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Research Article

STUDY OF BRAIN STEM AUDIOMETRY EVOKED POTENTIAL IN PATIENTS WITH TYPE 2 DIABETES MELLITUS IN A TERTIARY CARE CENTRE

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A R T I C L E I N F O

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A B S T R A C T

Introduction: Type 2 Diabetes mellitus is associated with various complications including neuropathy. Though Peripheral neuropathy has been thoroughly explored, central neuropathy is yet conspicuous area which needs to be elucidated using novel techniques. Brainstem Evoked Response Audiometry (BERA) is a sensitive technique to assess early impairment of the auditory nerve and of brain stem function which can be a surrogate marker for central neuropathy.

Objective: Present study was aimed to access brain stem evoked potential in patients of type II DM with controlled and uncontrolled blood sugar level groups.

Methodology: Two groups including controlled and uncontrolled T2DM were included in this study and their audiometric analysis was performed using Brainstem Evoked Response Audiometry. All testing was performed in sound treated room in which ambient noise level well within the permissible limits. Absolute latencies of wave I III & V in both ear and Interpeak latencies of wave I-III, III-V, I-V in both ears were recorded.

Result: Study groups were found to be matched for age (p=0.20), gender distribution (p=0.67) and duration of DM (p=0.441). FBS (p=0.001), PPBS (0.001) and HbA1c (p<0.0001) were found to be significantly higher in Group 2. Frequency of severe hearing loss (p<0.0001), deafness (p=0.0025), tinnitus (p=0.0017 and vertigo (p=0006) were significantly higher in Group 2. Comparison of latency between Group 1 and Group 2 was performed at difference level. Absolute latency V as well as interpeak latency III-IV were found to be significantly higher in uncontrolled DM group (Group 2).

Conclusion: This study suggests that if brain stem evoked response audiometry is carried out in diabetic patients, involvement of central neuronal axis can be detected earlier in patients and will help to reduce morbidity and early prevention and management.

INTRODUCTION

Type 2 diabetes mellitus is a chronic endocrinological entity characterised by syndrome of hyperglycemia due to relative or absolute deficiency of insulin. A diffuse peripheral polyneuropathy involving autonomic and peripheral nerves is a well-known complication of prolong Diabetes Mellitus. Diabetic neuropathy occurs in 50% of individuals with long-standing type 1 and type 2 DM with subjects with longer duration of hyperglycaemia being at higher risk. Obvious symptomatic stage of neuropathy is preceded by long asymptomatic subclinical stage. Those who are diabetic may suffer from hearing loss also. This hearing loss tends to be sensory neural, with subtle progression and usually bilateral. Loss of higher frequency is usually encountered. Brainstem Evoked Response Audiometry (BERA) is a non-invasive electrophysiological sensitive technique to assess and detect early impairment of the cochlear and retro cochlear pathway of hearing.

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The present study was aimed to access brain stem evoked potential in patients of type II DM with controlled and uncontrolled blood sugar level groups. Further, an attempt was made to relate abnormal brainstem evoked responses with the blood glucose level and central neuropathy.

MATERIAL AND METHODS

The present hospital bases observational case control study was conducted during July 2017 to September 2018 in ENT OPD Dr, B. R. A. M. Hospital which is a tertiary care centre. Study was approved by institutional ethical committee of Pt. J. N. M. M. C. (No. MC/Ethics/112, dated 17/09/18)and all the precautions were followed to comply with declaration of Helsinki. Total 96 diabetic subjects with 48 subjects each in controlled (i.e. HBA1C<7) and uncontrolled (i.e. HBA1C>7) diabetes group were selected by random sampling.

Subjects in age group 30 to 60 years who are biochemically proved having Type II diabetes mellitus having more than 2 year of duration of disease were included in the study.

Patient with acute complication of diabetes, history of ear discharge, associated endocrine disorder, head injury, neurological deficit, cerebrovascular accidents, noise exposure in past, history of drug intake known to cause central neuropathy or patients who has history of ototoxic drugs were excluded from study. Patients with history of hearing loss prior to diagnosis of diabetes were also excluded.

Subjects were recruited after informed and written consent. Past history and family history were enquired. Five milliliter of blood in fasting state was collected for fasting blood sugar (FBS) and glycated haemoglobin (HbA1c) and 2 ml of blood was collected 2 hours after food for post prandial blood sugar level (PPBS).

