



Original article

Effect of Hypertension and Hypercholesterolemia on Auditory Brainstem Response in Adults

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ABSTRACT

Introduction: Cerebrovascular comorbidity factors (CCF) namely hypertension (HT) and hypercholesterolemia (HC) has been associated individually to the abnormalities seen in absolute peak latencies (APL) and inter-peak latencies (IPL) of the auditory brainstem response (ABR). HT effects the upper brainstem at lower click stimulus rate and HC effects the lower brainstem at higher click stimulus rate. However, concomitant effect of HT and HC on ABR parameters are inadequate. **Material and Methods:** Total 200 (age 40 - 60 years) non-diabetic subjects were measured for total cholesterol (TC) and blood pressure (BP). They were divided equally into four groups based on the reported measures (HC for TC > 200mg/dl; and HT for BP > 140/90 mmHg) as Group A (normal TC and BP), B (HC, normal BP), C (HT, normal TC), and D (HT, HC). ABR at low click stimulus were then recorded from subjects, and APL and IPL of groups B, C and D were compared with group A. **Results:** Group C vs A: Significant increase (\uparrow) ($p < 0.01$) in APL of waves I, II and V, and IPL of waves III-V; Group D vs A: significant \uparrow in all APLs and IPLs; Group B vs A: no significant variation. **Conclusion:** HT was found to be stronger associated with abnormality in ABR whereas HC had a relatively weak association. But, their concomitant effect on ABR parameters demonstrated augmentation of the neuropathy of both upper and lower brainstem, reflecting the need for combined treatment of the CCFs.

KEYWORDS: Auditory brainstem response, hypertension, hypercholesterolemia.

INTRODUCTION

Auditory brainstem response (ABR) is an audiometric test used to evaluate the functioning of the brainstem in which a wave form is recorded from scalp electrodes in response to an auditory stimulus [1]. The waveform is characterised by two parameters namely, (a) absolute peak latency (APL): consisting of five peaks namely I, II, III, IV, and V; and (b) inter-peak latency (IPL): consists of three clinically important IPL's namely I-III, I-V, III-V [2, 3] respectively. As the auditory stimulus traverses, the five peaks of ABR are said to be generated chronologically by distinct parts of the auditory pathway of the brainstem namely the cochlear nerve, cochlear nucleus, superior olive, lateral lemniscus and inferior colliculus [4]. Therefore, the parameters of ABR may serve as a diagnostic measure to objectively assess abnormalities in different structures of brainstem [2, 3] and clinically diagnose the different retrocochlear and eighth nerve pathologies [5].

Abnormalities in ABR latencies have been associated with various cerebrovascular diseases (CeVD) [6-8]. For example, brainstem strokes and transient ischemic attacks involving the posterior cerebral circulation result in increased latency in ABR for wave V [6-8]. Disorders of anterior cerebral circulation also contribute to abnormalities in ABR [7]. It was also found that wave V latency in ABR was prolonged in depressed patients accompanied with vascular disease [9].

CeVD is associated with various modifiable risk factors like hypertension (HT), diabetes mellitus, obesity and hypercholesterolemia (HC) [10]. The risk factors could be present in an individual either as a stand-alone factor or in combinations. Studies have reported that the risk factors often tend to aggregate in an individual [11] particularly the vascular comorbidity factors HT and HC [12]. According to a recent study based on analysis of survey reports from 1988 to 1994, 1999 to 2004, and 2005 to 2010, it was concluded that occurrence of HT and HC has increased over the years

and 60.7% to 64.3% of the hypertensive population were also hypercholesteraemic [13]. On the other hand, protocols for combined treatment of HC and HT are still suboptimal [12, 13]. Individual effect of HT measured from the parameters of ABR has been found to affect the higher brainstem and is evident at lower frequency of auditory stimulus provided during ABR recordings [14, 15].

Similarly, individual effect of HC as measured from the parameters of ABR has been found on lower brainstem [16]. However, effect of HC has been found to be dependent on the frequency of the auditory stimulus and found evident only at higher frequency [16]. To our knowledge, the joint influence of HC and HT on brainstem functioning has never been investigated at any frequency of auditory stimulus. Since it has been found that presence of HC and HT reinforces the effect of each other in vascular damage [17], hence the present study aims to investigate the individual and concomitant effect of HC and HT on ABR parameters and hypothesises that synergistic effects of these comorbidity factors on the parameters of ABR (APL and IPL) might play an important role in augmenting neuropathy of the brainstem.

