Evaluation of brainstem auditory evoked potential in type 2 diabetes mellitus individuals

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ABSTRACT

Background: Diabetes mellitus (DM) is a group of common metabolic disorders that share the phenotype of hyperglycemia. The long term complication of DM includes diabetic neuropathy, which involves both central and peripheral nervous system. Objective of the study was to assess’ diabetic neuropathy in type 2 diabetes mellitus individuals using brainstem auditory evoked potential.

Methods: This study was carried out in the Neurophysiology Lab of Department of Physiology, Government Villupuram Medical College and Hospital (GVMCH), Villupuram, Tamil Nadu, India. The BAEP was performed in 50 patients with type-2 DM selected from the Diabetic OPD without overt hearing loss along with 50 age and gender matched controls with the exclusion of other possible causes which can cause peripheral and central neuropathies. BAEP was statistically analysed using Student independent unpaired ‘t’ test by IBM SPSS software 19.0 version.

Results: On analysis, the latencies I, III, V and Inter Peak Latencies (IPLs) III-V, I-V of BAEP revealed a significant difference between those of diabetes and those of controls (p<0.01).

Conclusions: These data reveal that there was a delay in both the latencies and IPLs which signifies the involvement of both the peripheral and central nervous system. The early diagnosis of brainstem defects may lead to improvement in treatment modalities of DM and decrease its morbidity. Thus BAEP might be used as a non-invasive tool to assess diabetic neuropathy.

Keywords: BAEP, Type-2 diabetes mellitus, Diabetic neuropathy

INTRODUCTION

Diabetes mellitus (DM) is a colossal worldwide health problem which causes serious health complication. DM can be broadly categorised into Type 1 and Type 2 Diabetes. Type 2 DM is more common than Type 1, which is mostly discovered by chance. Since Type 2 DM often has a long asymptomatic period of hyperglycemia, where many individuals may start developing complications even at the time of diagnosis of the disease.

The long-term complication of diabetes is diabetic neuropathy where there is both central and peripheral nerve damage. Though the pathophysiology of CNS abnormalities in DM is not clearly understood, the probable cause of the neuronal damage might be due to chronic hyperglycemia, blood brain barrier dysfunction angiopathy and others. 1-4

In detecting the evidence of central neuropathy, Coshum Durmuset al, Tothet al, Virtamenhi J et al found the involvement of central auditory pathway. 5-7

There are great number of researches done to detect the effect of diabetes mellitus on peripheral nervous system but not many have been done on the involvement of central nervous system in DM. Verotti A-et al found central neuropathy in diabetes mellitus patients by the use of evoked potential studies. 8 One of these methods is
Brainstem Auditory Evoked Potentials (BAEPs) which is a simple and non-invasive technique used to assess the auditory pathway upto the mid-brain. Shemer and Fennmesser first described it in 1967 and Hyde in 1987 gave its full explanation.

The purpose of this study was to determine the changes of BAEP in patients with type 2 diabetes mellitus.

**METHODS**

BAEP was performed in 50 patients with type-2 DM selected from the diabetic OPD in accordance with established diagnostic criteria by WHO, According to which:9

- Fasting level >126mg/dl
- Post prandial level >200mg/dl

**Inclusion criteria**

- Age: 20-60 yrs.
- Gender: both gender

**Exclusion criteria**

- Patients with family history of deafness
- Patients with ear disease
- Patients who are exposed to prolonged loud noise
- Patients taking ototoxic drugs
- Patients taking medication which might be expected to interfere with the functioning of CNS like Methyl dopa, reserpine, phenytoin, antipsychotic Antidepressants etc.
- Patients suffering from any concurrent diseases that affect the brain and Nervous system such as Uremia, Cerebro vascular stroke, hepatic encephalopathy etc.
- Patients with Hypertension, COPD, Multiple Sclerosis, Hypothyroidism, Hyperthyroidism.

Cases were matched with 50 age and gender matched healthy subjects. The patients and the control group were informed about the study, oral and written consent was obtained from them in the regional language.

**Data collection**

Data were collected regarding their demographics and selected medical information’s like their DM duration, treatment history, family h/o diabetes and complications like sensory symptoms (burning, tingling, numbness) in hand and foot.

They were then subjected to

- Neurological examination like Rinne, Weber and Absolute Bone Conduction test
- Blood glucose level(fasting and post prandial )

**Procedure**

The study was conducted in Neurophysiology Lab of Department of Physiology, GVMC&H, Villupuram after obtaining approval from Institution Ethical Committee, Villupuram. This was a case control study. By using the MEDICAID polyrite, BAEP procedure was performed according to the recommended standards of the American clinical neurophysiology society.10

**The method is summarised as follows**

After ENT examination, subjects were made to lie down in a couch and the electrodes were placed based on 10-20 International system of electrode placement. In order to measure the accurate latencies, sound higher than the hearing threshold was given according to Chippa KH et al.11

Monaural clicks of 2000at 90 dB were averaged by a filter setting of 100-3000Hz with masking sound of 40 dB in the contralateral ear. Two or more responses were obtained to show replicability. The signals thus produced were picked by the electrodes and were filtered, amplified, averaged and recorded.