Detailed ENT examination was performed including Otoscopy. Clinically hearing level was assessed by Rinne's, weber and absolute bone conductive tests using 512 Hz tuning fork (Fig. 1). After following above mention criteria and method, patients were finally selected for BERA. These were divided into two groups. Group 1- controlled blood sugar level (i.e. HBA1C<7) and Group 2 uncontrolled blood sugar level (i.e. HBA1C>7). BERA was recorded by GSI - AUDERA Audiometer. Click evoked ABR was performed in both ears monaurally. The testing was performed while patient was sleeping. Single channel recording was used in which non-inverting electrode was placed on the upper forehead, the inverting electrode was placed on mastoid of test ear and ground electrode was placed on mastiod of non-test ear. Electrode impedances were less than 5k, and inter-electrode impedance were less than 2k, Eartone -3A insert earphone was used to present the stimuli. At least 2000 click stimuli in rerefaction polarity presented at 30.1 click/sec repetition rate. Potentials were recorded in band - pass fitter setting 100 Hz 3000 Hz with an amplification factor of 1,00,000. Recording were started from 90 dBHL. ABR waveforms were analysed at 10ms time window setting. All testing was performed in sound treated room in which ambient noise level was within the permissible limits. Absolute latencies of wave I, III & V in both ear and interpeak latencies of wave I-III, III-V and I-V in both ears were recorded.

These data were compared with results obtained from the recordings of control group. Statistical analysis was done to compare and to see the signification of any variation. Students 't' test and Chi square test were performed as tests of signification and 'p' value <0.05 was considered as level of significance.

OBSERVATIONS AND RESULT

Over all age distribution showed middle age group (41-50)preponderance in type-II DM. Gender related frequency showed male predominance in type-II DM. Study included controlled and uncontrolled type 2 DM subjects (48 each) belonging to Group 1 and group 2. Various complaints such as deafness, tinnitus and vertigo were noted in 20 (20.8%), 18 (18.8%) and 20 (20.8%) subjects respectively.(Table1)

Two study groups were compared in respect to various parameters (Table-2). Both groups were found to be matched for age (p=0.20), gender distribution (p=0.67) and duration of DM (p=0.441). FBS (p=0.001), PPBS (0.001) and HbA1c (p<0.0001) were found to be significantly higher in Group 2. Frequency of severe hearing loss (p<0.0001), deafness (p=0.0025), tinnitus (p=0.0017 and vertigo (p=0006) were significantly higher in Group 2.

Table 1 General characteristics of study subjects

Characteristics	Age (Yrs)	Frequency	Per cent
Age (Years)	</=30	5	5.2
	31-40	24	25
	41-50	44	45.83
	51-60	23	23.95
Gender	F	34	35.4
	M	62	64.6
Type of DM	Controlled	48	50
	Uncontrolled	48	50
Deaf ness		20	20.8
Tinnitus		18	18.8
Vertigo		20	20.8

Table 2 Comparison of various parameters between Group 1 and Group 2

Characteristics		Group		Total	P Value
		Controlled DM (group 1)	Uncontrolled DM (group 2)		
Age (Years)		4.77± 2.97	4.33± 2.12		0.20
Gender	F	16	18	34	0.67
		33.33%	37.5%	35.4%	
	M	32	30	62	
		66.66%	62.5%	64.6%	
Duration of DM (Years)		4.77± 2.97	4.33 ± 2.12		0.441
FBS (mg/dl)		105.37 ± 24.80	166.64 ± 102.07		0.001
PPBS (mg/dl)		165.23 ± 29.86	215.39 ± 102.00		0.001
HbA1c (mg/dl)		6.55± 0.38	8.41± 1.67		<0.0001
Degree of hearing loss	Mild	45 (93.7%)	15 (31.2%)	60	<0.0001
	Moderate to severe	3 (6.25%)	33 (68.7%)	36	
Deafness	Absent	44	32	76	0.0025
		91.66%	66.66%	79.2%	
	Present	4	16	20	
		8.33%	33.33%	20.8%	
Tinnitus	Absent	45	33	78	0.0017
		93.75%	68.75%	81.2%	
	Present	3	15	18	
		6.25%	31.25%	18.8%	
Vertigo	Absent	43	32	76	0.006
		89.58%	66.66%	79.2%	
	Present	5	16	20	
		10.41%	33.33%	20.8%	

Comparison of latency between Group 1 and Group 2 was performed at difference level (Table 3). Absolute latency V as well as interpeak latency III-IV were found to be significantly higher in uncontrolled DM group (Group 2). Association of duration of diabetes mellitus with hearing loss is noted (Table 4).