MATERIALS AND METHODS

A hospital based cross sectional study was designed and conducted in the Department of Physiology, Gauhati Medical College and Hospital after obtaining Institutional Ethical Committee approval. 200 non-diabetic subjects (100 males and 100 females respectively) between the age group of 40 to 60 years, weighing 50-80 Kg's were recruited from the outpatient department. Subjects were divided equally into 4 groups (50 subjects/group) and were defined as following: Group A for subjects with normal cholesterol (<200 mg/dl) and normal blood pressure (BP; <140/90 mmHg and >110/75mmHg), Group B for subjects with HC (>200mg/dl) but normal blood pressure (<140/90mmHg and >110/75mmHg), Group C for subjects with normal cholesterol (<200mg/dl) but HT(>140/90mmHg), and finally group D for subjects with HC (>200 mg/dl) and HT(>140/90 mmHg). To ensure similarity between the four groups age and sex were matched. Patients affected by CeVD, neurological diseases, sensorineural hearing loss and cardiovascular diseases were excluded from the study.

Data collection procedure: The participants were asked to visit the physiology department of Gauhati Medical College where the experimental protocols and purpose were briefed. Following this, the recruited subjects signed a consent form to show their willingness to participate in the clinical procedures required in the study. BP was measured manually by a mercury sphygmomanometer on every subject for two consecutive days. Each day the measurement was taken twice and the average of a day was noted. The same was calculated the next day.

A subject was diagnosed as hypertensive if the grand average for two days of BP measured was above 140/90 mmHg. Those subjects were investigated and diagnosed as cases of essential hypertension who appeared in the OPD for the first time. Before advising any antihypertensive, they underwent a detailed ENT examination and their hearing

threshold was determined using pure tone audiometry (PTA). All subjects were found within the normal hearing threshold (0–25 dB) [18] and without any problems in hearing. The next step was to collect blood samples from the subjects. Venepuncture was performed in the antecubital fossa taking all aseptic and antiseptic measures. About 5ml of blood was drawn using disposable syringes. The blood was investigated for serum total cholesterol (TC) and random blood sugar (RBS) by following colorimetric enzymatic method. All subjects were within the normal range of RBS (79-140 mg/dl according to American Diabetic Association guidelines [19]).

Recording of ABR: The subjects were asked to lie down in a sound proof room. Electrodes were placed according to 10-20 International System of electrode placement. The active electrode was placed at the ipsilateral ear lobule (Ai), reference electrode at the vertex (Cz), and grounding electrode was placed at the forehead (Fz). Electrical impedance was kept below 5k Ω . Acoustic transients of stimuli (alternating clicks) were delivered through earphones to the ear being tested while the opposite ear was masked with white noise of 40 dB. ABR was recorded by giving 2000 click stimulus of 70 dB and each brief click is a square wave pulse of 0.1 msec. A click rate of 11/sec was used. A total of 2000 individuals weeps were recorded using filter band pass of 300-3000 Hz with artefact rejection level up to 25 micro volts. Two to three repetitions of the recording were done to ensure reproducibility. Recordings from both ears were averaged to obtain the APL of the waves from I to V, IPL of I-III, I-V and III-V, and amplitude ratio of V/ I.

Statistical analysis: Data's so obtained were analysed by means of two-tailed *t*-test for comparison of study groups (B, C, and D) with control (A). Further the multi-group comparison was done using one-way ANOVA. Where there was a significant difference, Turkey's honestly significant difference *post-hoc* test was used to identify the source of the significance.

RESULTS

There were 50 subjects comprising of 25 males and 25 females in each of the groups A, B, C, and D respectively. Mean and standard deviation (Mean \pm Std) of age (in years), weight (in Kg), height (in cm) and RBS (in mg/dl) of each group are as follows. Group A had age (47.5 \pm 6.27), weight (65.3 \pm 7.8), height (169.4 \pm 9.0), and RBS (103.62 \pm 28.18). Similarly, group B had age (49.59 \pm 6.32), weight (68.3 \pm 9.5), height of (169.89 \pm 12.2), RBS of (106.75 \pm 20.37). The range of group C for age (42.46 \pm 6.91), weight (70.54 \pm 9.5), height (165.89 \pm 12.2), RBS (106.75 \pm 20.37); and finally for group D are age (49.46 \pm 8.62), weight (73.35 \pm 9.6), height (166.56 \pm 6.87), and RBS (110.45 \pm 17.67). The (Mean \pm Std) of the parameters namely (systolic blood pressure (SBP), diastolic blood pressure (DBP), TC, and ABR) that were statistically analysed for significance are given in table 1. Parameters of study groups (B, C, and D) were compared with control group A. Beside every column of study groups (B, C, and D) the statistical significance (*p* < 0.01) is marked as S and non-significance as NS respectively.

Table1: Mean and standard deviation of SBP, DBP, TC, APL and IPL of ABR in the 4 groups.

