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A study of pattern reversal visual evoked potentials in newly diagnosed hypertensive patients.

KEYWORDS

Hypertension, VEP, P100 Latency , P100 Amplitude

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ABSTRACT

Introduction: Neuronal dysfunction in hypertension with multifactorial etiology involves white matter involvement and strongly associated with presence of retinal micro vascular lesions. Cortical lesions associated with optic nerve damage and retinopathy leads to visual disturbances. VEPs are the potential changes recorded from the scalp in response to visual stimuli. Since optic nerve is considered to be the part of brain, its subclinical involvement is likely hypertension. It is in this connection the present study involving visual evoked potential was done to see if there was any change in functional integrity of visual pathways in hypertension. The aim of the study was to evaluate the visual evoked potential in newly diagnosed hypertensive patients who have not taken any antihypertensive drugs before.

Methods: 50 cases were selected based on inclusion and exclusion criteria and compared with age, sex matched 50 controls. Study was conducted after getting informed consent, by using the RMS equipment and VEP readings had been taken by standard procedure.

Results: Study showed significant delay in P100 latency when analysed through unpaired student t test having p100 latencies for right eye 101.47±4.98 with p value of 0.0004 and left eye 101.76±5.02 with p value of 0.007 substantiating prechiasmal lesion.

Conclusions: Statistically significant delay in p100 latency suggests that the development of hypertensive retinopathy subclinically, occurs in very early stages of Hypertension, which is not detectable on routine clinical examination. VEP can be suggested for screening in high-risk individuals to evaluate the functional integrity of visual pathway in hypertension and as a key to unravel the mystery of hidden Hypertensive Morbidity and Mortality.

INTRODUCTION

Hypertension acts as a **silent killer** many years before overt end organ damage is clinically apparent. Hypertension causes vascular endothelial changes including hyalinization leading onto demyelination and brain infarction. Joint National Committee (JNC) VIII in 2013, defines and classifies Hypertension according to the following criteria:

- Normal - SBP: less than 120mmHg, DBP: less than 80 mmHg.
- Pre-Hypertension - SBP: 120-139mmHg, DBP:80-89 mmHg.
- Stage 1 Hypertension – SBP: 140-159mmHg, DBP: 90-99 mmHg.
- Stage 2 Hypertension – SBP: ≥160mmHg, DBP: ≥100 mmHg.

Hypertensive end organ damage causes Hypertensive vasculopathy, Hypertensive nephropathy, Hypertensive heart diseases like left ventricular hypertrophy, angina pectoris, ventricular arrhythmia, atrial fibrillation, etc. and Hypertensive cerebrovascular damage such as stroke, ischemic infarction, lacunar infarctions, microangiopathic complications, white matter lesions, etc. [1]. Hypertensive retinopathy is a condition characterized by a SPECTRUM OF RETINAL VASCULAR SIGNS in people with elevated blood pressure.[2] Retinal micro vascular abnormalities related to elevated blood pressure reflects the severity and duration of Hypertension which is present from its very early stages.[3,4] Hence the importance of refining risk stratification strategies, to ensure reliable detection of Hypertension related end organ damage before it becomes symptomatic, becomes pertinent. Retina provides window to study human circulation. Retinal arterioles can be visualised easily and non-invasively and share similar anatomical and physiological properties with cerebral and coronary microcirculation.[5] JNC lists retinopathy as one of the several markers of target organ damage in Hypertension. Signs of mild Hypertensive retinopathy are more common than expected occurring in nearly 10-15% of the adult population.[6] Hypertensive retinopathy can be an indicator of other complications in Hypertension.

The Visual Evoked Potential (VEP) tests the function of the visual pathway. VEPs are most useful for testing optic nerve function especially anterior visual conduction

Disturbance.[7] Unilateral infarction of anterior visual pathway was revealed by neurological signs in patients with Hypertension remaining undetected for long time.[8]

Recently studies has shown that P1 latency of visual evoked responseis delayed in pre-eclamptic women. Since optic nerve is considered to be the part of brain, its subclinical involvement is likely hypertension.

Studies showed the Hypertension caused a significant increase of lipid peroxidation in brain and retinal tissues in which were determined as markers of lipid peroxidation and the mean latencies of VEP were significantly prolonged in Hypertensive groups when compared with control groups.[9,10]

VEPs are sensitive indicators of optic nerve dysfunction. Since visual loss is a serious complication of Hypertension, VEP is measured in an attempt to evaluate the optic nerve damage in patients with Hypertension remaining undetected. This study aims to assess Hypertensive retinopathy subclinically by VEP in newly diagnosed Hypertensive individuals.