Table 3 Comparison of latency between Group 1 and Group 2

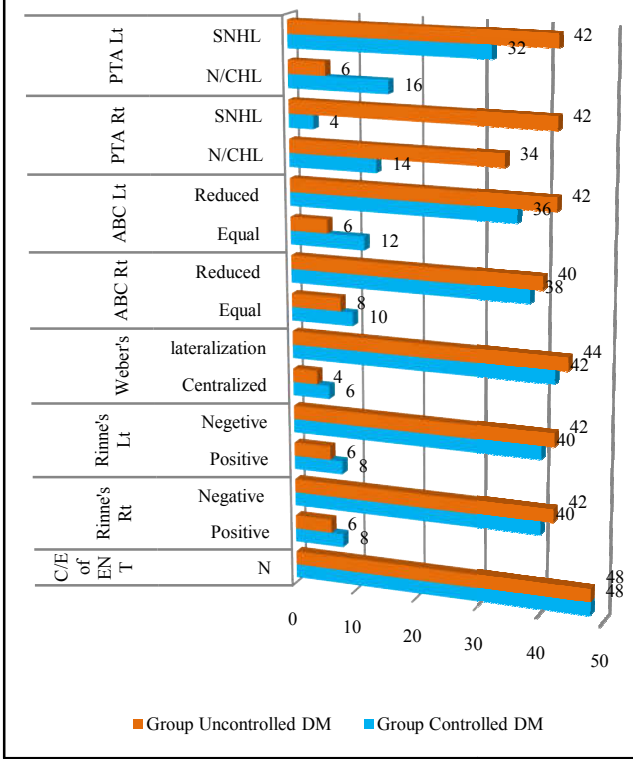
Characteristics	Group		P Value
	Controlled DM (group 1)	Uncontrolled DM (group 2)	
Absolute latency I	1.54 ± 0.14	1.58 ± 0.12	0.15
Absolute latency III	3.64 ± 0.19	3.62 ± 0.21	0.62
Absolute latency V	5.41 ± 0.16	5.55± 0.21	0.001
Interpeak Latency I-III	2.10±0.18	2.04±0.17	0.101
Interpeak Latency III-IV	1.79±0.15	1.92±0.23	0.001
Interpeak latency I-V	3.88± 0.18	3.99± 0.28	0.037

Maximum i.e. 3 (100%) hearing loss was found in patients having 8 to 10 or >10 years duration of diabetes followed by 6-8 years while minimum i.e. 3 (13.6%) hearing loss was found in patients having 2 or < 2-year duration (Table 4).

Table 4 Association of duration of diabetes mellitus with hearing loss

Duration of DM type II	No. of cases	Hearing loss present	Percentage
< 2 year	22	3	13.6
2-4 year	27	6	22.2
4-6 year	29	8	27.5
6-8year	12	10	83.3
8-10 year	3	3	100
>10 year	3	3	100

Fig.1 Various characteristics in study subjects with controlled and uncontrolled DM



DISCUSSION

The aim of this research was to study and compare central auditory neural transmission in controlled and uncontrolled diabetic patients. Only those diabetics were included in the study who did not have any complications of diabetes that result from microvascular changes. Thus, it is very obvious that here we tried to find out any silent changes in auditory neural pathway.

It is well known that diabetic patients develop peripheral and autonomic neuropathy. Conventional audiometric tests are not sensitive enough to detect the initial phases of the sensorineural hearing loss nor the site and pattern of pathological affection of brainstem auditory pathway.

Sheeu S. siddiqi *et al* showed that delay in absolute latencies and interpeak latencies by BERA demonstrate defect at level of brain stem and midbrain in long standing Type-II DM (Siddiqi SS *et al* 2013). Mishra Indira *et al* found that absolute latency I, III V and interpeak latency I-III, III-V, I-V were delayed in uncontrolled Type-II DM group as compared to controlled group of Type-II DM (Sushil M.I *et al* 2016).