**Statistical analysis**

The latencies and the Inter peak latencies were calculated and were statistically analysed using Student independent unpaired t’ test by IBM SPSS software 19.0 version.

P<0.05* is significant; P<0.01** is highly significant.

**RESULTS**

**Characteristics of the subjects**

In our study, a total of 50 diabetic patients and 50 healthy subjects, age and gender match were included. Twenty eight female and twenty two male were included in each group. The mean age of the subjects was 46.78±7.20 with age range of 20-60.Their basic data are listed in Table 1. There was no statistical difference between the cases and controls with regards to height and weight (p>0.05).

**Auditory function**

No subjective symptoms regarding the auditory pathology were found both in diabetic and control group. Neurological examination including Rinne, Weber and Absolute Bone Conduction were also normal.

**Blood glucose level measurement**

In our study, mean of fasting and post prandial blood glucose level in cases were 175.04±53.28, 257.48±99.23 respectively. There was a highly significant increase in fasting and post prandial blood glucose level in cases compared to the controls (p<0.01) as showed in table 2.
Comparison of the DM cases and controls in the BAEP study

Left ear

There was a very high significant increase in waves I, III, V and IPLs III-V, I-V (p<0.01) of Left ear in cases when compared to the control.

When compared to waves I, V and IPLs III-V, I-V (p<0.01) were highly significantly increased and wave III (p<0.05) was significantly increased in cases.

Right ear

The BAEP results on comparing with both cases and controls are listed in Table 3 and 4.

Table 1: General characteristics of the subjects.

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Controls</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>50</td>
<td>50</td>
<td>-</td>
</tr>
<tr>
<td>Gender (female/male)</td>
<td>28/22</td>
<td>28/22</td>
<td>-</td>
</tr>
<tr>
<td>Age mean</td>
<td>46.78±7.20</td>
<td>46.78±7.20</td>
<td>-</td>
</tr>
<tr>
<td>Age range</td>
<td>27-58</td>
<td>27-58</td>
<td>-</td>
</tr>
<tr>
<td>Height (cms)</td>
<td>162.40±6.80</td>
<td>160.90±8.09</td>
<td>p=0.318</td>
</tr>
<tr>
<td>Weight (kgs)</td>
<td>63.78±7.31</td>
<td>62.44±6.26</td>
<td>p=0.327</td>
</tr>
</tbody>
</table>

The Parameters were analyzed using Student independent unpaired 't' test; p<0.05* was taken as significant and P <0.01** was taken as highly significant.

Table 2: Blood glucose level measurement.

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Controls</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>175.04±53.28</td>
<td>93.92±7.42</td>
<td>p&lt;0.01**</td>
</tr>
<tr>
<td>Postprandial</td>
<td>257.48±99.23</td>
<td>108.22±8.74</td>
<td>p&lt;0.01**</td>
</tr>
</tbody>
</table>

The Parameters were analyzed using Student independent unpaired ‘t’ test. p< 0.05* was taken as significant.

Table 3: Comparison of the DM cases and controls in the BAEP study in left ear.

<table>
<thead>
<tr>
<th>Absolute latencies</th>
<th>Cases</th>
<th>Controls</th>
<th>t value</th>
<th>p value</th>
<th>Df</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1.60±0.15</td>
<td>1.47±0.15</td>
<td>4.083</td>
<td>&lt;0.01**</td>
<td>98</td>
</tr>
<tr>
<td>III</td>
<td>3.49±0.18</td>
<td>3.37±0.14</td>
<td>3.676</td>
<td>&lt;0.01**</td>
<td>98</td>
</tr>
<tr>
<td>V</td>
<td>5.31±0.22</td>
<td>4.82±0.25</td>
<td>10.241</td>
<td>&lt;0.01**</td>
<td>98</td>
</tr>
<tr>
<td>I-III</td>
<td>1.88±0.20</td>
<td>1.89±0.21</td>
<td>-0.301</td>
<td>0.764</td>
<td>98</td>
</tr>
<tr>
<td>III-V</td>
<td>1.83±0.21</td>
<td>1.45±0.24</td>
<td>8.136</td>
<td>&lt;0.01**</td>
<td>98</td>
</tr>
<tr>
<td>I-V</td>
<td>3.71±0.24</td>
<td>3.34±0.28</td>
<td>6.890</td>
<td>&lt;0.01**</td>
<td>98</td>
</tr>
</tbody>
</table>

The Parameters were analyzed using Student independent unpaired ‘t’ test; p< 0.05* was taken as significant & P<0.01** was taken as highly significant.

Table 4: Comparison of the DM cases and controls in the BAEP study in right ear.

