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Research Article

Pattern visual evoked potential in newly diagnosed hypertensive individuals

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ABSTRACT

Background: Neuronal dysfunction in hypertension with multifactorial aetiology 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 50 age, sex matched controls. Study was conducted after getting informed consent, by using the Medicaid polyrite instrument and VEP readings had been taken by standard procedure.
Results: Study shows 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 prechiasmal lesion.
Conclusions: Statistically significant delay in p100 suggests that the development of hypertensive retinopathy sub clinically, 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.

Keywords: Hypertension, VEP, Subclinical Retinopathy, Newly Diagnosed.

INTRODUCTION

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.

Epidemiology

Prevalence of pre-Hypertension is high among young subjects and stage 1, stage 2 Hypertension are high among older individuals.[1]

Throughout middle and old age blood pressure is directly related to vascular mortality, without any evidence of threshold down to at least 115/75 mmHg.[2] Age- sex specific prevalence of Hypertension showed progressive rise of systolic and diastolic Hypertension in women when compared to men. In participants above 40 years, SBP showed progressive increase up to eighth decade only in women. Only 58% of Hypertensive women and 52% of Hypertensive men were being treated with anti-Hypertensive drugs.[3]

Complications of Hypertension

Hypertension causes vascular endothelial changes including hyalinization leading onto demyelination and brain infarction. Such demyelination might lead to dementia through disconnection of subcortical-cortical association pathways.

Hypertension acts as a **silent killer** many years before overt end organ damage is clinically apparent. 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.[4]

Hypertensive retinopathy is a condition characterized by a SPECTRUM OF RETINAL VASCULAR SIGNS in people with elevated blood pressure.[5] Retinal micro vascular abnormalities related to elevated blood pressure reflects the severity and duration of Hypertension which is present from its very early stages.[6,7]

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.[8] 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.[9] 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.[10] Unilateral infarction of anterior visual pathway was revealed by neurological signs in patients with Hypertension remaining undetected for long time.[11] Recently studies has shown that P1 latency of visual evoked response is 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.[12,13]

- thiobarbituric acid- reactive substances (TBARS) and
- conjugated dienes (CD).

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.

Aim

The aim of the study was to evaluate the visual evoked potential (VEP) in newly diagnosed Hypertensive patients who have not taken any anti-Hypertensive drugs before.

Objectives

- To screen and diagnose the Hypertensive group in the age group 20-50 yrs.
- To exclude confounding factors.
- To evaluate VEP before the onset of medication for Hypertension.

METHODS

Study design: Observational
Type of study: Cross sectional study
Study site: Neurophysiology lab

Number of subject/samples

100 individuals with 50 each in Group I (case) and Group II (control) were considered.

Inclusion criteria

- Newly diagnosed Hypertensive patients (according to JNC 8 classification of Hypertension) both male and female attending Hypertensive OPD in our hospital.
- Age: 20-50 years.

Exclusion criteria

- Diabetes mellitus
- Hyperthyroidism
- Hypothyroidism
- Tuberculosis

- Acute respiratory illness
- Chronic obstructive pulmonary disease
- Spinal and chest wall deformities
- On medications confounding pulmonary functions
- Patients who have undergone chest surgeries
- Patients who are not cooperative
- Patients with Corneal Opacity
- Patients with Squint
- Patients with Glaucoma
- Patients with Cataract
- Patients with opthal surgeries
- Age: more than 50 years

Informed consent

Written and informed consent has been obtained from the subject in regional language (Tamil) as well as in English, as they are more than the age of 16.

Institutional ethical committee approval was obtained.

Material

By using MEDICAID POLYRITE instrument, VEP recordings are taken by standard procedure (Guideline 10, 2013).[14]

Procedure

Equipment set – up.

Montage

- Channel 1 –FPz – Reference Electrode
- Vertex – Cz- Ground electrode
- C – Oz – Active Electrode

Recording Condition

- Filter – high filter cut –100 – 300 hz.
- Amplification – 20,000 – 1,00,000
- Sweep duration – 300 msec
- Number of epochs – 100 are averaged
- Electrode impedence – Less than 5kΩ

Stimulation

- Black and white checker board will be used. Distance between subject and screen will be 100cms.
- Contrast – 80%
- Size of pattern – 14x16 minutes
- Rate of stimulation – 4-8Hz
- Mean luminance of central field 50 cd/m2
- Background luminance 20-40 cd/m2

Procedure

- The subject is asked to sit comfortably on a chair with their footwear.
- Each eye is tested separately.
- The other eye is kept covered with an opaque eye shield, which prevents the entry of light into that eye. The skin at the point of placement of the electrodes is cleansed with spirit.
- The electrodes were placed as per the Guidelines and then connected through the pre amplifier to the cathode ray oscilloscope.
- The subject is instructed to fix the gaze at the centre of the screen.
- The visual stimulus is delivered by photo stimulator at the frequency of 10 flashes/sec.

