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EFFECT OF GLYCEMIC CONTROL ON BRAIN STEM AUDITORY EVOKED POTENTIAL (BAEP) BASED ON HBA1C IN TYPE II DIABETES MELLITUS.

Physiology

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ABSTRACT

BACKGROUND: Diabetes mellitus is a complex metabolic disorder whose detrimental effects on various organ systems, including the nervous system are well known. Diabetes mellitus is becoming one of the most important health problems not only in developed countries but also in developing countries. Neuropathy is a common and frustrating long-term complication of diabetes. Diabetes may alter both the peripheral and central nerve functions but the peripheral manifestations of diabetic neuropathy are more frequently discussed in the literature than the impairment of cranial nerves.

MATERIAL AND METHODS: In the present study 90 subjects were enrolled considering the inclusion and exclusion criteria. They were divided into 3 groups Diabetics, Prediabetics, and Controls Evoked potentials offer the possibility to perform a functional evaluation of neural pathways in the central nervous system neurons. One of these methods is Brainstem Auditory Evoked Potentials (BAEPs). By this method, functional pathologies from the acoustic nerve to the upper part of brain stem and auditory cortex can be demonstrated at early stage. These are objective and non-invasive methods of investigation.

RESULT: Their HbA1c & BAEP was assessed. On comparing Glycemic levels based on HbA1c with BAEP of left ear we found a statistically increase in BAEP latency of wave III in uncontrolled diabetics as compared to controls, Prediabetics and controlled diabetics. (3.89±.06 ms vs. 3.63±.20 ms, 3.63±.28 ms and 3.69±.22 ms $p < .01$).But we found no statistically significant difference in comparing HbA1c with BAEP of right ear.

CONCLUSION: Our study showed that in diabetes patients of less than 5 yrs, with poor Glycemic control there was a unilateral abnormality of superior olivary nucleus in pons in auditory pathway, which may be interpret as beginning of central neuropathy in these diabetic patients. So this reveals that central neuropathy in auditory pathway begins earlier with poor Glycemic control. Maintaining good Glycemic control is very important in diabetes, as poor Glycemic control, even in short duration of diabetes, can lead to hearing loss.

KEYWORDS

BAEP; Diabetes mellitus; HbA1c; Hearing impairment.

INTRODUCTION:

According to the Indian Heart Association, India is the diabetes capital of the world with a projected 109 million individuals with diabetes by 2035 [1]. The disease currently affects more than 62 million Indians, which is more than 7.1% of India's adult Population [2].Data from prospective and cross-sectional studies consistently point to the fact that diabetic patients are more likely to develop micro- as well as macro-vascular conditions [3-5]. Prior to the onset of diabetes, many patients already show metabolic abnormalities, such as dyslipidemia, further contributing to the development of complication [6]. Neuropathy is a common and frustrating long-term complication of diabetes. Diabetes may alter both the peripheral and central nerve functions but the peripheral manifestations of diabetic neuropathy are more frequently discussed [7].

Central diabetic neuropathy is a newer concept and it can be detected by simple and non-invasive methods evoked potential [8]. Evoked potentials are electric signals from the central nervous system triggered in response to the stimulation of a receptor. These tests are characterized by very high sensitivity; they are non-invasive and have no side effects. Nerve tract damage increases the latency and reduces the amplitude of the response. They are extremely useful in clinical practice, as it is possible to ascribe changes in the wave latencies to specific anatomic structures in the central nervous system [9]. Brainstem Auditory Evoked Potentials (BAEPs) can evaluate functional pathologies from the acoustic nerve to the upper part of brain stem and auditory cortex at early stage. Lesions in these levels result in changes in BAEP amplitudes and latencies [10]. so, this study was conducted to evaluate CNS neuropathic changes in patients with type 2 DM with and without peripheral neuropathy.

AIMS AND OBJECTIVE:

Our study aimed to investigate the effect of Glycemic control on BAEP based on HbA1c levels.

MATERIAL AND METHOD:

The present study was carried out in Department of Physiology and Department of Biochemistry, Saraswathi Institute of Medical Sciences, Anwarpur, Hapur. The study was an open randomized comparative study.

Ethical Clearance from institutional ethical committee had been obtained. A written informed consent was taken for conducting the investigations and recording the various parameters.

SELECTION CRITERIA:

Inclusion criteria: Subjects with age 40 to 60 & with diabetes < 5 years.

