Study on brainstem auditory evoked potentials in diabetes mellitus

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ABSTRACT

الأهداف: لتحديد تغيرات نتيجة دراسة الجهد السمعي المستحث في جذع الدماغ (BEAP) لدى المرضى المصابين بداء السكري (DM).

الطريقة: أجريت دراسة على 50 مريض مصاب بداء السكري (54.2±9.9) عاماً، و 73 شخصاً سليماً (50.87±10.6) عاماً، تم اختيارهم في عيادة الأعصاب بمستشفى الإمام رازا – تابريز – ايران، خلال الفترة من أبريل 2006م وحتى يوليو 2007م. تم تصنيف المصابين بداء السكري وفقاً لنوع السكري (النوع الأول والنوع الثاني)، ومستوى سكر الدم عند الصيام (≥130mg/dl) ومستوى الهيموجلوبين (>7% and <7%).

النتائج: عند مقارنة عينات 50 مرضى السكري مع عينات 73 الأشخاص السليمين، لم يكن هنالك فرقاً ذو دلالة إحصائية بين نتائج الجهد السمعي المستحث في جذع الدماغ (BEAP) مع مستويات (FBS) سكر الصيام والهيموجلوبين (Hb1AC) ونوع السكري (p=0.496, p=0.151, p=0.683 على التوالي). كان هنالك اتحاد ذو معني كامل بين تأخير الموجة الثالثة والرابعة والخامسة وتأخير الذروة الأولى – الثالثة والثالثة – الخامسة لدى المجموعة المصابة بالسكري ومجموعة التحكم (p=0.035, p<0.0001, p=0.023, p=0.012). p=0.003).

خاتمة: لدى المصابين بداء السكري (DM) شذوذ (لا انتظامية) في نتيجة دراسة الجهد السمعي المستحث في جذع الدماغ (BEAP). يمكن استخدام دراسة الجهد السمعي المستحث في جذع الدماغ (BEAP) من أجل تقييم النقص في جذع الدماغ لمرضى السكري.

Objectives: To determine the changes of brain stem auditory evoked potential (BAEP) in diabetes mellitus (DM).

Methods: In a case-control study, 50 diabetic subjects (54.2±9.9 years) and 69 healthy subjects (50.87±10.6 years) were selected in the Clinic of Neurology, Emam Reza Hospital, Tabriz, Iran, from April 2006 to July 2007. Diabetic subjects were classified according to type of diabetes (type I and II), fasting blood sugar (FBS) level (≥130mg/dl) and glycosylated hemoglobin (HbA1C) (>7% and <7%).

Results: In a comparison of 50 diabetic samples and 69 non-diabetic samples, there was no significant difference between BAEP findings with FBS level (p=0.683), HbA1C (p=0.151), and type of diabetes (p=0.496). There was a meaningful association between latency of wave III (p=0.012), IV (p=0.023), V (p<0.0001), and interpeak latency of I-III (p=0.035) and III-V (p=0.003) in the diabetic and control group.

Conclusion: Subjects with DM have abnormalities in BAEP, and for evaluation of defects of the brainstem in diabetic patients usage of BAEP is recommended.

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Diabetes mellitus (DM) is one of the most frequent metabolic diseases, which cause different disabilities in many organs such as the brainstem. Brainstem is the place of the cranial nerves nuclei and pathway of sensory and motor tracts, therefore, early diagnosis of its abnormality may lead to early treatment and less subsequent mortality and morbidity. Brainstem auditory evoked potential (BAEP) can be used to record evoked potentials waves generated by neurons in the auditory pathway. By means of BAEP, it is possible to assess the integrity of neuronal brainstem generators and they are effective in evaluation of its functions.[1] Many studies have been performed for the evaluation of the association between BAEP abnormality and DM, but

these studies led to different results.[2,3] The most common abnormalities in these studies were the lengthening of the latency of waves III and V.[4-9] The earlier diagnosis of brainstem defects may lead to improvement in treatment modalities of DM and a decrease in morbidity and mortality.[1] The BAEP is effective and a less expensive test in evaluation of brainstem function.[10] The aim of this study was to assess BAEP abnormalities of diabetic subjects with type I and type II, compared to age and gender matched healthy subjects and to assess glycosylated hemoglobin (HbA1C), levels and fasting blood sugar (FBS) levels on BAEP results.