MATERIAL & METHODS:

Newly diagnosed Hypertensive patients (according to JNC 8 classification of Hypertension) both male and female attending Hypertensive OPD in our hospital.

The present work was conducted on 50 patients newly diagnosed hypertensive age range of 20-50 years. The patients were randomly selected without any bias for age, sex, types control and duration of the disease with 50 matched healthy volunteers serving as controls.

Exclusion Criteria: 1. Patients with history suggestive of diseases involving heart, renal system, liver and respiratory system, significant anemia (as per WHO criteria), electrolyte imbalance or

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resting abnormal ECG were excluded from the study.

2. Patients with cataract, squint, retinopathy, glaucoma or opacification or visual acuity < 6/18 with corrective lenses.

METHODS: All subjects selected for the study were subjected to a standardized protocol comprising of history, clinical examination especially ophthalmic and other necessary investigations following which they underwent visual evoked potential (VEP) testing.

Precautions required before performing the test: Washing hair the night before and avoiding hair chemicals, oils and lotions. Ensuring adequate sleep on previous night. Test conducted with corrective lenses, if worn. Any medications that cause drowsiness and affect the size of pupil should be avoided. Physical and mental relaxation.

Equipment: Visual evoked potential (VEP) was recorded with an RMS equipment equipped with pattern-shift stimulator television screen, signal amplifier with filters, computer system for averaging.

VEP Recording: VEP test was performed in a specially equipped electro diagnostic procedure room (darkened, sound attenuated room). Initially, the subjects were made to sit comfortably approximately 100 cm away from the pattern-shift screen. Subjects were placed in front of a video monitor displaying black and white checkerboard pattern. The checks of alternate black/white to white/black were displayed at a rate of approximately two checks per second. Every time the pattern alternates, the subject's visual system generates an electrical response that was detected and recorded by surface electrodes, which were placed on the scalp overlying the occipital and parietal regions with reference electrodes on the midline of frontal region (Fz). The subjects were asked to focus his gaze onto the center of the screen. Each eye was tested separately (monocular testing).

Stimulation Pattern: The visual stimuli were checkerboard patterns (contrast 70%, mean luminance 50 cd/m2) generated on a video monitor and reversed in contrast at the rate of two reversals per second. At the viewing distance of 100 cm, the check edges subtend a visual angle of 15 minutes with video monitor screen subtending an angle of 12.5°. The refraction of all subjects was corrected for the viewing distance.

Electrodes and Electrode Placement: Surface electrodes were fixed with paste in the following positions: active electrode at Oz (which is highest point on the occiput), reference electrode at Fz or 12 cm above the inion, ground on the vertex at Cz. The bioelectric signal was amplified (gain 20, 000), filtered (band-pass, 1-100 Hz), and 150 events free from artefacts were averaged for every trial.

RESULTS

Stastistical analysis was done using software SPSS. Values were expressed as Mean±S.D. Comparisons were made between groups by unpaired 't' test. p-values < 0.05, was considered as significant.

Control Group- There were 50 controls in this group ranging from 20-50 years of,

Mean age - 46.96±6.13 years.
Mean BMI - 23.04±1.82
Mean systolic BP - 109.24±7.38mmHg.
Mean diastolic BP - 73.21±7.36mmHg.

Hypertensive Group- There were 50 newly diagnosed, untreated hypertensive patients in this group ranging from 20-50 years of,

Mean age - 47.12±5.76 years.
Mean BMI - 23.07±2.61.
Mean systolic BP - 146.45±14.18mmHg
Mean diastolic BP - 94.56±9.22mmHg

Table-1 VEP parameters among the age, BMI, systolic and diastolic BP among the study groups.

Parameters	Study group	Mean±sd	P-value
Age	Case	47.12±5.76	0.893
	Control	46.96±6.13	
BMI	Case	23.07±2.61	0.947
	Control	23.04±1.82	
SBP	Case	146.45±14.18	0.0001
	Control	109.24±7.38	
DBP	Case	94.56±9.22	0.0001
	Control	73.21±7.36	

Table-2 Comprision of VEP parameters among the case and controls.

