RESEARCH ARTICLE

Comparative assessment of brainstem auditory evoked potentials in apparently healthy medical students with a family history of diabetes mellitus type 2

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ABSTRACT

Background: Neuronal studies on diabetes mellitus (DM) were previously based on peripheral and autonomic nerves. With the advent of Brainstem Auditory Evoked Potential (BAEPs), studies on sensory pathways in the central nervous system become easier and more productive. BAEPs is a non-invasive electrophysiological tool to detect retro-cochlear lesion. Hence, it is helpful to detect early Impairment of the auditory nerve and brainstem function. Aim and Objective: DM Type 2 (T2DM) is a known cause of neuropathy and in earlier course, it involves sensory nerves. T2DM runs in families and it has a genetic predisposition. BAEP is one of the methods to find out problems related to hearing by analyzing latencies of waveforms and inter-peak latencies. Hence, BAEPs in apparently healthy subjects with and without family history of T2DM is assessed. Materials and methods: This is a cross-sectional, casecontrol study. We have taken 110 volunteers from MBBS students of IMS, BHU of 17–23 years of age. Those with co-morbid conditions (eg. diabetes and hypertension), neurodegenerative diseases, neuropathy, schizophrenia, and those on ototoxic and neurotoxic drugs are excluded from the study. After taking consent and conducting a preliminary physical examination, BAEPs are recorded using a proper BAEP recording device. Statistical analysis is done using SPSS 2016 software trial version with Chi-square test. Results: The subjects with positive family history of T2DM in paternal grandfather showed deviation in latencies of BAEPs wave I (P < 0.001), wave III (P = 0.019), wave V (P = 0.033), and inter-peak latency between wave I and wave V (P = 0.019) from the normal values in the left ear. The subjects with positive family history of T2DM in paternal grandmother showed deviation from the normal in case of V/I % in the right ear (P = 0.016). Conclusion: The presence of T2DM in families can affect the wave latencies and inter-peak latencies of BAEPs.

KEY WORDS: Diabetes Mellitus Type 2; Brainstem Auditory Evoked Potentials; Wave Latencies; Inter-peak Latencies

INTRODUCTION

Diabetes Mellitus type 2 (T2DM) is a metabolic disease with hyperglycemia and various complications like neuropathy being very common. Damage to the small nerves may be the earliest detectable prominent sign in cases of glucose dysmetabolism. Reske-Nielsen et al., and Makishima and Tanaka., have shown the involvement of brain parenchyma in long-standing diabetes mellitus (DM), thereby suggesting central neuropathy. Durmus et al., Tóth et al., Scott-Brown et al. support the above finding in their respective studies. Vessels of the basilar membrane and stria vascularis thicken, stria vascularis atrophies and there is loss of outer hair cells in diabetic people leading to hearing loss. The lifetime risk of developing T2DM is markedly increased if any parent or...
first-degree relative is diabetic.[1] T2DM is a multifactorial disease, predisposition to the disease could be determined by many combinations of genetic variants (genotypes) and environmental factors.[8] Hence, due to the complex interplay of factors, it remains unknown how the disease genetics actually work even though it is known that there is a genetic predilection present.

Neuronal studies on DM were previously based on peripheral and autonomic nerves. With the advent of Brainstem Auditory Evoked Potentials (BAEPs), studies on sensory pathways in central nervous system become easier and more productive. BAEPs is a non-invasive electrophysiological tool to detect retro-cochlear lesion. Hence, it is helpful to detect early Impairment of the auditory nerve and brainstem function.[9] BAEPs provides an opportunity to evaluate the functional integrity of auditory pathway from the inner ear to the upper brain stem. Increased peak latencies with BAEP have been seen in T2DM patients, even in the young patients,[10] indicative of the central auditory pathway lesions in them.[11,12] Prolonged BAEP waveform peak latencies serve as an early indicator of subliminal subclinical central neuropathy since these observations are present even in the absence of clinical signs and symptoms of peripheral and central neuropathy.[11]

**Aim:** Relating the neuropathic effects of T2DM and possible detection of central neuropathy by BAEPs; it may well be hypothesized that young non-diabetic people with a positive family history of T2DM may be diagnosed with genetic predisposition to T2M based on the BAEPs changes due to the inheritance pattern of genes affecting the disease.

**MATERIALS AND METHODS**

The study protocol was approved by the Institute Ethics Committee. It was a cross-sectional casecontrol study, conducted from January 2019 to July 2019. A total of 110 apparently healthy subjects from MBBS students of IMS BHU were taken and their BAEP waves and inter-peak latencies analyzed. The sample size was chosen based on statistical analysis.

**Inclusion Criteria of Subjects**

Non-diabetic medical students of age group 17–23 years.