Methods. In a case-control study, 50 diabetic subjects with mean age of 54.2±9.9 (mean±SD) years range from 30-80 (20 male and 30 women) and 69 healthy subjects with mean age of 50.87±10.6 (20 male and 49 female)) were selected in the Clinic of Neurology, Emam Reza Hospital, Tabriz, Iran from April 2006 to July 2007. The Ethics Committee of Tabriz University of Medical Sciences approved this study and we obtained the patient's informed consent in Farsi language. Subjects with history of auditory diseases, space occupying lesions, degenerative diseases, cerebral vascular disorders, multiple sclerosis, migraine headache, or chronic renal failure were excluded. Although interpeak latency (IPL) are not significantly affected by peripheral hearing disorders, in case of necessity, peripheral hearing disorders including conductive hearing loss (external canal obstruction, tympanic membrane perforation, fluid in the middle ear) and sensorineural hearing loss (noise damage, Meniere's disease) were excluded by an Otorhinologist. Fasting blood sugar results were measured 3 times, and HbA1C measured once in diabetic subjects during this study and for determination of the effect of diabetes type on BAEP, diabetic subjects were divided into insulin-dependent (ID) and non insulin-dependent diabetes mellitus (NIDDM) groups. The HbA1C was used for determination of efficacy of diabetes control, it was divided into 2 groups, >7% and <7%, and FBS was >130mg/dl and <130mg/dl groups. The FBS and HbA1C were measured by chromatographic method (BioSystems S.A. Costa Brava 30, Barcelona, Spain). All subjects were evaluated with Neuroscreen® Plus TOENNIES (Jaeger, Wurzburg, Germany) with a frequency of 14 impulses per second totaling to 2000 impulses (recording was made at one frequency) between 8am and 12 am. An active electrode was placed in the right mastoid bone and earth electrode in the left mastoid and reference in the zone of scalp (C_Z). Silver chloride electrodes were used. For determination of click hearing threshold, click intensity is set initially at 50 dB, then it decreased in 5-dB steps until the subject can no longer hear the clicks and by then increasing intensity in 5-dB steps until the clicks can be heard. The BAEP results were interpreted for latency of waves I, II, III, IV, V and an IPL of waves I-III and III-V. The results were analyzed with SPSS 12 software and T-test, and results were considered meaningful at $p<0.05$.

Results. The mean age of diabetic subjects was 54.02±9.97 years (mean ± SD) with age range of 30-80, and in the healthy subjects was 50.87±10.61 years ($p=0.105$). The mean time of diabetes diagnoses was 8.74±7.12 years (1-28 years) and HbA1C average was 7.67±1.62, which in 22 subjects was less than 7%, and in 28 subjects was more than 7%. The mean of FBS was 194.93±79.5, and in 40 subjects was above 130 mg/dl and in 10 subjects less than 130 mg/dl. The type II DM group contained 31 subjects, and the type I DM group had 19 subjects. The right side latency of wave V and the left and the right sides IPL III-V were the most frequent abnormalities in our study, and we detected meaningful association between BAEP results in diabetic subjects and healthy subjects. This difference is detected in the waves from the central part of the auditory pathway that shows brainstem defects in diabetic subjects (**Table 1**). On comparison of the diabetic group with the control group, the latency of waves IV, V, and an IPL III-V in the right side and latency of wave III, V and an IPL III-V in left side had a meaningful relationship (**Table 1**). Comparison of mean latency of waves in the diabetic group with the control group showed a significant difference except in latency of waves I and II (**Table 2**). The comparison of the latency of waves and IPL in groups with FBS above 130 mg/dl with below 130 mg/dl had no meaningful relation, also HbA1C above 7% and below 7% had no effect on the latency of

Table 1 - Mean latency and interpeak latency in the right and left ear in diabetic and control subjects in our study.

Location/ BAEP wave	Diabetic group mean ± SD	Control group mean ± SD	*P*-value
Right ear			
I	1.64±0.14	1.62±0.11	0.308
II	2.73±0.22	2.71±0.15	0.744
III	0.383±0.26	3.72±0.14	0.017
IV	5±0.27	4.87±0.25	0.009
V	5.61±0.027	2.11±0.17	<0.009
I-III	2.19±0.27	2.11±0.17	0.069
III-V	1.84±0.22	1.74±0.15	0.004
Left ear			
I	1.64±0.12	1.64±0.12	0.998
II	2.69±0.2	2.7±0.18	0.576
III	3.82±0.19	3.75±0.17	0.049
IV	4.99±0.21	4.94±0.24	0.329
V	5.67±0.28	5.54±0.2	0.006
I-III	2.18±0.2	2.12±0.18	0.83
III-V	2.12±0.18	1.76±0.13	0.023

BAEP - brainstem auditory evoked potential

Table 2 - *P*-value detected from comparison groups with HbA_1C more than 7 and less than 7, and FBS more than 130 mg/dl and less than 130 mg/dl.

