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Original Research Article

A Comparative Study of Brainstem Evoked Response Audiometry in Diabetic and Nondiabetic Subjects

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Abstract: Type 2 diabetes mellitus is a common metabolic disorder characterized by variable impairment of the body organs and inappropriate hyperglycemia. This study was undertaken to evaluate auditory function and incidence of hearing impairment in patients with diabetes. In this case-control study, 130 type 2 diabetic patients aged 30 – 55 years and 130 age and sex matched, healthy volunteers were selected. The brainstem evoked response audiometry (BERA) was recorded with RMS EMG EP Marc-II machine. Parameters such as, absolute latencies of wave I, II, III, IV, and V, interpeak latencies I-III, I-V and III-V, were assessed separately for both the ears and analyzed by using unpaired student t-test. Further the cases were classified according to the duration of diabetes, blood glucose levels. Patients with type 2 Diabetes mellitus have subclinical hearing impairment as revealed by impaired auditory brainstem response. In this study diabetic patients showed delayed absolute latencies of wave III and V, IPL I-III and I-V in both the ears when compared to controls, while IPL III-V was delayed only in the left ear. There was a positive correlation between prolongation of latencies and duration of diabetes mellitus. The latencies were also found to be prolonged with altered blood glucose levels. The present study concludes that Patients with type 2 Diabetes mellitus have subclinical hearing impairment as revealed by impaired auditory brainstem response. Meticulous control of blood sugar levels is a must to prevent the early complications of diabetes, so that further damage to auditory pathway can be prevented.
Keywords: Diabetes mellitus; Hearing impairment; Brainstem evoked response audiometry (BERA).

INTRODUCTION

Type 2 diabetes mellitus is a common metabolic disorder characterized by variable impairment of the body organs and inappropriate hyperglycemia.

The prevalence of diabetes mellitus is increasing all over the world particularly in the developing countries. It has emerged as a major public health problem in our country. The WHO estimated that there were 31.7 million persons with diabetes in India in 2000 and that this number is likely to be 71.4 million in 2030[1]. India lead the world with largest number of diabetic subjects earning the dubious distinction of being termed the "Diabetic capital of theWorld"[2]

The association between hearing loss and diabetes mellitus (DM) has been debated since it was first reported by Jordao in 1857[3].

Diabetes–related hearing impairment has been described as sensorineural in origin, implying that the lesion may be cochlear or of the eighth cranial nerve, but evidence favoring a specific mechanism is insufficient[4].

High frequency progressive sensorineural hearing loss is reported to occur in the majority of the patients with DM because of cochlear and eighth nerve involvement[5].

Brainstem evoked response audiometry (BERA) is a simple, non-invasive procedure to detect early impairment of acoustic nerve and CNS pathway, even in the absence of specific symptoms. Brainstem auditory evoked potentials (BAEP) are recorded from the ear and vertex in response to brief auditory stimulation. They assess the conduction through the auditory pathway upto the midbrain. The recording is in the form of waves having peaks and troughs. There are

seven waves traditionally designated with roman numerals from I to VII occurring within 10 msec of the acoustic stimulus[6].

