

Brainstem Auditory Evoked Potentials in Type 2 Diabetes Mellitus

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ABSTRACT

The objective of this study is to analyze the effect of diabetes in auditory functions by using pure tone audiometry (PTA) and brainstem auditory evoked potentials (BAEP). The study was conducted using thirty consenting males with type 2 diabetes mellitus and thirty consenting age and gender matched controls. The PTA and BAEP were assessed. Independent samples t-test was used to compare differences between the two groups. In PTA, there was significant increase in mean auditory thresholds at all frequencies tested (250, 500, 1000, 2000, 3000, 4000, 8000 Hertz) in the diabetes group as compared to the control group. The right ear of the diabetes group showed significant increase in mean BAEP waves latencies I [1.85 ± 0.22 vs 1.66 ± 0.25 ms, $p=0.003$], II [3.01 ± 0.24 vs 2.69 ± 0.29 ms, $p=0.001$], III [4.25 ± 0.42 vs 3.87 ± 0.35 ms, $p=0.001$], IV [5.38 ± 0.43 vs 5.1 ± 0.32 ms, $p=0.007$], V [6.44 ± 0.5 vs 6.02 ± 0.22 ms, $p=0.001$] and interpeak latencies I-III [2.40 ± 0.42 vs 2.2 ± 0.29 ms, $p=0.039$], I-V [4.59 ± 0.51 vs 4.36 ± 0.28 ms, $p=0.033$] as compared to the Control group at 60 dB intensity. Acoustically asymptomatic diabetes patients showed significant increases in mean auditory thresholds, BAEP wave and interpeak latencies suggesting impairment of acoustic nerve function and lower brainstem region of the auditory pathway.

Keywords: Brainstem auditory evoked potential, Diabetes, Pure tone audiometry

INTRODUCTION

Diabetes mellitus is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin.¹ Type 2 diabetes is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased insulin production. Distinct genetic and metabolic defects in insulin action and/or secretion gives rise to the common phenotype of hyperglycemia in type 2 diabetes.² Diabetes is associated with chronic complications such as nephropathy, angiopathy, retinopathy, autonomic neuropathy, and peripheral neuropathy.³ Neuropathies affecting all cranial nerves except olfactory and hypoglossal nerve have been documented in diabetes. Retrospective studies show that as many as 50 percent of patients have some manifestations of auditory dysfunction and physiological analysis of temporal bones from diabetes patients revealed PAS-positive lesions of the capillaries in the stria vascularis.⁴

Brainstem auditory evoked potentials (BAEP) are signals generated in the auditory nerve and brainstem following an acoustic alternative click stimulus. The evoked responses consist of a series of waves generated entirely from the subcortical sites. BAEP are usually helpful in localizing the lesions in the brainstem. The waves of BAEP are I, II, III, IV and V. Wave I originates from the distal portion of the eighth cranial nerve, wave II from the cochlear nucleus, wave III from the superior olivary nucleus, wave IV from the lateral lemniscus and wave V from the inferior colliculus.⁵

Various reports have documented that diabetes affects vestibulo-cochlear nerve function and the auditory pathway. To date the location of the lesions in the auditory pathway is uncertain. The latency of wave V and interpeak latencies I-V and III-V were higher in the diabetes group as compared to the control group.⁶ The latencies of waves I, III, V and interpeak latencies I-III, III-V, and I-V were prolonged significantly in the study group when compared to the control group.⁷ Interpeak latency I-V was longer in the diabetes as compared to the control group.⁸ Therefore, the aim of the present study is to localize the lesions in the auditory pathway due to diabetes mellitus.

MATERIALS AND METHODS

The study was conducted on thirty male patients with diabetes and thirty, healthy, age and gender matched controls. All patients were under medication (oral hypoglycemic drugs such as metformin, gliclazide) and they were either newly diagnosed or follow up cases. The duration of diagnosed diabetes was measured using patient interviews. Patients were taken from the Department of Internal Medicine, B. P. Koirala Institute of Health Sciences (BPKIHS) within the age group 45-60 years. Subjects without known hearing defects were taken for the study. Subjects with a history of ear disease, family history of deafness, exposure to noise, head or ear trauma, cardiac disease, hypertension, chronic headache, air-bone gap more than 10 dB and any other illness which might affect the test results were excluded from the study.

