## **Original Research Article**

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# A study of auditory brainstem evoked responses in type 1 and type 2 diabetes mellitus patients with normal hearing

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#### **ABSTRACT**

**Background:** Diabetes mellitus (DM) is one of the most common metabolic disorders with millions of cases worldwide. Its effect on functioning of the central nervous system (CNS) and the peripheral nerves is a matter of current neurological research. Our study aimed to find out changes in auditory brainstem responses if any, in patients with type 1 and type 2 DM patients with apparently normal hearing.

**Methods:** 50 cases each of type 1 and type 2 diabetic patients with normal hearing were chosen along with 50 healthy controls. Pure tone audiometry and brainstem evoked response audiometry (BERA) was performed in all cases. The BERA results were interpreted for the latencies of waves I, II, III, IV and V and inter-peak latencies I-III, I-V and III-V.

**Results:** Significant delay in absolute latency of wave I, III, IV, V and inter-peak latencies I-V and III-V was seen in Type 1 diabetic patients. In type 2 diabetic patients, latencies of waves I, II, III, IV and V and inter-peak latencies I-III, I-V and III-V were significantly delayed. There was no statistically significant difference in latency delay between type 1 and type 2 DM. No relation was found with the duration of DM.

**Conclusions:** BERA is a non-invasive and easy to perform test that can detect minor CNS changes and can be used to detect peripheral (auditory nerve) and central neuropathy in diabetics even in absence of clinical signs and symptoms of deafness.

**Keywords:** Diabetes mellitus, Auditory brainstem responses, Central neuropathy

### **INTRODUCTION**

Diabetes mellitus (DM) is a condition characterised by poor glycemic control leading to a state of hyperglycaemia. It is one of the most common metabolic disorders affecting the human population with millions of cases world-wide. Reduced insulin secretion, decreased glucose utilisation and increased glucose production are the factors contributing to hyperglycaemia depending on the etiology of DM.<sup>1</sup>

In the early phase of DM, neuropathy can be clinically detected as a result of autonomic and peripheral nerve

function impairment. The involvement of the central nervous system (CNS) in diabetic neuropathy is also commonly seen.<sup>2</sup> It has been documented in the literature that long standing cases of diabetes mellitus is associated with progressive bilateral high sensorineural hearing loss starting at an earlier age than the normal population.<sup>3</sup>

Brainstem evoked response audiometry (BERA) is a simple and non-invasive procedure to detect the integrity and functioning of the eighth cranial nerve and the central auditory pathway. Brainstem auditory evoked response is the potential recorded from the ear and vertex in response to a brief auditory stimulation to assess the conduction

through the auditory pathway up to the midbrain. The normal BERA recording consists of five or more vertex positive and vertex negative waves arising within 10 ms of auditory stimulus. BERA study relies on the measurement of latencies and amplitude of waves arising after giving a sound higher than the hearing threshold. Consecutive waves on a BERA pattern from I to V reflect the electrical activity of the acoustic nerve, cochlear nuclei, superior olive, lateral lemniscus and inferior colliculus respectively. It can therefore be used to detect early impairment of functioning of the acoustic nerve and central auditory pathways even in the absence of specific signs and symptoms of clinical deafness.<sup>4,5</sup>

Our study was performed with the aim to detect any changes in auditory brainstem responses in patients with type 1 and type 2 DM patients with apparently normal hearing and their comparison with normal subjects, to find whether any correlation exists between the observed abnormalities (if any) with the duration and type of diabetes and to assess the utility of BERA as screening tool in early detection of diabetic neuropathy in patients with apparently normal hearing. In other words we have tried to find out if any there are any specific and predictable changes in the BERA responses in this group of patients before the clinical onset of sensorineural hearing loss.