GROUP	A (Mean ± SD)	B (Mean ± SD)	B with A	C (Mean ± SD)	C with A	D (Mean ± SD)	D with A
SBP	119.8 ± 10.90	116.83± 11.71	NS	164.16 ± 11.39	S	162.09 ± 9.70	S
DBP	82.3 ± 6.25	80.02 ± 9.95	NS	97.23 ± 9.02	S	96.98 ± 6.13	S
TC	169.3 ± 24.10	264.86± 25.32	S	168.52 ± 33.25	NS	269.01±26.19	S
APL I	1.26 ± 0.14	1.23 ± 0.12	NS	1.82 ± 0.08	S	1.78 ±0.15	S
APL II	2.49 ± 0.22	2.52 ± 0.12	NS	2.81 ±0.097	S	2.79 ± 0.09	S
APL III	3.68 ± 0.06	3.65 ± 0.17	NS	3.71 ± 0.07	NS	3.69 ± 0.12	NS
APL IV	4.78 ± 0.13	4.83 ± 0.12	NS	4.85 ± 0.13	NS	5.03 ± 0.17	S
APL V	5.34 ± 0.23	5.29 ± 0.12	NS	5.8 ± 0.10	S	5.84 ± 0.95	S
IPL I-III	1.86 ± 0.09	1.81 ± 0.12	NS	1.92 ± 0.23	NS	2.05 ± 0.15	S
IPL I-V	4.22 ± 0.15	4.24 ± 0.11	NS	4.36 ± 0.19	NS	4.30 ± 0.16	S
IPL III-V	1.82 ± 0.09	1.78 ± 0.11	NS	2.05 ± 0.19	S	2.001 ± 0.11	S
V/I ratio	139.64±16.12	149.73 ± 7.74	NS	156.22 ± 9.75	NS	159.40 ± 8.52	S

DISCUSSION

The aim of this study was to investigate the individual and combined effect HC and HT on ABR. For this, subjects were divided into three study (B, C and D) and one control group (A) based on the presence or/and absence of HC and HT. ABR was then recorded and three parameters namely APL, IPL and V/I ratio were analysed for significance ($p < 0.01$) between the study and control group (refer to table 1).

The group C (presence of HT and absence of HC) reflected significant prolongation of APL for waves I, II and V and IPL for III-V. This is in consistence with studies that reported similar APL and IPL prolongations in hypertensives compared with normotensives [14, 15]. Significant positive correlation between mean arterial pressure and APL of waves I, IV, V and IPLs I-V, III-V was also reported in hypertensive patients[20]. In concordance to other studies, the present study strengthens the claims that presence of HT can have neuropathic effects on the upper brainstem of auditory processing.

The group B (presence of HC and absence of HT) did not show significant variation in any of the ABR parameters. The result is inconsistency with the findings of Ben-David et

al. where they reported non-significant variation in ABR parameters in hyperlipidemic compared to normolipidemic subjects for similar click rate as used in the present study[16]. However, their study reported effects on ABR parameters (IPL I-V, and I-III) when the click stimulus was increased to 55 clicks/sec suggesting neuropathy of lower brainstem in hyperlipidemic subjects[16]. Similarly, another ABR study conducted at 39 clicks/sec reported delayed auditory processing at lower brainstem for individuals with HC [21].

Though the scope of the present study gets limited by the click rate (11/sec) utilised as auditory stimulus and it reports non-significant effects on ABR, however it cannot be ignored the role of HC on neuropathic effects of lower brainstem seems to be dependent on the stimulus frequency. Hence, the effect of HC on lower brainstem get subdued at lower frequency of auditory stimulus. However, the subtle effect of HC might get fostered at the same frequency by presence of other accompanying vascular risk factors and this, therefore broadens the horizons of the current study.

HC together with HT in group D was found to significantly prolong the APL and IPL at lower click stimulus rate of 11 clicks/sec. A similar findings was observed in the study of Karamitsos *et al* when the ABR response was compared between ischemic heart disease (IHD)patients and normal individual [22]. They found that the parameters of APL of waves I through V, the IPLs I-III, III-V, and I-V were significantly prolonged as also found in the present study at the same stimulus rate [22]. The present study strengthens the fact that HC augments HT effects of neuropathy of the brainstem as commonly seen in IHD patients. This may be explained by the fact that hypertension causes damage to the blood vessels which facilitates the deposition of cholesterol accelerating the atherosclerotic plaque formation, further reinforcing the synergistic effect of HT and HC [17].

Since atherosclerosis has been found to be strongly associated with micro infarcts formation [23], and hence the potential to cause neurological dysfunction [24] and coronary heart disease [25].Individual and combined effects of HT and HC have been reported on coronary heart disease where treating the individual factors (HT or HC) reduces the risk by 25%, whereas treating their combination reduces the risk by more than 35% [13]; and yet the combined treatment protocols are reported to be suboptimal [12, 13] The present study reports the synergistic effects of HC and HT on the neuropathy of brainstem and reinforces the need for concomitant treatment of these factors to reduce the overall vascular damages. Alternatively, these risk factors may be modified to prevent central nervous system decline.

CONCLUSION

HT was found to be stronger associated with abnormality in ABR whereas HC had a relatively weak association. But, their concomitant effect on ABR parameters demonstrated augmentation of the neuropathy of both upper and lower brainstem, reflecting the need for combined treatment of the CCFs.

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