Thirty healthy age and gender matched volunteers were recruited as a control group. The control subjects were selected among staff members of BPKIHS. These subjects did not have diabetes and were selected using the same exclusion criteria as above. The study was approved by the Ethical Review Committee of BPKIHS, Dharan, Nepal. Although the methods of measurements used in this study are entirely noninvasive, informed written consent was obtained from all participants.

Recording procedure

The recording was done in Neurophysiology Laboratory, Department of Basic and Clinical Physiology, BPKIHS, Dharan. The recording was done between 10:00 a.m. – 12:00 noon to minimize possible diurnal variation. Temperature of the recording room was kept comfortable at 26±2°C to avoid sweating or shivering.

Anthropometric Variables

Anthropometric variables of the subjects such as age, height, weight, and Body Mass Index (BMI) were measured. Age was recorded in full years. Height was measured in centimeters from top of the head to heel. Weight was measured in kilograms, bare footed with light clothing. BMI was calculated as body weight in kilograms divided by square of height in meters.

Cardio-respiratory variables

Cardio-respiratory variables of the subjects such as blood pressure, respiratory rate and heart rate were measured by using standard techniques.

Pure tone audiometry

Auditory thresholds of the subjects were measured using pure tone audiometry. The instrument used was Madsen electronics (Orbiter 922, version 2). Pure tone audiometry was used to test the hearing thresholds of the subjects at different frequencies (250, 500, 1000, 2000, 3000, 4000, 8000 Hertz).

Brainstem Auditory Evoked Potentials (BAEP)

Subjects were asked to come with their scalps washed free from oil or gel. BAEP of the subjects were measured by using Neuropack 2 (Nihon Khoden machine, NM-4205; H636, Japan) and earphone dynamic receiver ELEGA (Type DR-531; no. 237, Japan) in a sound proof room. The

recording (active) electrodes were placed on the mastoid region of both ears with a reference electrode at the vertex (Cz) according to the 10-20 international system. The ground electrode was placed centrally on the forehead (Fz) over the nose. Electrode impedance was less than 5 K Ω.

Acoustic click stimuli (monophasic square pulses of 0.1ms duration) of intensity 60 dB was given monoaurally at the rate of 10Hz. The contralateral ear was masked with continuous white noise at intensity of 40 dB. For each ear, evoked responses of 2000 click stimuli were averaged by a filter setting of 100 Hz and 3000 Hz.

Peaks of BAEP waves were determined by inspection. Latencies of waves I, II, III, IV, V and interpeak latency (IPL) I-III, III-V, I-V were measured from BAEP record.

Statistical analysis

Data of anthropometric variables, cardio-respiratory variables, pure tone audiometry and BAEP were normally distributed. So, independent samples t-test was used for comparisons between the diabetes and control groups. Data were analyzed with statistical software SPSS version 18.

RESULTS

Subject Characteristics

Average duration of disease since diagnosis was 9.45 ± 3.15 years.

Anthropometric variables

There were no significant differences among diabetes and control groups in terms of their age, height, weight and body mass index. (Table 1)

Cardio-respiratory variables

Systolic blood pressure, diastolic blood pressure, heart rate, and respiratory rate are shown in Table 2. There were no significant differences in those parameters between the diabetes and control groups.

Pure tone audiometry

Auditory thresholds of right ear at different frequencies of the diabetes and control groups are shown in the Figure 1. The mean auditory thresholds of both the right and left ears of the diabetes group were significantly higher than the control group in all frequencies tested.

Table 1. Comparison of Anthropometric Variables Between the Diabetes and Control Groups.

Variables	Diabetes (n=30) Mean ± SD	Control (n=30) Mean ± SD	p value
Age (years)	57.2 ± 6.2	55.3 ± 6.5	0.26
Weight (Kg)	65.6 ± 7.7	63.6 ± 5.5	0.25
Height (m)	1.6 ± 0.1	1.6 ± 0.1	0.81
BMI (Kg/m ²)	24.6 ± 2.7	23.8 ± 2.2	0.21

p<0.05 was considered statistically significant, BMI = body mass index

Table 2. Comparison of Cardio-respiratory Variables Between the Diabetes and Control Groups.