Exclusion criteria: Subjects with any complication of diabetes, any other cardio vascular disease or demyelinating disorder such as multiple sclerosis chronic smokers & alcoholics, history of ear disease, exposure to prolonged loud noise, intake of ototoxic drug, stroke, head injury or family history of deafness & taking any medication which might be expected to interfere with the functioning of central nervous system. Methyldopa, reserpine, phenytoin, Antipsychotic, antidepressants were excluded from the study. Randomly selected patients of either sex were taken after following the inclusion & exclusion criteria and divided into 3 groups:

Group-1 : 30 Normal (HbA1c less than 5.7%)
Group-2 : 30 Prediabetics (HbA1c -5.7 – 6.4%)
Group-3 : 30 known Diabetics (HbA1c -6.5% or more)

Quantitative determination of HbA1 was done using the glycated hemoglobin kit (Sigma diagnostics, St. Louwas, USA) in whole blood

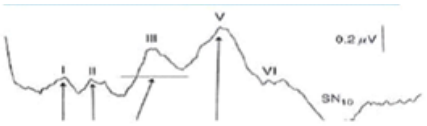
BRAIN STEM EVOKED RESPONSE

Recording techniques

The test was performed on RMS EMG.EP MARK II (RMS (P) LTD. Chandigarh). The subjects were instructed to have a head bath before coming for the test. They were asked to sit comfortably on a chair Cleaned Electrodes(ground electrode: (Fz),reference Electrode (Cz): Vertex, active Electrode (Oz): mastoid process were properly placed by using 10-20 conductive paste applied in the recess of electrode and then adhered to cleaned surface of their respective side. Standard silver chloride electrodes of 1 cm diameter were placed according to 10-20 International System. [11]. Filtering was employed to reduce the band width so that only important component of signals generated was recorded. Lesions in these levels result in changes in BAEP amplitudes and latencies [12]. The stimulus in the form of click was transmitted to ear via a transducer placed in inserted earphone or headphone and the subjects were instructed to listen to the tones

carefully. The waveforms of impulses generated at the level of Brain stem were recorded by the placement of electrodes over the scalp. The impulse recorded contained a series of peaks and troughs. The positive peaked were referred by roman numerals from I-VII.

Different wave pattern recorded were as follows:
I, II, III, IV, V, I-III, I-V, I-Ia, V-Va



STATISTICALANALYSIS:
The one way ANOVA was used to statistically analyze and compare the various proportions which were derived in the different groups. Pearson's Correlation was used for correlations. A p-value which was >0.05 was considered as non-significant, while a p value which was <0.05 was considered as significant and a p value which was <0.001 was considered to be highly significant.

RESULT:
When we compared Glycemic levels based on HbA1c with BAEP of left ear we found a statistically increase in BAEP latency of wave III in uncontrolled diabetics as compared to controls, Prediabetics and controlled diabetics. (3.89 ±.06 ms vs. 3.63 ±.20 ms, 3.63 ±.28 ms and 3.69 ±.22 ms p < .01) as in table 1.

TABLE-1: Glycemic levels based on HbA1c with BAEP of left ear.

Left Ear	Control	Pre diabetic	Controlled DM	Uncontrolled DM	ANOVA (F Value)
Wave I	1.80±.26	1.71±.29	1.80±.21	1.78±0.19	F =0.04 P = ns
Wave II	2.80±.26	2.84±.34	2.80±.28	2.83±.34	F =0.13 P = ns
Wave III	3.63±.20	3.63±.28	3.69±.22	3.89±.06	F =5.15 P = .003
Wave IV	4.7768± .22971	4.8781± .32978	4.7569±.20286	4.87447±.21993	F =1.504 P = ns
Wave V	5.6132± .33300	5.4000± .79152	5.6122±.25031	5.5280±.25364	F =1.119 P = ns
I-III	1.8314± .37906	1.9943± .67522	1.9816±.65876	2.1040±.22045	F = .773 P = ns
I-V	3.80±.79	3.74±.49	3.05±7.13	3.74±.40	F =.61 P = ns
III-V	1.97±.31	1.91±.33	1.92±.39	1.63±.25	F =1.01 P =ns
I-Ia	1.71±1.54	2.09±2.04	1.98±2.19	1.97±2.32	F =.14 P = ns
V-Va	2.13±1.44	1.98± 2.09	2.64±2.28	2.39±2.55	F =.49 P = ns

We found no statistically significant difference in comparing BAEP with HbA1c of right ear in table 2.