VEP Parameters	Study Groups	Mean ± SD	P-value
P100 Latency Right eye	Case	101.47±4.98	0.0004
	Control	98.37±3.26	
P100 Latency Left eye	Case	101.76±5.02	0.0007
	Control	98.74±3.48	
P100 Amplitude Right eye	Case	6.49±3.53	0.204
	Control	7.68±5.56	
P100 Amplitude Right eye	Case	6.36±3.78	0.135
	Control	7.82±5.73	

DISCUSSION

Present study was focussed to find out Visual Evoked Potentials in 50 newly diagnosed Hypertensive individuals and the mean age 47.12±5.67 years and mean BMI 23.07±2.61.
Of the 50 newly diagnosed Hypertensive individuals, 22 were female and 28 were male.

Blood pressure measurement among the groups on Comparison revealed statistical differences (p=0.0001, p=0.0001) as the newly diagnosed Hypertensive individuals had mean systolic blood pressure 37.21±6.9 mmHg, diastolic blood pressure 21.35±2.76 mmHg more than the controls.

The activation of the primary visual cortex and also due to the discharge of the thalamocortical fibers. N70 reflects the activity of the fovea and the primary visual cortex while N145 reflects the activity of the visual association area. The P100 is a prominent peak that shows relatively little variation between the subjects, minimal within-subject interocular difference, and minimal variation with repeated measurements over time [11]. Therefore, this paper focused more on the values of P100 latency and P100 amplitude among the groups which were examined.

Visual Evoked Potential is a non-invasive procedure, in which the latency obtained, followed by stimulation of sensory modalities for vision principally reflects the activity generated in the optic pathway and the primary visual cortex in brain. The major component of VEP is the large positive wave peaking at about 100 milliseconds. This "P100" or "p1"in the jargon of Evoked Potentials is very reliable between individuals and stable from about 5 years to 60 years. The mean peak latency of the P100 only slows about 1 millisecond per decade from 5 years old until 60 years old.[12] The P100 latency of Hypertensive group was delayed significantly than that of the control group in our study. This proves to be of clinical significance because even the mean peak latency variation of 1 millisecond per decade has marked effect on the prediction of retinopathy changes. Lipid peroxidation in brain and retinal tissues were associated with electrophysiological alterations recorded as changes in VEP in Hypertensive group. Additionally plasma renin activity was proved to be higher in patients with Hypertension. Retinal vascular changes occur in Hypertensive retinopathy occurs even in pre-Hypertensive stage.[13] Signs of mild Hypertensive retinopathy are more common than expected occurring in nearly 10-15% of the adult population (Resch M, et al, 2013). In Hypertension, changes in small arteries

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structure are basically of two kinds:

1. Inward eutrophic remodelling in which outer and lumen diameters are decreased, media/lumen ratio is increased and cross-sectional area of the media is unaltered.

2. Hypertrophic remodelling, in which media thickens to encroach on the lumen, resulting in increased media cross-sectional area and media/lumen ratio.

Inward eutrophic remodelling is predominantly exhibited by mild essential Hypertensive patients, whereas hypertrophic remodelling predominates in severe Hypertension such as secondary Hypertension.[14] All these changes contribute to demyelination of optic nerve which is one of the vulnerable areas of brain, leading to abnormal p1 latency in VEP which corresponds to P100 latency.[15] Unilateral infarction of anterior visual pathway was revealed by neurological signs in patients with Hypertension remaining undetected for long time. Studies have proven difference in P100 latency of right and left eyes have a higher prediction for prechiasmatic lesion. Our study has significant P100 latency when analysed through Levene''s test for equality of variances having p100 latencies for right eye 4.19±0.4 with p value of 0.003 and left eye 5.30±0.02 with p value of 0.000 substantiating the prechiasmal lesion. This indicates the initial signs of Hypertensive retinopathy may appear before BP elevation above WHO reference limits occurs (Pietro cugini, et al, 1998).[16]

This study suggests that Hypertension affect neural conduction of visual pathway and leads to Hypertensive retinopathy. The delayed p100 latency of VEP can be used as a tool to detect subclinical Hypertensive retinopathy in newly diagnosed Hypertensive individuals who are not under anti-Hypertensive medication.

CONCLUSION

According to our study, we conclude that statistically significant delay in P100 latency suggest that the development of Hypertensive retinopathy subclinically, occurs in very early stages of Hypertension, which can be detected by VEP even before the onset of overt retinopathy. P100 latency difference highlights the involvement of prechiasma ensuring the possibility of detection of subclinical retinopathy through VEP. This helps to prevent the further complications of Hypertensive retinopathy and categorize the schedule for management.

There was some limitation to the experiment was the small sample size of 50 subjects. An increased sample size could decrease experimental error and uncertainty.

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