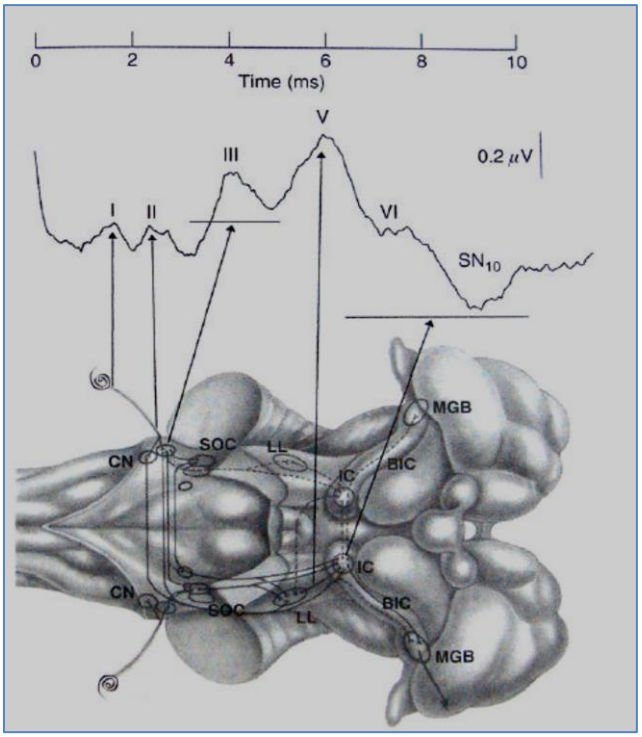

Fig-1: Anatomical correlation of the neural generators of BAEP

MGB – Medial geniculate body SOC – Superior olivery complex
IC – Inferior colliculus CN – Cranial nerve
LL – Lateral leminiscus MGB - Medial geniculate body

Generators of BAEPs:

Wave form	Generators
I	VIII nerve
II	Cochlear nucleus
III	Superior olivary nucleus
IV	Lateral lemniscus
V	Inferior colliculi
VI	Medial geniculate body
VII	Originate between medial geniculate body to auditory complex

It is suggested that BERA can demonstrate electrophysiologically any lesions from acoustic nerve to the brainstem and can be used in diabetics to show subclinical variances and central neuropathy.[7]

This study was undertaken to evaluate auditory function and incidence of hearing impairment in patients with Type 2 diabetes and to find whether any correlation exists between the observed abnormalities and the fasting blood glucose levels and duration of diabetes or not.

OBJECTIVES:

1. To analyse brainstem evoked response audiometry in diabetic subjects.
2. To compare the auditory brainstem response between diabetic subjects and age matched controls for the following parameters-
   a) Absolute latency of wave I, II, III, IV and V.
   b) Interpeak latencies I-III, I-V and III-V waves.

MATERIAL AND METHODS:

The study was conducted in the department of Physiology, J.J.M medical college, Davangere,between the period of Jan 2009 to Jan 2012. In this study 130 diabetic patients between 30 to 55 years attending medical outpatient department of Bapuji hospital and Chigateri General Hospital attached to J.J.M Medical College, Davangere were selected and 130 normal age

matched subjects were selected randomly from the general population.

Inclusion criteria:

- Age-group between 30 - 55 years
- Patients who are biochemically proved diabetes mellitus.
- Subject with more than 2 years of duration of diabetes mellitus.
- Normal healthy age matched controls between 30-55 years.

Exclusion criteria:

- Patients with acute complication of diabetes like diabetic ketoacidosis, nonketotic hyper-osmolar coma and hypoglycemia.
- Patients, who had history of ear discharge, associated endocrine disorder eg. Myxedema, headinjury, neurological deficit, cerebrovascular accident ornoise exposure in past.
- Patients with history of drug intake known to cause central neuropathy eg.Reserpine, alphamethyldopa, phenytoin and nitrofurantoin.
- Patients who had history of taking ototoxic drugs eg. Gentamycin, streptomycin, kanamycin, amikacin andquinine.
- Patients with history of hearing loss prior to diagnosis of diabetes.

The study and control group were selected as per inclusion and exclusion criteria. Written and informed consent was taken for the study after explaining the procedure and its significance in their vernacular language. A brief personal history was taken and a clinical examination of all the systems was done to exclude medical problems and to prevent confounding of results. Height and weight of the subject was recorded. Height was measured to the nearest 0.5 centimeters with wall mounted scale and weight measured to the nearest 0.5 kgs using a beam balance scale in light indoor clothing.

BERA recording:

After selecting the subjects, they were subjected to BERA testing on RMSEMG. EP MARK-II machine manufactured by RMS RECORDERS and MEDICARESYSTEM, Chandigarh.