Variables	Diabetes (n=30) Mean ± SD	Control (n=30) Mean ± SD	p value
SBP (mmHg)	120 ± 5.6	119 ± 6	0.27
DBP (mmHg)	78.6 ± 5.4	78.4 ± 4.5	0.91
HR (beats per minute)	76.3 ± 4.3	74.8 ± 4.2	0.19
RR (per minute)	14.5 ± 1.5	13.8 ± 2	0.18

SBP = systolic blood pressure, DBP = diastolic blood pressure, HR = heart rate, RR = respiratory rate, p<0.05 considered statistically significant.

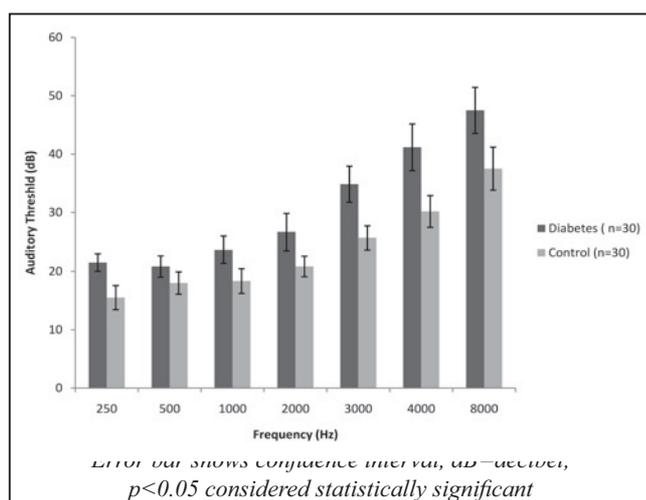


Figure 1. Comparison of Mean Auditory Thresholds of Right Ear at Different Frequencies Between the Diabetes and Control groups.

Brainstem Auditory Evoked Potentials (BAEP)

The absolute latency and IPL of different waves of both the right and left ears of the diabetes and control groups at 60 dB sound intensity are given in the Table-3. Latencies of waves I, II, III, IV, V and interpeak latencies I-III, I-V were significantly increased in the diabetes group as compared to the control group.

DISCUSSION

There were significant increases in mean auditory thresholds at all frequencies tested in the diabetes group as compared to the control group. Our findings are in agreement with the

findings of Frisina *et al*, in which four pure tone average (PTA) groups were computed: PTA-1 (0.5, 1, 2 kHz), PTA-2 (1, 2, 4 kHz), PTA-3 (4, 8, 9 kHz), and PTA-4 (10, 11, 12, 14 kHz).⁹ For all frequencies, diabetes patients consistently needed more sound intensity for threshold detection. Similarly, there were significant differences in the auditory thresholds at all frequencies from 250 Hz to 8000 Hz between the diabetes and control groups and all the hyperglycemic subjects showed sensorineural hearing loss changes on audiogram.¹⁰ Diabetics had a poorer hearing threshold than the non diabetics.¹¹

We evaluated the BAEP of both ears of both the diabetes and control groups at 60 dB sound intensity. Compared to healthy controls, the diabetes group showed significant increase in wave latencies I, II, III, IV, V and IPL I-III, I-V at 60 dB sound intensity. Lengthening of the latencies of waves I, II, and III indicate that lesions are in the distal portion of auditory nerve, cochlear nucleus, and superior olivary nucleus respectively.⁵ This suggests that there is a defect throughout the auditory pathway from spiral ganglion to superior olivary nucleus. Lengthening of IPL I-III suggests lower brainstem pathology. The increase in latencies of waves IV, V and IPL I-V was due to an increase in IPL I-III, as IPL III-V was comparable between the diabetes and control groups. This finding suggests that projections from the superior olivary nucleus to inferior colliculus are seemingly intact. According to our results, lengthening in wave latency and IPL indicates that the pathology affected both the peripheral and the central nervous system structures.

