

TYPE-2 DIABETES MELLITUS AND BRAIN STEM EVOKED RESPONSE AUDIOMETRY: A CASE CONTROL STUDY

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ABSTRACT

BACKGROUND AND OBJECTIVE

Type-2 Diabetes Mellitus (T2DM) causes pathophysiological changes in multiple organ system. The peripheral, autonomic and central neuropathy is known to occur in T2DM, which can be studied electrophysiologically.

AIM

Present study is aimed to evaluate functional integrity of auditory pathway in T2DM by Brainstem Evoked Response Audiometry (BERA).

MATERIAL AND METHOD

In the present case control study, BERA was recorded from the scalp of 20 T2DM patients aged 30-65 years and were compared with age matched 20 healthy controls. The BERA was performed using EMG Octopus, Clarity Medical Pvt. Ltd. The latencies of wave I, III, V and Wave I-III, I-V and III-V interpeak latencies of both right and left ear were recorded at 70dBHL.

STATISTICAL RESULT AND USE

Mean±SD of latencies of wave I, III, V and interpeak latency of I-III, I-V and III-V were estimated of T2DM and healthy controls. The significant differences between the two groups were assessed using unpaired student 't' test for T2DM and control groups using GraphPad QuickCalcs calculator. P value <0.05 was considered to be significant.

RESULT

In T2DM BERA study revealed statistically significant ($p < 0.05$) prolonged latencies of wave I, III and V in both right (1.81±0.33ms, 3.96±0.32ms, 5.60±0.25ms) and left (1.96±0.24ms, 3.79±0.22ms, 5.67±0.25ms) ear as compared to controls at 70dB. Wave III-V interpeak latency of left ear (1.87±0.31, 1.85±0.41ms) and wave I-III (2.51±0.42ms, 1.96±0.48ms) and III-V (2.01±0.43ms, 1.76±0.45ms) of right ear was prolonged in diabetic patient as compared to controls, although no significant difference was obtained ($p < 0.05$).

INTERPRETATION AND CONCLUSION

Increase in absolute latencies and interpeak latencies in T2DM patients suggest involvement of central neuronal axis at the level of brain stem and midbrain.

KEYWORDS

Type 2 Diabetes Mellitus, Central Neuropathy, Brainstem Evoked Response Audiometry.

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INTRODUCTION

Diabetes mellitus is an endocrinological and metabolic disorder that involves the dysregulation of use and/or the production of insulin, the hormone that is required for regulation of glucose in the body. Hyperglycaemia or elevated blood glucose levels is the hallmark characteristic of the disease.¹ T2DM is characterized by a resistance to the action of insulin, a relative deficiency of insulin production or both. Insulin resistance leads to deficiency in the necessary insulin action required for the proper metabolism of carbohydrates, fats and proteins.¹ It is associated with high morbidity and mortality due to its macrovascular and microvascular complications like myocardial infarction, hypertension, peripheral vascular disease, neuropathy, nephropathy and retinopathy.²

Diabetic neuropathy can be classified as peripheral, autonomic, proximal or focal affecting different parts of the body in various ways. Autonomic and peripheral neuropathy, nephropathy, retinopathy and hearing impairment are some of the late complications of T2DM.² Micro- and macro-angiopathic disturbances and myelin degeneration are responsible for late onset of neuropathy. Diabetes related hearing impairment has been described as sensory neural in origin, implying that the lesion may be cochlear or of the eighth cranial nerve, but evidence favouring a specific mechanism is insufficient.³ High frequency progressive sensorineural hearing loss is reported to occur in the majority of the patients with diabetes mellitus because of cochlear and eighth nerve involvement.⁴

It is suggested that Brain Stem Auditory evoked potential (BERA) can demonstrate electrophysiologically any lesion from acoustic nerve to Brain stem and can be used in diabetics to show subclinical variances and central neuropathy.⁵ At present BERA has become a routine part of the standard audiological test battery. It is based upon the study of electrical potential generated by auditory pathway in response to sound stimuli.

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Their latencies are quite specific and their reproducibility is very good. The differences in latencies between these peaks are measure of the conduction time between the brainstem generators. Interpeak latencies I-III, III-V and I-V are indicative of central conduction from brainstem to mid-brain level in auditory pathway.⁶

With this background present study was undertaken to evaluate auditory function and detection of central neuropathy in patient with T2DM.

