Effect of Elevated Mean Arterial Pressure (MAP) and Pulse Pressure (PP) on Auditory Brainstem Responses

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Abstract: Auditory evoked potential testing serves as a non-invasive clinical tool in the characterization of the electrophysiological phenomena of neural excitation, conduction and transmission across auditory pathways. The electrophysiological correlation of changes in sensory function in primary hypertension has already been studied in terms of effects of SBP and DBP on waves of auditory brainstem responses (ABR). In the present study, the correlation of MAP and PP with ABR was observed to explore the possible interaction of cardiovascular regulatory mechanisms with the auditory pathway at brainstem levels. BAEPs recordings were performed on 50 known hypertensives (WHO Guidelines) aged between 40-60 years of either sex attending Medical OPD of Guru Nanak Dev Hospital, Amritsar along with 50 age- and sex-matched normotensive controls, using EEG electrodes on an RMS EMG, EP MARC II (PC-based) machine. The data were statistically analysed by way of independent t-test and regression analysis and assessed by Levene’s test for equality of variance. Auditory threshold increased significantly in the hypertensive group compared with controls (p < 0.05). There was a significant prolongation of absolute peak latencies of waves I, and V and inter peak latency III-V in the hypertensive group. However, no significant difference was observed in other parameters of BAEPs. We established a highly significant correlation of rise in MAP with absolute peak latency of wave V and inter peak latency III-V along with a significant positive correlation of elevated pulse pressure with inter peak latency III-V. These findings suggest that central vasomotor control system interacts with generator of wave V of the ABRs in the midbrain region in delaying the absolute peak latency of this wave in primary hypertension.

Keywords: Auditory brainstem responses, Hypertension, Mean arterial pressure, Pulse pressure, auditory pathways.

INTRODUCTION

Essential hypertension usually clusters with other cardiovascular risk factors such as ageing, being overweight, insulin resistance, diabetes, and hyperlipidaemia increases risk for cerebral, cardiac, and renal events. Subtle target-organ damage such as left-ventricular hypertrophy, microalbuminuria, and cognitive dysfunction occur early in hypertensive cardiovascular disease, although catastrophic events such as stroke, heart attack, renal failure, and dementia usually happen after long periods of uncontrolled hypertension only [1].

Many mechanisms may operate to initiate and sustain hypertension. In afferent systemic arterioles, malfunction of ion pumps on sarcolemmal membranes of smooth muscle cells may lead to chronically increased vascular tone. Central nervous system dysfunction occurs frequently in patients with essential hypertension [2]. This might be due to arterial or arteriolar spasm in the blood vessels of the brain [3], that in combination with fibrinoid degeneration of small arteries leads to microinfarction and brain oedema in a severe case of hypertension. Additionally, hypertension predisposes small penetrating cerebral arteries to atheromatous changes, leading to lacunar infarctions in the gray nuclei and white matter. The dysfunction of brainstem regulatory mechanisms of blood pressure in essential hypertension interacting with sensory neuronal substrate might cause a variety of clinical features of motor or sensory deficits [4]. The current study was aimed to explore such changes in neural generator activity and sensory conduction in CNS caused by the effect of elevated mean arterial pressure (MAP) and pulse pressure (PP) by monitoring auditory evoked potentials in patients of essential hypertension. To our best of knowledge, our study is first of its kind in evaluating the changes in ABRs in terms of MAP and PP.
MATERIALS AND METHODS
Following ethical approval by the ethical committee of the institute, the study was conducted on 50 patients of essential hypertension of age group 40-60 years, attending Medical OPD of Guru Nanak Dev Hospital, Amritsar and 50 normotensive subjects (age and sex matched).

Selection of hypertensive subjects
The criterion of considering a patient hypertensive was a BP > 140/90 mmHg based on the average of 2 or more readings taken during each of his/her visits to the outpatient department.

These subjects were not on any antihypertensive medication. The patients were divided into various groups depending upon the grade of hypertension, as per WHO Guidelines. The WHO blood pressure classification includes 3 grades of hypertension.

<table>
<thead>
<tr>
<th>WHO/ISH Classification of Hypertension</th>
<th>Blood Pressure</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mm Hg)</td>
<td>140-159</td>
<td>160-179</td>
<td>≥ 180</td>
<td></td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>90-99</td>
<td>100-109</td>
<td>≥ 110</td>
<td></td>
</tr>
<tr>
<td>DBP, diastolic blood pressure; SBP, systolic blood pressure</td>
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</table>

All the patients were interviewed on a pre-tested proforma that included clinical history. These subjects were investigated and diagnosed as cases of essential hypertension.

