-frontal circumference of the POAG patients and control subjects are summarized in Table 1.** Which shows that male patients are more in number than females and high intraoccular pressure was present in glaucoma patient group than control group.

Table 2: **Comparison of** Parameters of **PR-VEPs** in **Study Groups**

Parameters	POAG	Control	p value	
N75 latency (ms)	83.24 ±7.140	73.65 ±9.76	<0.001	Statistically Significant
P100 latency (ms)	118.47 ±5.377	108.95 ±9.085	<0.001	
N145 latency (ms)	166.88 ±9.780	152.47 ±9.831	<0.001	
P100-N75 amplitude (µv)	2.828±1.622	5.383±3.436	<0.001	

Table 2 shows significantly prolonged all latencies and reduced p100 amplitude in PAOG patients than Controls.

Table 3: **Pearson Correlation Coefficient (r) of Various Parameters of PR-VEP In Relation To IOP of Study Groups**

Parameters	PAOG (r)	Control (r)
N75 latency (ms)	0.02595	- 0.0234
P100 latency (ms)	0.04841	0.1721
N145 latency (ms)	0.07638	-0.1889
P100-N75 amplitude (µv)	-0.2088	0.1474

Table 4: **Correlations between the visual field indices and the latency time and amplitude of P100 in POAG patients**

	Latency time (r value)	**Amplitude (r value)**
POAG MD(dB)	-0.08210	0.02083
POAG sLV(dB)	-0.19930	0.06375

Discussion: Primary open angle glaucoma (POAG) is the most common form of glaucoma in India **a**s reported in most of the prevalence studies in the country by Jacob et al [5], Das K et al [6], Dandona et al [7].

Glaucoma is a condition in which an elevation of intra ocular tension is believed to cause pressure on the retinal nerve fibers bundles as they course into the optic nerve and is associated with the loss of visual function; this is known to produce an alteration of the VEP waveforms. Demyelination of the optic nerve can result in increased latency **and**

compressive damage can typically reduce amplitude.[8]

About 20% to 30% of optic nerve fibers may have suffered permanent damage before there is any detectable visual field loss in glaucoma.[9,10] Several previous studies have pointed out that structural loss of retinal ganglion cells (RGC) precedes visual field (functional) impairment. This has led to an increasing interest in electrophysiological testing in glaucoma in the past few years.[11,12]

The present study found that the latency of **N75,** P100**, N145** was **significantly** delayed and the amplitude of P100 was **significantly** reduced **(< 0.01)** in POAG patients when compared with that of control subjects**. Our result** is consistent with previous investigations reported in glaucoma patients in the past by Parisi et al [13], Bach [14], Horn [2], Grippo et al [15], Tong [16], Vaegan and Hollows [17].

Furthermore, we found the MD values in the POAG patients were negatively correlated with the latency time of P100, which is in agreement with previous studies by Horn [2] **and Parisi et al** [13].

The routine techniques recommended to detect damage resulting from glaucoma include intraocular pressure measurement, optic disc evaluation and visual field testing. New technologies such as confocal scanning laser ophthalmoscopy (CSLO) and optical coherence tomography(OCT) have become available that provide quantitative, reproducible and objective measurements of the optic nerve head and retinal nerve fibre layer thickness.[18] But high cost currently precludes their generalized use. Threshold perimetry is time consuming, fatiguing for the patient and shows a significant learning defect.[19] As compared to all these tests Visual evoked potential is less time consuming, cost effective and objective test.

Conclusion:

The significant changes of glaucoma observed on Visual evoked potential we can conclude that t**he** impaired visual cortical responses **in** glaucoma patients can be revealed by electrophysiologica**l** method before the changes detected on perimetry. **V**isual evoked potentials provide alternate way to assess functional impairments in glaucoma. VEPs should b**e** use in academic institutions to objectively assess the integrity of the afferent visual pathway. Pattern VEP can be objective electrophysiological tool for monitoring patient with progression of optic nerve pathology in glaucoma patients. VEPs aid in the diagnosis of glaucoma in the clinical office setting.

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