<table>
<thead>
<tr>
<th>Absolute latencies</th>
<th>Cases</th>
<th>Controls</th>
<th>t value</th>
<th>p value</th>
<th>Df</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1.59±0.20</td>
<td>1.45±0.15</td>
<td>3.933</td>
<td>&lt;0.01**</td>
<td>98</td>
</tr>
<tr>
<td>III</td>
<td>3.48±0.21</td>
<td>3.40±0.18</td>
<td>2.105</td>
<td>&lt;0.05*</td>
<td>98</td>
</tr>
<tr>
<td>V</td>
<td>5.29±0.23</td>
<td>4.84±0.23</td>
<td>9.553</td>
<td>&lt;0.01**</td>
<td>98</td>
</tr>
<tr>
<td>I-III</td>
<td>1.89±0.25</td>
<td>1.93±0.19</td>
<td>-0.973</td>
<td>0.333</td>
<td>98</td>
</tr>
<tr>
<td>III-V</td>
<td>1.80±0.17</td>
<td>1.45±0.21</td>
<td>9.061</td>
<td>&lt;0.01**</td>
<td>98</td>
</tr>
<tr>
<td>I-V</td>
<td>3.7±0.31</td>
<td>3.37±0.24</td>
<td>5.961</td>
<td>&lt;0.01**</td>
<td>98</td>
</tr>
</tbody>
</table>

The Parameters were analyzed using Student independent unpaired ‘t’ test; p< 0.05* is taken was significant and P <0.01** was taken as highly significant.

DISCUSSION

Patients with DM may have progressive, sensory neural hearing loss which could be sub clinical.12-18 Report from American Clinical Society also stated that sensory neural hearing loss is more common among DM than non DM subjects. In present study, on observing, we found that the latencies of the cases and controls were decreased...
when compared with the normal values as illustrated by Chippa et al, but on comparing the latencies between the cases and controls, there was a highly significant increase in the latencies of the cases.11

In present study, we found significant increase in wave I, III, V and IPLs III – V and I – V on both ears when compared to the control group but IPL I – III showed no significance.7,19,27 Though there was no significant hearing loss in the Diabetic cases, we observed prolongation of wave I in cases which revealed that the disorder had started peripherally. This suggests that they might have sub clinical hearing impairment.

Lengthening of latency III, V implied that there might be brainstem dysfunction as suggested by Donald MW et al.18 Studies like Toth et al, Durmus et al, Al-Azzawi and Miraza, Dileo et al also showed a meaningful association between the latency I, III, V when compared to the control group.5,6,19,20

Regarding IPL elongation of IPLs III-V and I-V with normal I-III showed an evidence of conduction delay within the central auditory pathway. Numerous authors had reported that BAEP latencies showed an increase central conduction time in the auditory pathway even in the absence of hearing loss.6,28

Thus significant increase in wave I, III, V and IPLs III-V and I-V indicate that both central and peripheral pathways were affected. This was in concordance with Fidele et al, who found that peripheral transition time (wave I) and central transition time (IPL I–V) were significantly delayed in the diabetics as compared to the normal.29

This suggest that the probable pathology might be in cochlear and the central auditory pathway and main pathological finding in the diabetic patients was demyelination of the VIII cranial nerve and the atrophy of the spiral ganglion of the cochlear. The probable pathogenesis might be primarily, high metabolic demands of the inner ear and auditory pathway which lead to the excessive accumulation of sugar, sorbitol and fructose in the nerve and damage it. This could make them the target of the disease even before the evidence of micro vascular complications.30-32 This is followed secondarily by microangiopathy.

Though these abnormalities were present at different level from auditory nerve to the brainstem, Brainstem auditory evoked potential could help in detecting the pathology at an early stage even before the appearance of overt complications.33

BAEP is considered advanced than audiometry because CNS involvement could not be tested by audiometry and to detect auditory nerve functions audiometry requires the cooperation of the subject and external conditions which might affect the results.34 But BAEP does not require the cooperation of the subject as it is resistant to sleep sedation and anaesthesia and not affected by external environment.35,36 Thus BAEP could be used as a simple non-invasive, effective tool to assess the abnormalities of the entire auditory pathway even before the onset of specific symptoms in diabetic patients.

CONCLUSION

In present study we observed significant increase in latencies I, III, V and IPLs III-V, I-V. Present study suggests that if BAEP was carried out in diabetic patients early impairment of the entire auditory pathway could be detected even before the onset of any clinical signs and symptoms.

Hence, such a useful and cost effective procedure might be used routinely as a part of standard audiological test battery in all diabetes mellitus patients to evaluate neuropathy subclinically. Further, improvement in the treatment modality might influence and reduce the BAEP abnormalities.

Limitation

- In this study only Type 2 DM patients were involved
- Present sample size was not enough to extrapolate the result to the whole population.
- We have taken the fasting blood glucose level to measure the glycemic control instead of HbA1c

Scope for further researches

- BAEP should be carried out in broad spectrum of patients to standardise the results
- Cohort study could be carried out to emphasise the effectiveness of the procedure

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES


