ORIGINAL RESEARCH PAPER

Physiology

Volume - 7 | Issue - 2 | February - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

BAEP Variations in patients of Type 2 Diabetes mellitus and Normal individuals – an observational analytical study.

KEYWORDS

Brainstem auditory evoked potential , Inter peak latency, cranial nerve abnormalities .

Dr Shweta P. Bhagat

Tutor, Department of Physiology, Mahatma Gandhi Institute of Medical Sciences, Sewagram, Wardha, Maharashtra, India.

Dr Shobha S. Pajai

Associate Professor, Department of Physiology, Mahatma Gandhi Institute of Medical Sciences, Sewagram, Wardha, Maharashtra, India.

ABSTRACT Brainstem auditory evoked potential (BAEP) is a simple non invasive electrophysiological procedure to detect early impairment of acoustic nerve and central nervous system (CNS) pathways even in the absence of specific symptoms. Aim - Aim of the present study was to compare the BAEP (Brainstem auditory evoked potential) variations in patients of type 2 diabetes mellitus and normal individuals. Methods – This was an observational analytical study comparing two groups cases & controls carried on 100 subjects (50 cases and 50 controls). BAEP parameters including absolute latencies of each wave (I,II,III,IV & V) & inter peak latencies (IPL) I-III , I-V & III-V were measured in all study participants. Results - Absolute latencies of all the waves and inter peak latencies I-III, I-V & III-V in both ears were significantly prolonged in type 2 diabetes mellitus patients than that of control group suggesting abnormality in neural conduction. Conclusions – BAEP is a most helpful technique for an early diagnosis of central and cranial nerve abnormalities in diabetic patients.

Introduction

Currently diabetes is one of the biggest health concerns which the world is faced with, according to the World Health Organization (WHO)1,2. WHO defines diabetes as "a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces" 3. Approximately 171 million people worldwide are suffering from diabetes. This number is expected to become more than double by 2030 without intervention. Diabetes is behind every 1 in 20 deaths from all causes and approximately four million annual deaths are because of complications of diabetes i.e. six deaths every minute or one death every 10 seconds. India has been called "the diabetes capital of the world," and it has been estimated that 41 million Indians have the disease and "every fifth diabetic in the world is an Indian".[1,2]

Type 2 diabetes mellitus is associated with micro vascular and neuropathic complications affecting the retina, kidney, peripheral arteries, and peripheral nerves. The pathologic changes accompanying diabetes could cause injury to the vasculature or the neural system of the inner ear, resulting in sensorineural hearing impairment.[4] Mechanisms possibly for diabetes labrynthopathy consists of microangiopathy at the cochlea, neuropathic brainstem involvement, metabolic effect hyperglycemia or hypertriglyceridemia, hyperviscosity resulting vascular problems, or a combination of above factors. The metabolic disturbances may be accompanied by temporary alteration in the intraneural vessel in the form of increased vascular permeability.

The typical hearing impairment which is associated with diabetics is a bilateral sensorineural hearing loss occurring due to neuropathy. Clinically overt neuropathy symptoms manifests only after several years of onset of diabetes, but it can be detected much earlier with the help of electrophysiological tests.[5,6]

Most of the clinical and diagnostic studies have focused on peripheral and autonomic nerves. With the refinement of brainstem evoked response audiometry (BERA), patients have abnormal auditory nerve and brainstem response to an acoustic stimulus and seem to be more prone to develop sensorineural hearing loss. Brainstem auditory evoked potentials (BAEP) are recorded from patient's ear and vertex following response to brief auditory stimulation.

BEAP is a simple non invasive procedure to detect early impairment of acoustic nerve and CNS pathways even in the absence of specific symptoms. They assess the conduction through the auditory pathway upto the midbrain. BAEP consists of five or more waves occurring within 10 msec of the acoustic stimulus. The working hypothesis in most of the BAEP studies has assigned waves I, II, III, IV and V to the segment of the auditory nerve closest to the cochlea, cochlear nucleus, superior olivary complex, lateral lemniscus and inferior colliculus respectively.[7]

Many studies have evaluated the association of BAEP abnormalities and type 2 diabetes mellitus, but these have given variable results [8,9]. There is also a lack of adequate data on BAEP changes in diabetics in India, mainly as very few studies have been done here. The present study was done to compare the BAEP variations in type 2 diabetes mellitus (DM) and normal individuals.

Materials and Methods

Observational analytical study comparing two groups (cases & controls) was carried out in Mahatma Gandhi Institute of Medical Sciences located in central India. Cases were all diagnosed patients of type2 Diabetes mellitus from 30 to 60 years of age group depending upon criteria of HbA1c > 6.5 as per guidelines of American Diabetes Association for Diabetes mellitus. Age and Sex matched normal healthy subjects with cases like hospital staff and relatives of patients accompanying them were selected as controls. Patient diagnosed to have type 2 diabetes mellitus or on diabetic treatment and willing to participate in study were included in study. Patients with other possible causes of neuropathy like hypothyroidism, alcoholism, liver disease & patients having history of ear disease, exposure to prolonged loud noise, intake of ototoxic drug, head injury or family history of deafness were excluded from study.

Total 100 study participants were included (50 controls and 50 Type 2 diabetes mellitus patients). Sample size was estimated using Abnormal BAEP in normal subjects – 10%; Abnormal BAEP in patients of Type2 DM – 40%; Confidence level (α 5%) - 95 % and Power of study – 90% Sample size estimated was 44 in each group.