**Exclusion Criteria of Subjects**

- Presence of Diabetes, Hypertension, or other comorbid conditions leading to neuropathies
- Subjects with neurodegenerative diseases. For example., Parkinson’s disease, Alzheimer’s disease
- Subjects with hearing disorders or a family history of the same
- The use of ototoxic and sedative drugs. For example., Antipsychotics, Antidepressants, Methyldopa, Reserpine, Phenytoin, etc
- Subjects with psychiatric disorders
- Strokes, severe head injuries
- Subjects with peripheral neuropathy.

Peripheral neuropathy was excluded by performing the pressure tests with back of a pencil, proprioceptive test (sense of position of proximal and distal joints by rotating in various directions, keeping them in particular position, and asking the subject to keep the other limb in the same position with his eyes closed for the entire process), pain test using a pinprick and tendon pinch, tactile localization and discrimination, temperature tests using cold and warm objects.

Body height was taken by asking the individual to stand firmly on flat ground against a rigid wall, a flat object slid down up to the head and the height noted using a measuring scale fixed to the wall. Weight was taken using a digital device. Body mass index was calculated by dividing the weight in kilograms by the square of height in meters. The respiratory rate was counted. Pulse rate was calculated using radial arteries of both hands and all parameters were noted. Blood pressure was noted using a sphygmomanometer. BAEPs were carried out using a proper BAEPs device called BERAGRAPH (Medicaid systems, 389, Industrial area, Phase-II, Chandigarh) under standard conditions. The subject was instructed to be comfortable by all means. The skin of the forehead and both the mastoid processes were made grease free. Any jewelry, cell phones, or other devices were removed based on their potential ability to interfere with the process. The active electrode was properly placed onto the vertex so that it keeps its position throughout the recording and the reference electrode was placed on the mastoid. The ground electrode was positioned over forehead. The headphone was in position, low filter was 100 Hz and high filter was 10 kHz. Brief click monaural stimuli were used at 55 dB 2000 times (1/s) and the wave pattern was noted. The normal range of sound perception of an apparently healthy individual is approximately from 20 dB to 80 dB with slight individual variations, provided the perception is not that of noise. 55 dB lies within this favorable range, thus, 55 dB has been used to avoid subjective bias. We recorded all waves in the rarefaction setting. The room was soundproof. At least two readings from each ear were taken to confirm the reproducibility of waveform; the absolute latencies of waves I to V and inter-peak latencies I-III, I-V, III-V were recorded along with V/I ratio percentage (V/I%). The entire process is conducted after taking proper consent from the subject. Following parameters are recorded during the BAEPs study:

- Wave I: Acoustic nerve (1.4 ms–1.8 ms).
- Wave II: Cochlear nucleus (2.8 ms).
- Wave III: Superior olivary nucleus (3.6 ms–4.1 ms).
- Wave IV: Nucleus of lateral lemniscus (5.1 ms).
- Wave V: Inferior colliculus (5.5 ms–6.0 ms).
- Wave VI: Medial geniculate body.
- Wave VII: Originates between medial geniculate body to auditory complex.[13]

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Inter-peak latency I-III: 1.6 ms–2.6 ms.
Inter-peak latency I-V: 3.5 ms–4.5 ms.
Inter-peak latency III-V: 1.4 ms–2.4 ms.
Normal V/I%: 50–300%.

Statistical analysis was done using SPSS 2016 software trial version by Chi-square test.

RESULTS

Family history of T2DM in Paternal Grandfather

Of 110 subjects, 95 (86.4%) have no history of T2DM in paternal grandfather and 15 (13.6%) have the history.

Comparing the proportion of subjects in the normal latency range of the first wave of the left ear, there is a marked decrease in the case of those with their paternal grandfather having a history of T2DM (26.7%) as compared to those without the history (57.9%); it is observed from Table A1. While the proportion in the decreased latency does not vary much with the family history stated, the increase in latency may be attributed to the family history while comparing the two groups (40% in those with a positive history and 6.3% without). The results are statistically significant. In the right ear for wave I the results also showed increased latency in subjects with family history of T2DM in paternal grandfather though it is statistically not significant (P = 0.139).

No significant association was found in subjects with family history of T2DM in paternal grandfather with BAEPs waves I, III, V of the right ear, inter-peak latencies I-V of right ear, I-III of both ears, III-V of both ears, and V/I% ratio.

Table A2 shows that the proportion of subjects within normal range of latency of 3rd wave in the left ear is almost double in case of positive family history of T2D in paternal grandfather (66.7% as compared to 34.7%). Decreased latency was almost 2 times more in the subjects without family history of the same (65.3%) compared to 33.3% with positive family history. No one showed increased latency. The results are statistically significant. A few changes were also found in wave III of the right ear, but they were statistically not significant (P = 0.840).