Procedure in brief: Recording of BERA was carried out in a quiet and dimly litroom .Subjects were asked to lie down comfortably on a bed in a fully relaxed state. The skin at the point of placement of electrodes was cleaned with spirit. Using electrode paste surface electrodes were placed at the vertex (Cz), both mastoid (Ai &Ac) forehead (ground). The resistance was kept below 5 K. Monoaural auditory stimulus consisting of rarefaction clicks of 100 microseconds were delivered throughelectrically shielded earphones at a rate of 11.1/sec. Contralateral ear was masked with pure white noise of 40 dB. A band pass of 150-3000 Hz was used to filter out undesirable frequencies in the surroundings. Responses to 2000 click presentations were averaged for 10 msec.

Parameter studied: BERA threshold for each ear with absolute latencies of wave I, II, III, IV and V waves. Interpeak latencies (IPL) of I-III, I-V and III-V were considered from the recording for comparison among diabetic and non-diabetic controls as well as diabetics of different durations.

Statistical analysis:

The results are expressed as mean and standard deviation, separately for right and left ear. Unpaired t-test was used for intergroup comparisons, p-value of 0.05 or less has considered as statistical significance.

RESULTS:

The basic data i.e. age, sex, height, weight and body surface area did not show any statistical significance between the diabetics and controls ($P > 0.05$), but there was a statistically highly significant difference between the mean FBG levels of both the groups ($P < 0.001$), the values being much higher in diabetic patients. The duration of T2DM in our subjects ranged from 1-15 years, the mean value being 11.38 ± 6.14 years (Table 1).

Furthermore, since all corresponding mean BAEP wave latencies are comparable between right and left ear, in both diabetic and control subjects [Tables 2 and 3] thus, it is clear that the right-left latency asymmetry is within normal limits in both these groups.

A comparison between the mean values of the various wave latencies and IPLs was done separately for both the ears, in diabetics and controls [Table 4].

It was seen that the absolute latencies of wave III and V, and mean IPL I-III and I-V were highly significantly in both the ears in diabetics as compared to controls (P values being < 0.005).

Also, the mean IPL III-V was significantly higher in diabetic, but only with left ear stimulation ($P = 0.02$), while it was comparable with control group, with left ear stimulation. None of the differences between the mean latencies of waves I, II,IV were statistically significant between both the groups ($P > 0.05$), with either ear stimulation.

Correlation between latencies of BERA and duration of diabetes mellitus

A comparison between the mean values of the various absolute latencies and IPLs was done separately for both the ears, in diabetics of less than 10 years, diabetics of more than 10 years duration and controls [Table 5].

Correlation between latencies of BERA and blood glucose level in diabetics

A comparison between the mean values of the various absolute latencies and IPLs was done separately for both the ears, in diabetics with blood glucose level less than 140 mg/dl and more than 140 mg/dl [Table 6].

Table 1: Anthropometric parameters in Controls & Cases

Basic characteristics	Case (n=130)	Control (n=130)	Significance
Age in years	46.73 ± 5.96	46.75 ± 6.06	P>0.05
Sex	M:67.5% F:32.5%	M:67.5% F:32.5%	P>0.05
Height in cm	164.27 ± 7.97	164.18 ± 7.85	P>0.05
Weight in kg	68.03 ± 11.55	68.25 ± 11.90	P>0.05
BSA in m^2	1.73 ± 0.16	1.74 ± 0.17	P>0.05
FBS (mg/dl)	117.6±16.84	72.8±4.62	P<0.05
Duration of disease (years)	11.38±6.14	NA	NA
Inference	Samples are age, sex, height, weight and BSA matched (P>0.05)		

Table 2: Comparison of BAEP waveform latencies (in msec) between the right and left ear in patients with T2DM