VEP Parameters

The following parameters were considered during the study:

- Latency of N 75ms
- Latency of P100ms
- Latency of N 145 ms
- Amplitude of P100 – N75 μV.

RESULTS

Statistical analysis has been done using SPSS software 16 version and the parameters has been analysed using student independent unpaired 't' test.

- $p<0.05$* is significant.
- $p<0.01$* is highly significant.

Control Group

There were 50 cases (32 female and 18 male) in this group ranging from 20-50 years of,

- Mean age - 44.06±6.336 years.
- Mean BMI - 22.10±1.619.
- Mean systolic BP - 111.20±7.183mmHg.
- Mean diastolic BP - 71.20±7.461mmHg.

Normal VEP waveform of the control group is shown in Figure 1.

Hypertensive Group

There were 50 newly diagnosed, untreated Hypertensive patients (32 female and 18 male) in this group ranging from 20-50 years of,

- Mean age - 44.08±5.907 years.
- Mean BMI - 22.18±2.919.
- Mean systolic BP - 144.60±14.172mmHg.

- Mean diastolic BP - 95.80±10.120mmHg.

Abnormal representative VEP wave pattern of Hypertensive group in which P100 latency is delayed is shown in Figure 2.

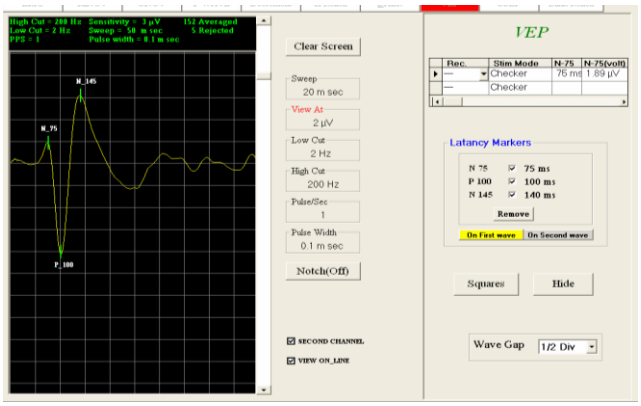

Figure 1: Normal VEP wave showing p100 latency at 100 milli second.

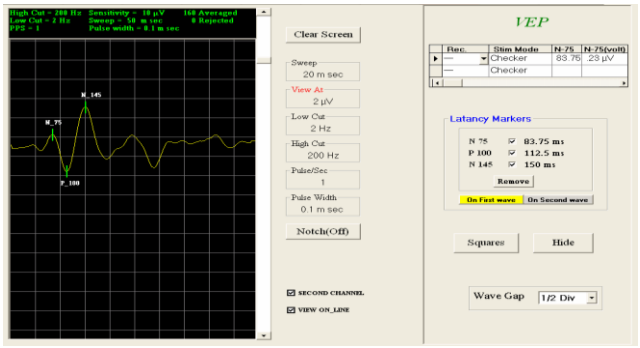

Figure 2: Abnormal VEP wave shows prolonged p100 latency.

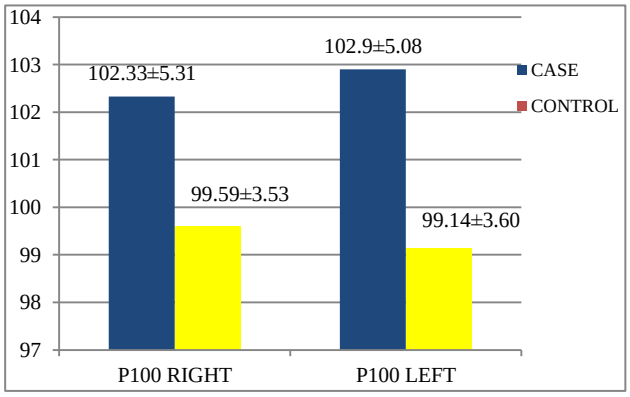

Figure 3: P100 values of cases and controls of right and left eyes.

Difference in P100 latency of right and left eyes has 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.

Table 1: Comparing age, BMI, systolic pressure and diastolic pressure among the case and the controls.