The patients with any associated diseases like diabetes mellitus, ischemic heart disease (IHD), cerebrovascular disease, renal disease and having any clinical auditory abnormality or subjective symptoms of hearing loss, were excluded from the study. The patients were explained the procedure and written consent was taken before carrying out the procedure.

The controls were having a diastolic pressure < 90 and systolic pressure below 140 mm of Hg.

ABRs were performed on an outpatient basis, in the Department of Physiology, Government Medical College, Amritsar using RMS EMG EP Mark II 2CH (PC based) machine. The subjects were asked to wear earphones and electrodes placed on the top of head (vertex) and mastoid process. Active electrode was placed at ipsilateral mastoid process (Ai), reference electrode was placed at Cz and Grounding electrode was placed at the forehead (Fz). Electrical impedance was kept below 5kΩ. Auditory stimuli were delivered through the earphones to the ear being tested while masking the other one with white noise of 40 dB.

BAEPs were recorded using standardized technique after giving 2000 sound click stimuli of intensity 70dB above normal hearing threshold, at 11/s frequency and 0.1ms duration. The signals picked up by the electrodes were recorded using filter band pass of 300-3000 Hz with artefact rejection level up to 25 microvolts. 2 to 3 repetitions of the recording were done to ensure reproducibility i.e. – latency measured on separate recordings agreed with each other within 0.1 m sec or less.

The following parameters were measured for analysis of BAEPs in the patients and controls-
- Absolute latency of wave I to V
- Inter peak latencies (IPLs)
- Amplitude of wave I and V
- Amplitude ratio of wave V/I

RESULTS
Control Group
There were 50 subjects in this group between 40 and 60 years of age with average being 51.1 ± 6.9 years. They had mean weight: 64.0 ± 5.6 kg, height: 166.3 ± 5.6 cm, body surface area: 1.73 ± 0.09 kg/m², SBP: 121 ± 5.5 mmHg, DBP: 78.4 ± 3.5 mmHg, MAP: 92.6± 3.5 mm Hg, PP: 42.6± 4.8 mm Hg.

Hypertensive Group
There were 50 subjects in this group with their age between 40 to 60 years, average being 50.2 ± 5.9 years. They had an average weight: 67.3 ± 5.8 kg, height: 166.4 ± 7.0 cm, body surface area: 1.75 ± 0.11 kg/m², SBP: 148.6 ± 15.5 mmHg, DBP: 97.2 ± 7.5 mmHg and MAP: 114.4 ± 9.06 mmHg, PP: 51.3± 9.8 mm Hg.

Since values of ABRs of left and right ear did not vary significantly, an average of the 2 ears was calculated and composite data are given.

On comparing the ABRs between the study and control groups, there was statistically highly significant prolongation of latency of waves I and wave V, along with inter peak latency III-V in the hypertensives compared to control group (P < 0.001 ). The peak amplitudes of wave I and V were observed to be significantly decreased in the hypertensive group. The mean arterial pressure showed highly significant positive correlation with wave V (r=0.57) and inter peak latency III-V(r=0.65) while pulse pressure was found to be significantly correlated with inter peak latency III-V (r=0.32).
Table 1: Absolute Latencies, Inter-Peak Latencies and Amplitude Ratio in hypertensives as compared with normotensives. Data is presented as mean ± SD.

<table>
<thead>
<tr>
<th>Absolute Latency (ms)</th>
<th>Normotensive</th>
<th>Hypertensive</th>
</tr>
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<tbody>
<tr>
<td>Wave I</td>
<td>1.62±0.20</td>
<td>1.78±0.19**</td>
</tr>
<tr>
<td>Wave II</td>
<td>2.72±0.19</td>
<td>2.73±0.21</td>
</tr>
<tr>
<td>Wave III</td>
<td>3.75±0.15</td>
<td>3.66±0.22</td>
</tr>
<tr>
<td>Wave IV</td>
<td>4.82±0.21</td>
<td>4.75±0.26</td>
</tr>
<tr>
<td>Wave V</td>
<td>5.54±0.21</td>
<td>5.80±0.24**</td>
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<tr>
<th>Inter peak Latency (ms)</th>
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<tbody>
<tr>
<td>I-III</td>
<td>2.11±0.28</td>
<td>1.88±0.32</td>
</tr>
<tr>
<td>I-V</td>
<td>3.91±0.314</td>
<td>4.02±0.36</td>
</tr>
<tr>
<td>III-V</td>
<td>1.79±0.21</td>
<td>2.13±0.20**</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Amplitude wave I&amp;V</th>
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</thead>
<tbody>
<tr>
<td>I-Ia</td>
<td>0.51±0.34</td>
<td>0.32±0.18*</td>
</tr>
<tr>
<td>V-Va</td>
<td>0.56±0.32</td>
<td>0.43±0.24*</td>
</tr>
<tr>
<td>Amplitude ratio V/I</td>
<td>1.68±1.55</td>
<td>1.75±1.57</td>
</tr>
</tbody>
</table>