BAEP wave	HbA1C		*P*-value	FBS		*P*-value
	>7%	<7%		>130 mg/dl	<130 mg/dl	
I	1.64±0.09	1.64±0.11	0.936	1.62±0.08	1.64±0.11	0.534
II	2.67±0.22	2.73±0.14	0.251	2.70±0.14	2.71±0.19	0.902
III	3.79±0.18	3.86±0.22	0.204	3.83±0.22	3.82±0.19	0.937
IV	4.95±0.15	5.04±0.23	0.119	5.01±0.28	4.99±0.18	0.713
V	5.62±0.26	5.74±0.28	0.151	5.66±0.31	5.67±0.27	0.897
I-III IPL	2.15±0.16	2.23±0.24	0.185	2.21±0.23	2.18±0.19	0.683
III-V IPL	1.83±0.21	1.86±0.17	0.523	1.82±0.25	1.85±0.18	0.655

BAEP - brainstem auditory evoked potential, HbA_1C - glycosylated hemoglobin, FBS - fasting blood sugar, IPL - interpeak latency

Table 3 – *P*-value detected from comparison between BAEP results in type I and type II diabetes.

BAEP waves	*P*-value Type I	*P*-value Type II
I	0.634	0.213
II	0.353	0.279
III	0.031	0.079
IV	0.013	0.093
V	0.006	0.007
I-III	0.37	0.301
III-V	0.015	0.026
I	0.634	0.213

BAEP - brainstem auditory evoked potential

waves (**Tables 1 & 2**). In comparison of subjects in the type I DM groups with control groups, latency of waves III, IV, V and IPL III-V had meaningful association and comparison between type II DM with control group showed a significant difference detected in the latency of wave V and IPL III-V (**Table 3**). However, comparison between DM type I and II with each other had no meaningful association.

Discussion. Our study did not detect any relationship between type of diabetes and BAEP results (p=0.497), however, Durmus et al[11] reported a relation between waves latency III and V and type of diabetes, and Das et al[12] showed a significant association only in type II. Al-Azzawi and Mirza[16] reported no relation between type of diabetes and BAEP results, similar to our study.

Our study showed no relation between levels of HbA1C and results of BAEP similar to the Leon-Morales[14] study. In our study, the FBS mean was 194.93±79.50 and in the Diaz Leon-Morales et al[14] study, this was 170±66.6, in 2 studies, there was no relation between FBS level and BAEP abnormality. In our study, the latency of wave I increased more than the normal level in 20% of diabetic subjects, however, in comparison with the control subjects there was no significant association (p=0.583), in contrast to the studies by Toth et al[15], Durmus et al[11], Al-Azzawi and Mirza,[16] and Di Leo et al,[17] which showed a meaningful association. In our study, the latency of wave II was abnormal in 26% of diabetic subjects, and in comparison with the control group there was no meaningful difference (p=0.910), in Toth et al[15] study, this comparison showed meaningful difference, however, in other studies this wave was not recorded. The abnormality of latency of wave III in our study was 36% and in comparison with the control group this difference was significant (p=0.012), Toth et al,[15] Durmus et al,[11] Al-Azzawi and Mirza,[16] and Di Leo et al[17] also detected this relation in their studies, but Akinci et al[13] did not detected this relation. Regarding the latency of wave IV, the abnormality was detected in 16% of our diabetic subjects and there was a meaningful difference detected with the control group (p=0.023), Akinci et al[13] also confirmed this relation, but other studies did not point to this wave. Our BAEP results for latency of wave V show abnormality in 50% (p<0.0001). Both Toth et al[15] and Durmus et al[11] (p=0.05), Di Leo et al[17] and Al-Azzawi and Mirza[16] (p=0.008), and Diaz de Leon-Molares et al[14] (p<0.01) also recorded this relation. The comparison of IPL of I-III between diabetic group and the control group were abnormal in 24% (p=0.035) and this relation was confirmed by Toth et al,[15] Al-Azzawi and Mirza,[16] and Dolu et al,[18] but Diaz de Leon-Molares et al[14] showed this relation only in type II diabetic subjects, and Akinci et al[13] and Di Leo et al[17] only in type I diabetic subjects. Regarding III-V IPL, we detected abnormalities in 44% of diabetic subjects

with a meaningful association (p=0.003), and Toth et al,[15] Al-Azzawi and Mirza,[16] Dolu et al,[18] and Diaz de Leon-Molares et al[14] confirmed this association.

The increase of latency or interpeak latency of waves of BAEP even in the absence of any clinical signs may show brainstem dysfunction. The results of BAEP can be used in evaluation of brainstem dysfunction in diabetic subjects, however, for standardizing BAEP results and detecting the association between BAEP results and severity of disease more researches must be carried out.

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