Parameters	Study group	N	Mean±sd	P value
Age	Case	50	44.08±5.907	0.987
	Control	50	44.06±6.336	
BMI	Case	50	22.18±2.919	0.866
	Control	50	22.10±1.619	
SBP	Case	50	144.60±14.172	0.000
	Control	50	111.20±7.183	
DBP	Case	50	95.80±10.120	0.000
	Control	50	71.20±11.20324	

Age and BMI were found not be significant (0.987 and o.866); but the Systolic BP and Diastolic BP were found to be highly significant (p 0.000) validating the case population.

Table 2: Comparing the VEP parameters among the study groups.

Vep parameters	Study group	N	Mean±sd	P value
N75 r	Case	50	75.2600±10.28757	0.189
	Control	50	72.4160±11.20324	
N75 l	Case	50	74.4400±7.50672	0.006
	Control	50	70.2600±7.32917	
P100 r	Case	50	102.3300±5.30797	0.003
	Control	50	99.5880±3.52794	
P100 l	Case	50	102.8950±5.07598	0.000
	Contro	50	99.1400±3.60278	
N145 r	Case	50	138.6600±13.06408	0.969
	Control	50	138.5550±13.68750	
N145 l	Case	50	138.0300±13.73126	0.436
	Control	50	135.8700±13.85809	
Amplitude r	Case	50	7.4912±5.84065	0.111
	Control	50	5.9646±3.21880	
Amplitude l	Case	50	5.6428±3.49021	0.110
	Control	50	4.7370±1.92022	

P100L, both right and left eye, n 75 were highly significant (p 0.003 and p 0.000) Right and left eye P100 latency difference highlights the involvement of prechiasma ensuring the detection of subclinical retinopathy.

On comparing the control and the Hypertensive group, age and BMI were found not be significant; but the Systolic BP and Diastolic BP were found to be highly significant (Table 1 and Figure 3).

The value of P100 latency in these Hypertensive patients was 102.3300±5.30797 and 102.8950±5.07598 comparable with the normotensive controls being 99.5880±3.52794 and 99.1400±3.60278 of right and left eye respectively (Table 2).

Of all the VEP parameters P100 latencies of both the eyes show highly significant p value being p<0.003 and p<0.000 of right and left eye respectively and is given in figure3.

DISCUSSION

The study was focussed to find out Visual Evoked Potential in 50 newly diagnosed Hypertensive individuals and the mean age 44.08±5.907 years and mean BMI 22.18±2.919.

Of the 50 newly diagnosed Hypertensive individuals, 32 were female and 18 were male. This is in concurrence as stated by Shyamal Kumar das, et al, 2005 and Priscilla IghoPemu, et al, 2008. The predicted reasons were increasing family stress and obesity which is common in middle aged women.[15]

Blood pressure measurement among the groups on comparison revealed statistical differences (p=0.000,p=0.000) as the newly diagnosed Hypertensive individuals had mean systolic blood pressure 33±10.1mmHg, diastolic blood pressure 24±9.3mmHg more than the controls.

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.[16]

The P100 latency of Hypertensive group was on an average 3.72±4.3 more 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[17] 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 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.[18] 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.[19] 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).[20]

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

Cortical lesions associated with optic nerve damage and retinopathy leads to visual disturbances. Unilateral infarction of anterior visual pathway was revealed by neurological signs in patients with hypertension which remains undetected for long time.

Evoked potentials are commonly used in clinical practice to study development and clinical disorders related to central nervous system. Our study has shown significant change in the latencies of VEP in newly diagnosed Hypertensive patients who have no clinically significant retinopathy.

Statistically significant delay in P100 latency suggests 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.
Right and left eye 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 not only Hypertensive retinopathy but also thorough screening of end organ damage and categorize the schedule for management.

Summary

- Functional integrity of visual pathway is not well documented in Hypertension.
- The present study aimed to screen and diagnoses Hypertension in the age group of 20-50 years, excluding confounding factors and evaluates visual evoked potentials (VEPs) before they are on medication for Hypertension.
- Pattern reversal visual evoked potentials (VEPs) were recorded in 50 newly diagnosed Hypertensive individuals and compared with 50 age and BMI matched normotensive individuals.
- In our study, female newly diagnosed Hypertensives were more than the male in accordance with the earlier studies highlighting the fact of family stress and obesity.
- P100 latency was significantly higher than the control suggestive of subclinical retinopathy even before the diagnosis of Hypertension.
- Inter eye latency difference also revealed significant P100 latency variation, highlighting the prechaismal involvement in subclinical retinopathy.
- The study concludes that VEP changes at the early stage of Hypertension or in the newly diagnosed cases where retinopathy is not detectable on routine clinical examination may if assessed allow the identification of the subclinical retinopathy as a key to unravel the mystery of hidden Hypertensive Morbidity and Mortality.

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