MATERIALS AND METHODS

The present study was conducted in the Department of Physiology, LNMCM Bhopal with the approval of institutional ethical committee.

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Patients were referred to Department of ENT for complete check-up to exclude any ear pathology. Patients with acute complications of diabetes like diabetic ketoacidosis, non-ketotic hyperosmolar coma, history of ear discharge, associated endocrinal disorder, history of drug intake known to cause central and peripheral neuropathy or ototoxic drug were excluded from the study.

Based on inclusion and exclusion criteria and willingness of subjects to participate in the study 20 T2DM patients (Age 30-65 years, Male-12, Female-08) and 20 healthy controls (Age 30-65 years) were selected for the study. Proper history and anthropometric measurements of all the subjects included in the study were done. Complete clinical examination including general systemic and audiometric examination were done. Biochemically random blood glucose was estimated to confirm T2DM by GOD POD method.⁷

Bera was recorded using EMG Octopus by Clarity Medical Pvt. Ltd. with 2 amplifiers hardware version 2.5 and software version 4.2 in sound proof room with patient in relaxed supine position. Prior to the test the procedure was explained to the patient. Skin of the forehead and of mastoid process were cleaned with acetone soaked swab. Then electrodes were properly cleaned and placed using 10-20 conductive paste applied in the recess of electrode and was then adhered to cleaned surface of their respective side. Standard silver chloride electrodes of 1cm diameter was placed according to 10-20 International System.⁸

Ground Electrode: Fz

Reference Electrode (Cz): Vertex

Active Electrode (Oz): Mastoid Process

The stimulus was given using head phone. The stimulus rate was set at 11 clicks/sec., sweep speed was set at 1ms/div., low filter was set at 100Hz and high filter at 3KHz. Recording were taken at 70dBHL for 3KHz frequency with rare click stimulus. Averaging was done for 2000 epochs. Impedance was kept less than 5kΩ. At least 2 recordings were taken to confirm the re-reproducibility of wave form and the absolute latencies of wave I, III and V and interpeak latencies I-III, III-V, and I-V were recorded.

Results of T2DM patients were compared with those of the healthy subjects. Mean±SD of absolute latencies of wave I, III, V and interpeak latencies I-III, III-V and I-V were calculated. The significant difference between the two groups were assessed using unpaired student 't' test. P value <0.05 was considered statistically significant.

OBSERVATION AND RESULT

Sl. No.	Parameters	Control Group	Diabetic Group	t-value	p-value
1	Age (Years)	47.25±6.41	51.75±11.15	1.56	NS
2	*RBG (mg/dl)	101.35±27.07	178.31±76.58	4.23	<0.00
3	Height (cm)	157.10±10.36	154.42±1.90	0.91	NS
4	Weight (Kg)	62.73±10.20	62.26±13.27	0.12	NS
5	BMI (Kg/m ²)	25.47±4.10	26.08±5.04	0.42	NS

Table 1: Comparison of anthropometric measurements between control and diabetic group

*Random blood glucose was found to be higher in diabetic patients as compared to control group.

Wave Latency (ms)	Control Group (n=20)	Diabetic Group (n=20)	t-value	p-value
I	1.62±0.29	1.96±0.24	4.03	<0.0001*
III	3.63±0.25	3.79±0.22	2.14	<0.05*
V	5.41±0.37	5.67±0.25	2.60	<0.01*
I-III	2.02±0.41	1.60±0.61	-	-
I-V	3.89±0.36	3.71±0.39	-	-
III-V	1.85±0.41	1.87±0.31	0.71	NS

Table 2: Comparison of absolute latencies & inter peak latencies of left ear in control group and in patients with Type 2 diabetes mellitus at 70dB

*P<0.05 statistically significant, NS- not significant

Statistically significant delay in absolute latencies of wave I, III, V of left ear in diabetic group as compared to control group was recorded. Although wave III-V interpeak latency was found to be higher in diabetic patients as compared to controls, but difference was not statistically significant.