Measurement		Right ear Mean ± SD	Left ear Mean ± SD	*P* value
Absolute latencies (ms)	**I**	1.67 ± 0.23	1.69 ± 0.23	0.483
	II	2.67 ± 0.17	2.65 ± 0.28	0.487
	III	3.62 ± 0.32	3.61 ± 0.23	0.772
	IV	4.84 ± 0.29	4.79 ± 0.45	0.289
	V	5.78 ± 0.40	5.71 ± 0.59	0.264
Inter peak latencies (ms)	**I-III**	1.88 ± 0.30	1.87 ± 0.41	0.822
	I-V	3.97 ± 0.39	3.98 ± 0.67	0.883
	III-V	1.97 ± 0.34	1.99 ± 0.50	0.706

Table 3: Comparison of BAEP waveform latencies (in msec) between the right and left ear of controls

Measurement		Right ear Mean ± SD	Left ear Mean ± SD	*P* value
Absolute latencies (ms)	**I**	1.63 ± 0.08	1.65 ± 0.07	0.397
	II	2.64 ± 0.26	2.63 ± 0.19	0.723
	III	3.51 ± 0.21	3.53 ± 0.22	0.454
	IV	4.78 ± 0.27	4.73 ± 0.24	0.116
	V	5.33 ± 0.18	5.30 ± 0.16	0.156
Inter peak latencies (ms)	**I-III**	1.78 ± 0.13	1.75 ± 0.20	0.153
	I-V	3.80 ± 0.19	3.77 ± 0.18	0.192
	III-V	1.91 ± 0.18	1.89 ± 0.15	0.331

Table 4: Comparison of BERA between Diabetics and Healthy Controls

Side	Measurement		Controls		Diabetics		Controls v/s Diabetics
			Mean	SD	Mean	SD	P value
Left Ear	Absolute latencies (ms)	I	1.65 ± 0.07		1.69 ± 0.23		0.06
		II	2.63 ± 0.19		2.65 ± 0.28		0.50
		III	3.53 ± 0.22		3.61 ± 0.23		0.004 **
		IV	4.73 ± 0.24		4.79 ± 0.45		0.18
		V	5.30 ± 0.16		5.71 ± 0.59		0.001 **
	Inter peak latencies (ms)	I-III	1.75 ± 0.20		1.87 ± 0.41		0.003 *
		I-V	3.77 ± 0.18		3.98 ± 0.67		0.001 **
		III-V	1.89 ± 0.15		1.99 ± 0.50		0.029 *
Right Ear	Absolute latencies (ms)	I	1.63 ± 0.08		1.67 ± 0.23		0.062
		II	2.64 ± 0.26		2.67 ± 0.17		0.27
		III	3.51 ± 0.21		3.62 ± 0.32		0.001 **
		IV	4.78 ± 0.27		4.84 ± 0.29		0.08
		V	5.33 ± 0.18		5.78 ± 0.40		0.001 **
	Inter peak latencies (ms)	I-III	1.78 ± 0.13		1.88 ± 0.30		0.001 **
		I-V	3.80 ± 0.19		3.97 ± 0.39		0.001 **
		III-V	1.91 ± 0.18		1.97 ± 0.34		0.08

Unpaired t test, *Significant, ** Highly significant

Table 5: Comparison of BERA parameters with relation to duration of type 2 diabetes mellitus

Side	Measurement		Controls (n=130)	Diabetics (< 10yrs) (n = 54)	Diabetics (> 10yrs) (n = 76)	Controls v/s Diabetics (< 10yrs)	Controls v/s Diabetics (> 10yrs)	Diab.(<10yrs) v/s Diab. (> 10yrs)
			Mean±SD	Mean±SD	Mean±SD	P Level	P Level	P Level
Left Ear	Absolute latencies (ms)	I	1.65 ± 0.07	1.68 ± 0.23	1.69±0.28	0.15	0.11	0.75
		II	2.63 ± 0.19	2.65 ± 0.28	2.68±0.36	0.50	0.16	0.45
		III	3.53 ± 0.22	3.61 ± 0.23	3.78±0.22	0.004 **	0.001 **	0.001*
		IV	4.73 ± 0.24	4.76 ± 0.45	4.78±0.54	0.50	0.33	0.74
		V	5.30 ± 0.16	5.71 ± 0.59	6.01±0.58	0.001 *	0.001 **	0.001*
	Inter peak latencies (ms)	I-III	1.75 ± 0.20	1.83 ± 0.41	1.91±0.45	0.04 *	0.003 **	0.13
		I-V	3.77 ± 0.18	3.90 ± 0.67	4.12±0.76	0.03*	0.001 **	0.01*
		III-V	1.89 ± 0.15	1.92 ± 0.50	2.01 ±0.51	0.51	0.01*	0.15
Right Ear	Absolute latencies (ms)	I	1.63 ± 0.08	1.65 ± 0.23	1.68±0.29	0.34	0.06	0.35
		II	2.64 ± 0.26	2.66 ± 0.17	2.68±0.19	0.46	0.15	0.37
		III	3.51 ±0.21	3.58 ± 0.32	3.64±0.42	0.04 *	0.002*	0.19
		IV	4.78 ±0.27	4.80 ± 0.29	4.83±0.26	0.56	0.13	0.38
		V	5.33 ± 0.18	5.70 ± 0.40	5.82 ±0.37	0.001*	0.001 **	0.01
	Inter peak latencies (ms)	I-III	1.78 ± 0.13	1.84 ± 0.30	1.91±0.34	0.03*	0.001 **	0.08
		I-V	3.80 ± 0.19	3.89 ± 0.39	4.11±0.29	0.01*	0.001 **	0.001*
		III-V	1.91 ± 0.18	1.96 ± 0.34	1.98±0.36	0.1	0.04*	0.6

Unpaired t test, *Significant, ** Highly significant

Table 6: Comparison of BERA parameters with relation to blood glucose levels in type 2 diabetes mellitus patients

Side	Measurement		Bl.Glucose< 140 (n =62)	Bl.Glucose> 140 (n = 68)	BGL<140 v/s BGL>140
			Mean ± SD	Mean ± SD	P Level
Left Ear	Absolute latencies (ms)	I	1.66±0.28	1.72 ± 0.21	0.06
		II	2.61±0.36	2.67 ± 0.24	0.11
		III	3.58±0.22	3.66 ± 0.21	0.003*
		IV	4.74±0.54	4.80 ± 0.55	0.33
		V	5.56±0.58	5.97 ± 0.50	0.001**
	Inter peak latencies (ms)	I-III	1.85±0.45	1.89 ± 0.39	0.44
		I-V	3.94±0.76	4.05 ± 0.70	0.23
		III-V	1.95 ±0.51	2.02 ± 0.58	0.30
Right Ear	Absolute latencies (ms)	I	1.65 ± 0.23	1.67 ± 0.29	0.53
		II	2.66 ± 0.17	2.69 ± 0.18	0.17
		III	3.61 ± 0.32	3.64 ± 0.40	0.51
		IV	4.82 ± 0.29	4.87 ± 0.28	0.16
		V	5.73 ± 0.30	5.89 ± 0.32	0.001*
	Inter peak latencies (ms)	I-III	1.85 ± 0.30	1.90 ± 0.33	0.20
		I-V	3.93 ± 0.39	4.01 ± 0.41	0.11
		III-V	1.94 ± 0.34	1.99 ± 0.35	0.24

Unpaired t test, *Significant, ** Highly significant

DISCUSSION:

Central diabetic neuropathy is a newer concept and it can be detected by simple and non-invasive methods. One of these methods is BERA. By this method, functional and autonomic pathologies from the acoustic nerve to the upper part of the brainstem can be demonstrated at an early stage. Lesions at these levels results in changes in BERA amplitudes and latencies. Evaluation of these changes might help to determine early sub clinical neurological dysfunctions in diabetes mellitus[8].