** Indicates 'p' < 0.001; *Indicates p<0.05

DISCUSSION

Hypertension affects the sensory conduction across auditory pathways. A pioneer study in north India reported prolongation of latency of all waves of ABR along with IPL III-V [5]. In another study, 55 essential hypertensive patients and 55 normal elderly subjects between the ages of 55-99 years were selected. ABRs were measured along with serum cholesterol and triglyceride levels. The results of the ABR demonstrated that the latencies of wave V, IPL I-V and IPL III-V were prolonged compared with normal elderly subjects. The patient’s duration of illness and the complications of hypertension had an influence on hearing disorders in relation to the ageing process. Hence they concluded that the hearing disorders in the elderly people are a result of long duration of illness and the complications of hypertension [6].

In our study the absolute peak latency of waves I, and V along with IPL III-V was significantly higher in hypertensives compared to controls (p<0.05). In addition the peak amplitudes of wave I and wave V were significantly diminished in the study group compared with controls.

The mean arterial pressure showed highly significant positive correlation with wave V(r=0.57) and inter peak latency III-V(r=0.65) and pulse pressure showing a positive correlation with inter peak latency III-V (r=0.32), which was statistically significant (p<0.05).

Our study has been substantiated by the findings of Karamitsos et al. who studied ABRs in 30 patients of ischaemic heart disease and in an equal number of healthy age matched control subjects. The parameters measured were absolute latency of waves I through V, the inter peak latencies I-III, III-V, and I-V, and the peak amplitudes of wave I, III, and V. The measured absolute latencies and inter peak latencies were found to be significantly increased, and the peak amplitudes were found to be diminished in the study group. Hence BAEPs may become part of the noninvasive assessment in IHD and essential
hypertension patients [7]. Auditory brainstem-evoked responses were conducted on 28 patients with otologic symptoms (pulsatile tinnitus, hearing loss, aural fullness) secondary to benign intracranial hypertension syndrome. Abnormalities consisting mainly of prolonged inter peak latencies were detected in one third of these patients. It is speculated that the pathophysiologic mechanisms responsible for these auditory brainstem-evoked abnormalities are stretching-compression of the cochlear nerve, caused by the intracranial hypertension and/or primary edema. Normalization or improvement was noticed in the majority of the patients after management of intracranial hypertension. Since the number of patients in this study was small, the diagnostic and prognostic value of this test needs further evaluation [8]. Significant prolongation of waves IV, V and VII of ABRs were also seen in rabbits with intra-cranial hypertension compared with controls [9]. Another study [10] showed that raised blood pressure in pre-eclamptic women may affect the vascular responses of the blood vessels in brain and cause ischaemic delay in P1 latency of visual evoked potentials. This may also explain the delay in ABR latencies in hypertensive cases. Narrowing and sclerosis of small penetrating arteries in the subcortical regions of the brain are common findings on autopsy in chronic hypertension. [11-14].

Further on the basis of regression equation finding it was observed that the absolute peak latencies of wave V in five cases and inter peak latencies III-V in three cases fell beyond the 99 percent tolerance limit of controls, thus showing abnormal BEAPs.

Latencies of Auditory Brainstem Responses (ABR) reflect the neural conduction velocity in the corresponding segment of auditory pathways. A delay of absolute latency (AL) of wave I and wave V in hypertensive study group suggests the sensory deficit both at the level of auditory nerve and auditory pathways in the brainstem. Further, the effect of the elevated mean arterial pressure is at the brainstem level as depicted by highly significant positive correlation with wave V.

As the inter peak latencies provide information about the time required for processing from one site in the auditory pathway to the next site, so our observations further suggest that auditory information processing time is affected more particularly from pons to midbrain (IPL III-V) of auditory pathway with elevation in mean arterial pressure and pulse pressure.

CONCLUSION
Our findings suggest that central vasomotor control system interacts with generator of wave V of the BAEPs in the midbrain region in delaying the absolute peak latency of this wave in primary hypertension. Further work is required to elaborate these findings.

REFERENCES