#### **METHODS**

This prospective study was carried out in the Department of ENT and Head Neck Surgery, Government Medical College, Patiala from February 2012 to September 2013 and included a total of 150 subjects with apparently normal hearing. Subjects were divided into three groups:

- Group 1- 50 type 1 DM subjects.
- Group 2- 50 type 2 DM subjects.
- Group 3- 50 non-diabetic healthy subjects (controls).

Subjects in the age group of 25-60 years were taken and only proven cases of type 1 and type 2 DM by history, clinical examination and blood investigations were included in the study. Patients with history of any ear disease like chronic otitis media, previous ear surgery and exposure to prolonged loud noise, intake of ototoxic drugs, meningitis, head trauma, stroke or family history of hearing impairment were excluded. Patients taking any medication which might be expected to interfere with the functioning of CNS (e.g., methyldopa, reserpine, phenytoin, antipsychotics and anti-depressants) were also excluded from this study. Any patient with an abnormal pure tone audiometry test was also automatically excluded from the study.

Informed consent was obtained from all individual participants included in the study. Detailed history was taken and clinical examination was done. Detailed ear, nose and throat examination was done. Biochemical

studies for fasting blood sugar (FBS) and random blood sugar (RBS) levels were done in every case.

Subjects were first tested by pure tone audiometry (PTA) and then BERA was performed. Correct procedure of the test was explained to all subjects and the findings were recorded on a predesigned proforma. Pure tone audiometry was performed using ELKON eda 3N3 multi audiometer in a sound proof room. Both air and bone conduction were tested for frequencies between 500-8000 Hz and 500-4000 Hz respectively. Pure tone average was calculated for three frequencies i.e., 500 Hz, 1000 Hz and 2000 Hz for both ears.

For BERA, RMS EMG EP MARK II apparatus was used and test was performed as per the procedure given in the manual supplied by RMS Recorders and Medicare Systems Pvt. Ltd. The subject's vertex, middle of forehead and both the mastoid processes were cleaned with spirit gently to avoid impedance. Active electrode was placed over the vertex, reference electrode on the left and right mastoid processes and ground electrode over the forehead just above the nasion using standard electrode paste.

All the electrodes were plugged in a junction box and skin to electrode impedance was monitored and was kept below 5 k $\Omega$ . The sound stimulus was given in the form of "broad band clicks" by headphone attached to the headset at the rate of 11.1 Hz and 0.1 millisecond duration. 2000 clicks were given at an intensity of 70 dB level above the individual perceptual hearing threshold. The later was estimated by doing pure tone audiometry prior to this test.

The BERA results were interpreted for the latencies of waves I, II, III, IV and V and interpeak latencies (IPL) I-III, I-V and III-V. The BERA results of patients with DM were classified according to the duration of disease (those with DM less than 10 years duration and those with DM for more than or equal to 10 years). Evaluation of the data was carried out by independent student's t-test for unpaired data. 'p' value less than 0.05 and 0.005 were considered significant and highly significant respectively.

#### **RESULTS**

In this study, total 150 subjects were included and divided into three groups. Mean age of type 1 and type 2 diabetic subjects was 41.7±11.75 years and 48.24±6.23 years respectively in this study. The mean age of controls was 45.54±7.49 years. There was no statistical significant difference between mean age of both diabetic and control groups. However, the mean FBS and RBS levels were much higher in diabetics. There was no statistically significant difference between pure tone average of diabetic subjects and controls in both ears and pure tone average lies within normal hearing thresholds (Table 1).

Auditory brainstem response morphology was normal in all groups. Wave latencies were prolonged in diabetic

groups as compared to control group in both right and left ear. In type 1 DM patients, mean absolute latencies of waves I, III, V and IPL III-V of both ears and latency of wave IV in right ear and IPL I-V in left ear were significantly prolonged (p<0.05) as compared to control group (Table 2). In type 2 DM patients, absolute latencies of all waves and inter peak latencies show significant

difference (p<0.05) in comparison with controls in both ears except wave II latency and IPL I-III on right side which show no significant difference (Table 3). When the two diabetic groups were compared with each other, latency prolongation was more pronounced in type 2 DM patients, but the difference was not statistically significant.