Table A3 shows that the proportion of subjects within normal range of latency of 5th wave in the left ear is slightly greater in cases of positive family history (53.3%) of T2D in paternal grandfather as compared to those without the similar family history. Decreased latency of the 5th wave of the left ear is present in significantly more subjects without the positive family history stated (52.6%) as compared to those without it (40%). No subject without family history showed increased latency while only one subject showed increased latency in the other group. The data here is statistically significant. A few changes were also found in wave V of the right ear, but they were statistically not significant (P = 0.536).

Table A4 shows that the proportion of subjects within normal range of inter-peak latency between wave I and wave V in the left ear is significantly more in the case of subjects without a positive family history T2DM (94.7%) as compared to those with a positive family history of T2DM (73.3%). The decrease in this proportion may be justified by the higher proportion of subjects with decreased interval (20.0%) and increased interval (6.7%) when we compare the data to the subjects without the stated family history (4.2% with decreased interval and 1.1% with increased interval). The data here is statistically significant. A few changes were also found in inter-peak latency I-V of the right ear but they were statistically not significant (P = 0.602).

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<th>Table A1: Wave I of left ear (IL) - Paternal grandfather</th>
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<td>T2D in paternal grandfather</td>
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<th>Table A2: Wave III of the left ear (IIIL) - Paternal grandfather</th>
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<th>Table A3: Wave V of the left ear (VL) - Paternal grandfather</th>
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Family History of T2D in Paternal Grandmother

About 95 (86.4%) out of 110 subjects lacked history of T2D in paternal grandmother while the other 15 (13.6%) possessed that history.

Table B1 shows that the proportion of individuals in the normal range of value of V/I%R in both groups is almost equal. However, the proportion of individuals showing increased value is higher in the group without the history of T2DM in paternal grandmother (36.8%) with respect to the group with that history (20%). The proportion of individuals showing a reduced value is higher in the group having T2DM (13.3%) in paternal grandmother when we compare it to the other group (1.1%). The results are statistically significant. A few changes were also found in V/I% of the left ear but they were statistically not significant ($P = 0.652$).

No significant association was found in subjects with a family history of T2DM in paternal grandmother with BAEPs waves, interpeak latencies, or V/I% ratio of the left ear.

History of T2DM in Father

No significant association was found in subjects with a family history of T2DM in father with BAEPs.

History of T2DM in Mother

No significant association was found in subjects with family history of T2DM in mother with BAEPs.

History of T2DM in Maternal Grandfather

No significant association was found in subjects with family history of T2DM in maternal grandfather with BAEPs.

History of T2DM in Maternal Grandmother

No significant association was found in subjects with family history of T2DM in maternal grandmother with BAEPs.

DISCUSSION

As per the study conducted, we have observed a greater proportion of subjects with T2DM in paternal grandfather showing increased latency of wave I of both ears as compared to those without the history but the findings of left ear are statistically significant. Konrad-Martin et al.[14] also found in a study that there were differences between wave latencies of the right and left ear, though they were not able to explain the exact reason for this difference. Similarly, there are more studies which have found differences between the waveform latencies of the right and left ear.[11,13] When it comes to the wave III and wave V of the left ear, we have seen that positive history of the same normalizes the latencies, albeit the latencies being more in them with respect to those without the history that have a significantly more proportion of subjects showing decreased latency of the waves. The inter-peak latency between the wave I and wave V of the left ear showed deviation from normal in case of T2DM in paternal grandfather. In case of paternal grandmother, there is no significant association between BAEPs waves and T2DM history except V/I % in the right ear where deviation of values below normal range was found.

In this study, we found that there is no significant association between BAEPs waves and family history of T2DM in father, mother, maternal grandfather, and maternal grandmother.

Mishra et al.[16] concluded that BAEPs in uncontrolled diabetic patients can detect the early complication of neuropathy. Sumner et al.[1] says that diabetic neuropathy is an early detectable sign. Omar says that T2DM is a multi-factorial disease depending on genetic and environmental pathways. With relation to the above, we may be able to get a line as to how we may use BAEPs as a screening tool for T2DM.

It is a well-known fact that T2DM has a tendency to run in families and it also involves most of the nerves, especially sensory nerves in its earliest course.[17] This could be a possible explanation for deviation of BAEPs waves in apparently healthy subjects with family history of T2DM in this study.
Limitations of this Study

(a) The sample of subjects is gathered from a pool of medical students. Hence, there is a selection bias. (b) Age group of subjects is limited to 17–23 years. (c) Sample size of the study is relatively small.

CONCLUSION

We conclude that the presence of family history of T2DM can affect BAEPs waves in apparently healthy subjects in their early lives before any significant symptoms appear. So, in near future, with the help of further studies in this field, BAEPs can be established as a screening tool to detect the predisposition of the apparently healthy subjects to T2DM.

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