In our study we found that there was lengthening in latencies of wave III and V, IPL I-III and I-V in diabetic patients when compared to controls ($p<0.05$). While IPL III-V was delayed only in left ear ($p<0.05$).The absolute latencies of waves I, II and IV however, remained unchanged on either side.

The delay in latencies of waves III and V, IPL I-III and III-V signifies conduction delay from the most peripheral part of the auditory pathway to the pons and mesencephalon. This may be due to demyelination which results in delay of the latter wave components. Similar findings were reported earlier by Abdulkadiroglu *et al.* [9], Di Leo *et al.* [10].

Correlation between BERA response and duration of diabetes

In our study we found that absolute latencies of waves III and V were prolonged in diabetic patients with duration of illness more than 10 years when compared to diabetic patients with less than 10 years of illness. Also absolute latencies of waves III and V were significantly prolonged in both these groups when compared to controls ($p<0.05$).

From the above findings we can say that there is a positive correlation between the duration of diabetes and lengthening of latency. This condition can be explained due to sub clinical ischemia, which can develop during diabetic process like atherosclerosis and sorbitol accumulation.

The present study concurs with findings of Naini *et al.* [11], which showed that short term diabetes mellitus patients have minor abnormality in their BERA response, while those having diabetes for 10-19 years, the duration of absolute latency in wave III to V had increased by 0.3 msec, as compared to the control group.

We found a lengthening in the IPL I-III and I-V in both the ears in diabetics with increase in duration of illness when compared to controls, also diabetic patients with more than 10 year duration of illness showed significant delay in IPL III-V when compared to controls.

Abnormal BERA responses were more common in diabetic patients with duration of illness more than 10 years. Microangiopathy is responsible for diabetic neuropathy, which is a long term complication and this explains a higher incidence of abnormal BERA responses in patients with prolonged illness. These findings are similar to those reported by Das P *et al*[12], who concluded that longer the duration of diabetes the chances of hearing loss is more across all the ranges of frequencies.

Correlation between BERA response and blood glucose levels in diabetic patients

We found that absolute latencies of wave III and V in left ear were delayed in diabetics with increased blood sugar levels when compared to diabetics with good metabolic control ($p<0.05$), while right ear showed delay only in latency of wave V, compared to those patients with good metabolic control ($p<0.05$).

Similar findings were reported by Pessine *et al.* The relationship between hearing loss at different frequencies and metabolic control revealed that poor glycemic control leads to hearing loss at all frequencies, but much higher in mid and high frequencies[13].

Though our study is by no means exhaustive, it does provide a glimpse about the effect of type 2 diabetes mellitus on hearing, which brings about changes in BERA parameters.

Also since only very few studies have been done on this aspect, further research is needed to study the effect of type 2 diabetes mellitus on hearing. BERA abnormalities in diabetes initially seem to appear due to central impairment of the auditory pathway which gradually involves the peripheral parts in due course of time.

Thus BERA can be of clinical importance for the diabetes, as it may reflect the degree of neural affection in the auditory pathway and may alert the patients for adequate glycemic control, which can resist the neuropathic progression any further.

CONCLUSIONS AND RECOMMENDATIONS:

In this study, significant differences in BERA latencies were seen between T2DM patients and healthy controls. From our study we can say that duration of illness and presence of high fasting blood glucose levels are definite risk factors for the development of central neuropathy. Therefore it is important to have a good glycemic control in order to avoid involvement of auditory nerve resulting in hearing impairment.

As diabetes is rampant in our country, it is necessary to consider the “hearing status as a long term complication of diabetes”.

It is recommended to perform an audiometric test initially on all the diabetic patients and to keep this as an “initial record of auditory examination of patients”. Also, performing this test every year on a regular basis could help the physician to up-date their record of the hearing status of the patients as well as to give the necessary guidance in regard to the control of diabetes to them.

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