Table 1: Mean and SD of various parameters in group 1 (type 1 DM), group 2 (type 2 DM) and group 3 (control) subjects.

Parameters	Group 3 (Controls) (Mean±SD)	Group 1 (type 1 DM) (Mean±SD)	Group 2 (type 2 DM) (Mean±SD)
Age (years)	45.54±7.49	41.7±11.75	48.24±6.23
Weight (kg)	67.38±11.74	67.58±9.08	69.26±11.42
Height (cm)	159.8±9.84	159.84±7.39	160.06±7.8
FBS (mg/dl)	79.68±6.13	123.32±21.07	131.76±24.33
PTA (dB) left ear	16.87±3.41	17.40±3.50	15.90±3.83
PTA (dB) right ear	15.84±3.76	16.84±3.90	16.07±3.76

Table 2: BERA results of patients in group 1 (type 1 DM), group 2 (type 2 DM) and group 3 (control) subjects in left ear and their comparison.

Waves and IPL (in ms)	Control (group 3) (Mean±SD)	Type 1 DM (group1) (Mean±SD)	Type 2 DM (group 2) (Mean±SD)	P value group 1-3	P value group 2-3	P value group 1-2
Wave I	1.60±0.11	1.68±0.20	1.71±0.14	0.014*	0.000*	0.344
Wave II	2.70±0.18	2.76±0.23	2.79±0.20	0.172	0.028*	0.493
Wave III	3.65±0.19	3.83±0.23	3.88±0.21	0.001*	0.000*	0.241
Wave IV	4.77±0.20	4.86±0.25	4.92±0.25	0.079	0.002*	0.196
Wave V	5.51±0.17	5.75±0.25	5.83±0.28	0.000*	0.000*	0.172
IPL I-III	2.09±0.22	2.15±0.12	2.17±0.18	0.076	0.043*	0.542
IPL III-V	3.91±0.17	4.07±0.20	4.11±0.26	0.000*	0.000*	0.384
IPL I-V	1.83±0.24	1.92±0.18	1.94±0.27	0.034*	0.027*	0.635

<sup>\*</sup>Significant (p<0.05).

Table 3: BERA results of patients in group 1 (type 1 DM), group 2 (type 2 DM) and group 3 (control) subjects in right ear and their comparison.

Waves and IPL (in ms)	Control (group 3) (Mean±SD)	Type1 DM (group1) (Mean±SD)	Type2 DM (group 2) (Mean±SD)	P value group 1-3	P value group 2-3	P value group 1-2
Wave I	1.59±0.14	$1.70\pm0.22$	1.76±0.17	0.005*	0.000*	0.125
Wave II	2.73±0.21	2.77±0.31	$2.80\pm0.25$	0.478	0.111	0.508
Wave III	3.69±0.19	3.83±0.25	3.93±0.22	0.002*	0.000*	0.051
Wave IV	4.69±0.24	4.90±0.29	4.87±0.28	0.000*	0.001*	0.654
Wave V	5.56±0.28	$5.80\pm0.29$	$5.89\pm0.23$	0.000*	0.000*	0.084
IPL I-III	2.10±0.21	2.13±0.13	2.15±0.21	0.381	0.308	0.729
IPL III-V	3.97±0.25	4.10±0.25	4.13±0.23	0.009*	0.001*	0.528
IPL I-V	1.86±0.31	1.97±0.22	1.96±0.22	0.063	0.067	0.967

<sup>\*</sup>Significant (p<0.05).

Diabetic patients were divided according to the duration of disease into two categories: a) duration less than 10 years and b) duration more than or equal to 10 years. For type 1 diabetic group, number of patients under each category was 27 and 23 respectively (Table 4). Similarly

for type 2 DM group, the division was 26 and 24 patients respectively. There was no statistically significant difference (p>0.05) between latency of waves, inter peak latencies and amplitude with duration of disease <10 years and those with  $\ge$ 10 years in both left and right ear in both groups of DM patients (Table 4 and 5).