Wave Latency (ms)	Control Group (n=20)	Diabetic Group (n=20)	t-value	p-value
I	1.60±0.29	1.81±0.33	2.13	<0.05
III	3.56±0.34	3.96±0.32	3.83	<0.001
V	5.33±0.51	5.60±0.25	2.12	<0.05
I-III	1.96±0.48	2.51±0.42	1.33	NS
I-V	3.45±0.32	3.72±0.48	-	-
III-V	1.76±0.45	2.01±0.43	1.79	NS

Table 3: Comparison of absolute latencies and interpeak latencies of right ear in normal subjects and in patients with diabetes mellitus at 70dB

Absolute latencies of wave I, III and V was significantly prolonged in diabetic as compared to controls. Wave I-III and III-V interpeak latency was found prolonged in diabetic as compared to control, but difference was not statistically significant.

DISCUSSION

BERA represents the electrical events generated along the auditory pathway recorded from the scalp by far field averaging methods.^{9,10} The response to a click consist of 6 or 7 small vertex positive waves recorded in the first 10ms after the stimulus. Wave I is produced by the acoustic nerve activity that wave II can reflect the activity of the cochlear nucleus with a contribution from the auditory nerve, that Wave III can be referred to the generators in the superior olivary complex and the lateral lemniscii, that the wave IV-V complex is generated in the axons and/or nuclei of the lateral lemniscii and probably also from inferior colliculi.¹¹

Peripheral neuropathy along with involvement of central neuronal axis associated with diabetes is responsible for myriad of symptoms.¹² Degenerative abnormalities of the brain tissue and atrophy of the spiral ganglion of the cochlea in the patients of diabetes mellitus suggests the presence of central neuropathy.¹³ T2DM subjects are more prone to develop sensory neural hearing loss.¹⁴ Friedman et al.¹⁵ and Goldsher et al.¹⁶ reported sensory neural deafness in 55% and 94% T2DM patients with neuropathy. In the present study abnormal BERA was recorded in 80% T2DM patients in left ear and 98% cases in right ear. Asymmetrical recording may be due to less duration of the disease in maximum number of cases. Studies in the literature have disagreed about the duration of disease and control of diabetic status to complications.^{17,18} Contrary to the findings of Olsson et al.¹⁹ and Reske et al.²⁰ who concluded brain involvement in longstanding diabetes.

Study by Triana et al.²¹ also found loss of sensory hair cells in cochlea in diabetics resulting in cochlear hearing loss.

Gupta R, et al. (2014).²² in their study on 25 T2DM patients found prolonged wave III and V, interpeak I-III, III-V, III-V at 70dB. They reported abnormal findings in 18 cases.

Similar to our study prolonged wave I and wave III latency was seen in T2DM as compared to control. Wave V latency was normal in maximum number of cases in both right and left ear.

Wave I-III interpeak latency was delayed in right ear in 55% cases in T2DM suggesting delayed transmission of auditory pathway of diabetes at level of brainstem and midbrain. Similar prolongation of wave I-III and I-V interpeak latency was reported at 70dB by Siddique et al. (2014).⁷ and Fiddle et al. (1984).²³

In our study, 04 patients with duration >10 year presented with prolonged wave I latency in 75% patients. Although neither significant prolongation nor any correlation could be established with duration of disease similar to Verma A.¹³ et al. Sharma Ravindera.²⁴ and Siddiqui et al. (2014).⁷ reported delayed BERA in 92.3% and 91% patients with duration >10 years respectively.

Abnormal brainstem evoked responses were more in patient with duration >10 years is reported by many authors.^{13,24} Microangiopathy, a long-term complication explain the cause of abnormal BERA in long duration T2DM (10 years) as reported by Jorgenson et al. (1962).²⁵

Some studies.²¹ found that the hearing loss is irreversible even after the control of diabetes, so we recommend appropriate preventions to be taken in T2DM patients before the development of complication.

CONCLUSION

BERA is simple non-invasive procedure to detect early impairment of acoustic nerve and CNS pathway central neuropathy in diabetes mellitus. CNS involvement does not seem to be related with duration of diabetes or presence of chronic complications. BERA recording can represent an objective clinically useful non-invasive procedure to stress the early impairment both of the auditory nerve and of brainstem function is not related to blood glucose level. However, duration of illness and presence of peripheral neuropathy are definite risk factor for the development of central neuropathy.

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