Table 3. BAEP Wave and Interpeak Latency Comparisons Between the Diabetes and Control Groups.

Latency (ms)	Right ear Diabetes n=30 Mean ± SD	Right ear Control n=30 Mean ± SD	p value	Left ear Diabetes n=30 Mean ± SD	Left ear Control n=30 Mean ± SD	p value
Wave I	1.85±0.22	1.66 ± 0.25	0.003	1.86 ± 0.24	1.71 ± 0.18	0.011
Wave II	3.01 ± 0.24	2.69 ± 0.29	0.001	2.96 ± 0.29	2.71 ± 0.22	0.001
Wave III	4.25 ± 0.42	3.87 ± 0.35	0.001	4.16 ± 0.4	3.84 ± 0.29	0.001
Wave IV	5.38 ± 0.43	5.1 ± 0.32	0.007	5.38 ± 0.42	5.02 ± 0.31	0.001
Wave V	6.44 ± 0.5	6.02 ± 0.22	0.001	6.52 ± 0.56	6.01 ± 0.29	0.001
I - III interpeak	2.40 ± 0.42	2.2 ± 0.29	0.039	2.3 ± 0.38	2.13 ± 0.26	0.043
III - V interpeak	2.19 ± 0.53	2.16 ± 0.32	0.77	2.36 ± 0.55	2.18 ± 0.36	0.123
I - V interpeak	4.59 ± 0.51	4.36 ± 0.28	0.033	4.67 ± 0.58	4.3 ± 0.33	0.004

p<0.05 considered statistically significant, ms=milliseconds, recording was done at 60 dB sound intensity.

Earlier study also showed lengthening in I, III, V waves latencies and I-III and I-V IPL in the patients compared to the control group.¹² Latencies for waves I, III, and V and IPL I-V were significantly longer in the diabetes patients than in the control group.¹³

Our findings support the results obtained by Gupta *et al* regarding significant delay in latencies of waves III, IV, V and IPL III-V, I-V in males with diabetes.¹⁴ Our findings also support the results obtained by Talebi *et al* regarding the significant delay in latency of waves III, IV, V.¹⁵ However, we did not observe any delay in IPL III-V in diabetes as reported by this study. Our results also support those reported by Durmus *et al* regarding significant delay in latencies of waves III and V.¹⁶ However, we also revealed a significant prolongation of latencies of waves I, II, IV and IPL I-V in diabetes subjects, which was not observed by them. The significant increase in latency of wave V and IPL I-V was also observed in our study.¹⁷ However, we also revealed significant rise in latencies of waves I, II, III, IV and IPL I-III, which were not revealed by both of these studies. Similarly, latencies of BAEP waves were significantly impaired in diabetes subjects as compared to controls.¹⁹ Peripheral transmission time (wave I) and central transmission time (IPL I-V) were also significantly delayed in diabetes subjects. The delay in central conduction time in diabetes may be related to neurodegenerative changes. A recent study suggested that insulin resistance in diabetes increases oxygen toxicity and apoptosis of neurons. This mechanism further promotes insulin resistance and neurodegenerative changes in the brain of patients with diabetes.²⁰ In contrast to our study, patients with diabetes showed an increase of wave V latency and interpeak I-V and III-V latencies. The brainstem responses suggested normal VIII nerve function but impaired neural conduction time within the brainstem.⁶ In another study, the latency of wave I was found to be equal in the diabetes and control groups. This suggests that the eighth nerve transmission to the level of the cochlear nucleus was not altered in diabetics. The latency of wave III and V was delayed significantly in the diabetic group as compared to the control group at 70, 80, and 90 dB. The delay in the latency of wave III and V in the diabetics indicate neuropathy at brainstem and midbrain level in the auditory pathway. The interpeak latency I-III, III-V, and IV was delayed in the diabetic group, which suggests delayed transmission of the auditory stimulus in the auditory pathway of diabetics at the level of brainstem and midbrain.²¹ Acoustically asymptomatic diabetic patients showed significant increase in auditory thresholds, BAEP waves and interpeak latencies suggesting impairment of acoustic nerve function and auditory pathways to the level of the superior olivary nucleus.

Conflict of interest: None

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