Mitchell *et al* found that Patients with diabetes for 10 years or longer had worse hearing thresholds at each frequency compared with those with diabetes for less than 10 years (Mitchell *et al* 2009). In our study also sensorineural hearing loss was found more with increase in duration of diabetes.

Meyerhoff and Shrewsbury *et al* In their screening survey, it was found that diabetic patients were mostly affected by tinnitus of hypoglycemia and hyperglycemia.

Akkuzu *et al* observed clinical incidence of tinnitus was confirmed in diabetes mellitus patients (Akkuzu *et al* 2004). Swain SK *et al* In their study conducted on the Indian population of 240 Diabetic patient, it was found that 29 % of affected patient suffered from tinnitus along with the other associated problems like vertigo etc (Swain SK *et al* 2014).

In our study also we found significantly higher frequency of tinnitus, vertigo and hearing loss in uncontrolled DM subjects as compared to controlled diabetic subjects which is in accordance with above studies.

Mishra Indra *et al* found a positive correlation in controlled and uncontrolled group of diabetes with hearing loss. Which was found statically highly significant ($p<0.001$) (Sushil M.I *et al* 2016). Godfred A. *et al* observed that poor glyemic control in the study population showed a positive association with the severity of hearing loss.

Panda and Prabhakar *et al*, compared subjects of diabetes with peripheral neuropathy and diabetes without peripheral neuropathy and found delay in absolute latencies of wave III and V and prolonged interpeak latencies of I-III and I-V in diabetic with peripheral neuropathy as compared to diabetics without neuropathy.

Mehra *et al*.1985 recorded BERA in Type-2 diabetes individuals and found that the 8th cranial nerve transmission till the level of cochlear nucleus to be normal. The delay in latencies of wave III, IV, V and interpeak latencies I-III and I-V were also found delayed.

Durmus *et al* measured the delay in neural conductance along the auditory pathway in diabetes patients. Their auditory brainstem response (ABR) recording revealed that absolute latencies of wave I, III, and V were prolonged significantly in the diabetes group when compared with the control group (Durmus C *et al* 2004). Patients with diabetes had significantly delayed latencies of wave III and V in the right ear and significantly prolonged interpeak I-III and I-V latencies in both ears. Al- Azzawi & Mirzaalso observed that the significant prolongation of latency of wave V and IPL I-III and I-V in diabetics (Al-Azzawi *et al* 2004).

The significant increase in latency of wave V, IPL I-III and I-V in T2DM, as reported by Gupta *et al* (Gupta *et al* 2010). Konrad Martin *et al* also reported a significant delay in latency of wave V and IPL I-V of T2DM patients (Konrad Martin D *et al* 2010). Habib *et al* reported a significant rise in latency of wave V and IPL I-V of T2DM patients (Habib *et al* 2011). Pooja Baweja *et al* showed that wave V and IPL I-V were significantly delayed, while the IPL I-III was significantly delayed, in females with T2DM (Baweja *et al* 2013).

In our study we found that no significant difference was detected between two groups regarding interpeak latency I-III. Interpeak latency at III-V and I-V was found to be significantly higher in uncontrolled type-II (group II) DM subjects compared to controlled type-II (group I) DM subject. Also, no significant difference was detected between two groups regarding absolute latency at I and III. Absolute latency at V was found significantly higher in uncontrolled DM subjects.

It is also obvious that blood sugar level of diabetic patients should be under control limits which delays complications like auditory neuropathy and prevent permanent damage of hearing Repeated audiological evaluation with BERA is the key to know the hearing status of diabetes patients especially in case of prolonged controlled diabetic and uncontrolled diabetic patients to prevent irreparable damage of hearing.

CONCLUSION

It is well known that diabetes mellitus causes peripheral and central neuropathy. The problem of central subclinical neuropathy has not been studied extensively because of difficulty in detecting latent electrophysiological disturbances of central nervous system by conventional audiometric tests. They are neither sensitive enough to detect the initial phases of sensorineural hearing loss nor capable of identify the site and pattern of affection to auditory pathway. Thus, we conclude that diabetic patients suffer not only from peripheral and autonomic neuropathy but also central neuropathy which is duration dependent. This study suggests that if brain stem evoked response audiometry is carried out in diabetic patients, the involvement of auditory pathway can be detected earlier and will help to reduce morbidity and early intervention and precautions to improve the quality of life of the patients.

***Conflict of interest**:* The authors declare no conflict of interest.

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