Table 4: Comparison of BERA parameters in relation to the duration of type 1 DM.

Paramete	rs		Duration <10 years (n=27) Mean±SD	Duration ≥10 years (n=23) Mean±SD	t value	P value
(111 1115)		I	1.65±0.17	1.72±0.23	1.33	0.190
Left ear		II	2.72±0.21	2.80±0.24	1.31	0.197
	Waves	III	3.80±0.19	3.87±0.26	1.18	0.246
		IV	4.81±0.22	4.91±0.28	1.30	0.201
		V	5.71±0.20	5.79±0.31	1.08	0.286
	IPL	I-III	2.15±0.12	2.15±0.12	0.01	0.987
		I-V	4.07±0.19	4.07±0.22	0.05	0.962
		III-V	1.92±0.14	1.92±0.23	0.04	0.967
	Waves	I	1.69±0.19	1.71±0.26	0.30	0.766
		II	2.76±0.30	2.78±0.32	0.20	0.840
		III	3.83±0.23	3.83±0.28	0.01	0.990
Right ear		IV	4.86±0.22	4.93±0.36	0.82	0.419
		V	5.78±0.22	5.82±0.36	0.46	0.648
	IPL	I-III	2.14±0.15	2.12±0.11	0.51	0.612
		I-V	4.09±0.16	4.11±0.32	0.27	0.788
		III-V	1.95±0.11	1.99±0.30	0.59	0.560

<sup>\*</sup>Significant (p<0.05).

Table 5: Comparison of BERA parameters in relation to the duration of type 2 DM.

Parameter	s (in ms)		Duration <10 years (n=26) Mean±SD	Duration ≥10 years (n=24) Mean±SD	t value	P value
	Waves	I	1.72±0.16	1.71±0.12	0.39	0.699
		II	$2.79\pm0.23$	$2.78\pm0.17$	0.14	0.891
		III	3.88±0.26	3.89±0.16	0.23	0.823
T 6.		IV	4.96±0.29	4.88±0.19	1.22	0.267
Left ear		V	5.84±0.35	5.81±0.19	0.50	0.623
	IPL	I-III	2.16±0.19	2.18±0.17	0.57	0.571
		I-V	4.12±0.31	4.00±0.20	0.32	0.749
		III-V	1.97±0.34	1.91±0.17	0.70	0.485
	Waves	I	1.76±0.19	1.77±0.16	0.20	0.843
		II	2.78±0.26	2.83±0.24	0.77	0.445
		III	3.91±0.25	3.94±0.20	0.41	0.686
Right ear		IV	4.84±0.33	4.91±0.23	0.87	0.389
		V	5.85±0.28	5.93±0.16	1.33	0.192
	IPL	I-III	2.14±0.23	2.15±0.19	0.27	0.789
		I-V	4.09±0.28	4.17±0.16	1.18	0.246
		III-V	1.93 ±0.25	1.99±0.17	0.99	0.326

<sup>\*</sup>Significant (p<0.05).

#### DISCUSSION

Diabetes is a complex multisystem disease that requires routine monitoring and control of blood glucose levels for preventing/delaying the onset of complications affecting the renal, visual and peripheral nervous system. Although the peripheral nervous system in DM has been investigated a lot in the literature, the term 'central neuropathy' has been unknown until recently. BERA represent a non-invasive procedure for monitoring CNS involvement in diabetes. By means of this test, functional

and autonomic pathologies from the acoustic nerve to the upper part of the brainstem can be demonstrated at an early stage. Lesions at various levels result in changes in amplitudes and latencies of specific waves of the BERA tracing according to their site of origin. Evaluation of these changes might help to determine early subclinical neurological dysfunction in DM.