TABLE-2: comparing BAEP with HbA1c of right ear.

Right Ear	Control	Pre diabetic	Controlled DM	Uncontrolled DM	ANOVA (F Value)
Wave I	1.83 ±.19	1.72±.25	1.79±.23	1.80±.21	F = .94 P = ns
Wave II	2.90±.35	2.73±.31	2.75±.24	2.98±.34	F = 2.98 P = .03
Wave III	3.69±.25	3.61±.21	3.64±.23	3.71±.21	F = .71 P = ns
Wave IV	4.79±.25	4.85±.21	4.76±.21	4.80±.19	F = .56 P = ns
Wave V	5.57±.51	5.67±.23	5.64±.27	5.55±.24	F =.53 P = ns
I-III	1.88±.29	2.07±.76	1.84±.41	1.91±.23	F = 1.00 P = ns
I-V	3.83±.35	3.94±.40	3.84±.35	3.75±.41	F = .85 P = ns
III-V	1.94±.34	2.03±.25	2.00±.40	1.83±.41	F = .98 P = ns
I-Ia	1.41±1.60	2.08±2.05	2.12±2.11	1.87±1.94	F = .64 P = ns
V-Va	2.20±2.24	2.00±1.89	2.68±2.08	3.28±2.82	F = 1.18 P = ns

DISCUSSION
The present study intended to show the effect of Diabetes on Auditory Pathway. We found in BAEP that there was a delay in wave III and inter peak latency in I-III and III-V in left ear in diabetics. This delay in absolute latency and inter peak latency indicates neuropathy at level of pons superior olivery nucleus. Studies by Reske Neilson et al., and Makishima et al., showed degenerative abnormalities of the brain tissue and atrophy of the spiral ganglion of the cochlea in patients of DM [13,14] thereby, suggesting the presence of central neuropathy. Based on histological findings, they concluded that microangiopathy of the stria vascularis was the main causative factor leading to central neuropathy in these patients [15]. The delay in the central conduction time in DM may be related to the neurodegenerative changes occurring in these patients. Some recent studies, suggested that insulin resistance in T2DM, not only leads to a compromise in the cell survival, metabolism and neuronal plasticity, but also increases oxidative stress and apoptosis of neurons. Also, an increase in the ceramide generation and a subsequent rise in its trafficking across the blood brain barrier, promotes further insulin resistance and neurodegenerative changes in the brain of patients with T2DM [16]. Makishima and Tanaka had noticed that in patients with type-2 diabetics spiral ganglia in basato middle turn of the cochlea tends to get atrophied along with the demyelination of the eighth cranial nerve [17].

The mean latencies of wave III and IPL III-V in left ear were significantly higher in uncontrolled diabetes as compared to controlled diabetes, Prediabetics and normal which shows that patients with uncontrolled diabetes are at more risk of development of central neuropathy.

Our results are consistent with other studies. A study done by Mishra et al [16] showed that the mean value of BEAP latencies of wave I,III,V and IPL of I-III,,III-V,I-V were significantly higher in uncontrolled diabetes as compared to control diabetes. Similarly Pozzessere et al reported that evoked potential abnormalities are correlated with Glycemic control [17]. Zivkovic et al [18] analysis of BAEP revealed a significant difference in the absolute latency of wave V for the right ear and the difference in inter-wave latencies I-V for the right and the left ears between well-controlled Glycemic and the poorly-controlled Glycemic was of borderline significance. However Mahnaz et al found no relation between levels of HbA1c and BAEP similar to the Leon-Morales study (19). We found only unilateral abnormality in BAEP latencies i.e. only left ear was involved. This may be due to the fact that duration of diabetes in all patients enrolled in the study group was less than 5 years. So this may be interpreted as just the beginning of central neuropathy. Moreover the delay in latencies of wave III was significant only in patients with uncontrolled diabetes revealing the fact that central neuropathy has started earlier in patients with poor Glycemic control.

CONCLUSION:
we can conclude that maintaining good Glycemic control is very important in diabetes irrespective of duration to prevent neurological complications as poor Glycemic control even in short duration of diabetes can lead to auditory neuropathy.

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