A delayed auditory brainstem response (ABR) in diabetic patients was first reported by Donald et al. They demonstrated latency increases particularly in the late

components of ABRs and proposed the term 'central diabetic neuropathy'.<sup>6</sup> After that various studies done by Toth et al, Fedele et al, Lisowska et al, Durmus et al, Fawi et al and Alam et al also indicated the delay of BERA waves and inter peak latencies in diabetic patients.<sup>2,7-11</sup> However, significantly prolonged wave I in type 1 DM patients in present study was not in agreement with study by Fawi et al.<sup>10</sup> Delay in IPL I-III was not significant in this study which is in contrast to results by above studies. Contrasting the results of our study, Verma et al found no abnormalities in the ABR recordings of 22 insulin treated diabetics and concluded that central neural pathways were not involved, at least initially in DM.<sup>12</sup>

In type 2 DM patients, there was a statistically significant delay in waves I to V in both left and right ears except wave II in the right ear which showed no significant difference as compared to controls. The inter peak latencies were significantly delayed in left ear along with a significant delay of IPL III-V in right ear. So our study correlates with study of Durmus et al, Alam et al, Sharma et al and Forogh et al. <sup>9,11,13,14</sup> The prolongation of wave I, is inconsistent feature in the literature as a few authors like Fawi et al and Talebi et al had shown no meaningful difference between diabetics and non diabetics. <sup>10,15</sup>

Wave I, produced by acoustic nerve activity (index of peripheral transmission time) and the IPL I-V or central transmission time i.e., considered as most reliable index of brainstem function were significantly impaired in diabetic patients as compared to controls in our study. findings indicate peripheral and central disturbances in the auditory pathway and they match with results of Fedele et al who also demonstrated signs of peripheral as well as central neuropathy in the ABR recordings in insulin dependent diabetic patients. According to a normal hearing threshold in diabetic patients, delayed wave I could be due to reduced conduction velocity in the auditory nerve that occurred secondary to diabetic neuropathy and indicate that the disorder is peripheral (distal to the nucleus). Prolonged IPL I-III, III-V and I-V explains retro cochlear and brainstem involvement. 14,16,17

It is noteworthy that comparison of ABR prolongation in two types of DM has not achieved much attention in previous studies. Durmus et al found statistically significant difference between latency of wave III and wave V (p<0.05) in two types of diabetes and no significant difference between inter peak latencies in their study. Our study stated no meaningful association between two types of diabetes similar to study by Talebi et al. 15

It has been well accepted that the incidence of diabetic complications increases with the duration of the disease. Donald et al and Fedele et al used ABR and found no correlation between the delay in wave latency in DM and duration of disease. <sup>6,7</sup> In our study, the difference between the latencies of all waves, inter peak latencies was not

significant (p>0.05) when the latencies in patients having DM for less than 10 years were compared to those having longer duration of disease. On the other hand, Seidi et al studied young patients with type 1 DM and found that latencies of ABRs correlate highly with the duration of disease. But Gupta et al and Sharma et al also concluded that abnormal wave latencies were related to the duration of illness in type 2 diabetic patients. Als

#### **CONCLUSION**

Electrophysiological studies like BERA are easy to perform and non-invasive test that may detect minor CNS changes at an early stage of diabetes and can be used in detecting peripheral (auditory nerve) as well as central neuropathy in diabetics even in absence of clinical signs and symptoms of deafness. It seems that a latent period is needed for the development of clinically detectable hearing loss. In view of this study, it is clear that screening of diabetic patients should be done individually for hearing assessment, and for those patients with abnormal evoked potentials, identified early in the course of the disease, special care should be paid to the metabolic regulation of the DM before a permanent disturbance along the 8th nerve takes place. Hence, it is recommended that BERA testing may also be included in the routine screening procedures of diabetic patients like fundus examination and microalbuminuria assessment.

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