Ethical clearance from college Institutional Ethics Committee was obtained . History taking included personal and socio-demographic details, occupational history, presenting complaints, past history, family history. Interview was followed by thorough clinical examination. Complete ENT check up by way of otoscopic examination, tuning fork tests to rule out peripheral hearing loss. Required investigations were done. HbA1c levels was assessed in the clinical biochemistry lab of the hospital. Confidentiality of the study subjects were assured and maintained throughout the study.

Volume - 7 | Issue - 2 | February - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

Brainstem auditory evoked potentials (BAEP) recordings

The BAEP procedure is safe and noninvasive ; recordings were performed in a quite room at constant room temperature of 30^0c . Electrode application was according to the International 10/20 System of Electrode Placement with one channel setting.

Subjects were in a supine position on the examination bed and their neck muscles were relaxed by placing pillows under their heads . Patient's hairs were oil free for placing electrodes over the head. Silver chloride cup electrode were attached on each mastoid prominence (A1,A2), at the vertex (Cz , as the reference electrode) and on the forehead (G, as a ground electrode). All the electrodes were cleaned with spirit before applying over patient's head. Then recording paste was applied over the electrode and placed over the prepared area. A cotton ball was placed over the electrode to prevent drying and subsequent loss or shifting of the electrode. The electrode impedance were checked and were kept lower than 3000 ohms . . The subjects wore earphones and were advised to sleep during the investigation. Stimulus in the form of click was transmitted to the ear via a transducer placed in the inserted ear phone. Alternate (condensation and rarefaction) clicks were presented monaurally through earphones at a repetition rate of 11.1 per second. The intensity of the click stimulus was 90 dB , while a white masking noise at a level of 60 dB applied on the contra-lateral non – stimulating ear, in order to ensure reproducibility. Electrical activity were filtered with a low filter frequency at 100 Hz & high filter frequency at 3 KHz. Analysis time was 10ms with a sweep speed of 1ms/Division, two recordings were taken for each ear. The wave forms of impulses generated at the level of brainstem were recorded..

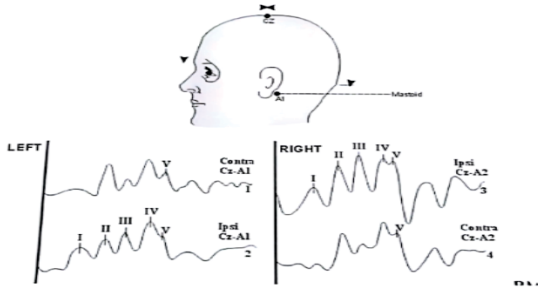

Figure –showing Electrode placement in Brainstem auditory evoked potential.

Absolute latencies were measured from the stimulus to the positive peaks. The absolute latencies of wave I ,II, III , IV and V were measured and the inter peak latencies (IPLs) between the wave I-III , III-V and I-V were also measured from peak to peak of two defined waveforms and hearing threshold for all subjects were measured. Descriptive and inferential statistics were applied . p<0.05 is considered as level of significance.

Results

Table 1: Comparison of anthropometric data and HbA1c levels in diabetic and control subjects

Variables	Diabetic Group (n =50)	Controls Group (n= 50)	Significance
Age (years) (Mean ±SD)	48.42±7.66	46.86±6.97	P= 0.11 NS
Sex M:F	29:21	32:18	p = 0.57 NS
Height (cms) (Mean ±SD)	157.98±5.47	158.84±6.56	P = 0.11 NS
Weight (kgs) (Mean ±SD)	62.32±8.24	59.50±6.11	P = 0.24 NS
HbA1c(%)	7.78±1.23	4.91±0.56	P = 0.0001 S

n: Number of subjects, NS: Non significant (p > 0.05), S: Significant (p< 0.05), SD: Standard deviation, M: Male, F: Female .

The baseline parameters like age, height and weight did not show any statistical significance between the diabetics and controls ($P > 0.05$), It was obvious that Hb1Ac was statistically highly significant difference between both the groups ($P < 0.001$), the values being higher in diabetic. (Table 1)

Table 2 : Comparison of absolute latencies (in msec) in two groups in right and left Ear

	BEAP Absolute Latencies	Control Group (n=50)	Diabetic Group (n=50)	t-value	p-value
Left Ear Mean±SD	**I**	1.54±0.15	1.92±0.31	7.48	0.0001,**S**
	II	2.59±0.19	2.94±0.31	6.68	0.0001,**S**
	III	3.62±0.28	3.99±0.30	6.14	0.0001,**S**
	IV	4.88±0.28	5.20±0.30	5.56	0.0001,**S**
	V	5.44±0.23	5.80±0.36	5.89	0.0001,**S**
Right Ear Mean±SD	**I**	1.56±0.18	2.41±0.37	14.36	0.0001,**S**
	II	2.61±0.15	3.15±0.34	10.14	0.0001,**S**
	III	3.61±0.16	4.28±0.42	10.38	0.0001,**S**
	IV	4.92±0.38	5.39±0.42	5.62	0.0001,**S**
	V	5.40±0.50	6.17±0.41	8.31	0.0001,**S**

BEAP: Brainstem auditory evoked potential, n: Number of subjects, S: Significant (p< 0.05) , SD: Standard deviation .

Furthermore, since the corresponding mean BAEP absolute latencies in all wave form shows statistical significant difference in both diabetic and control subjects in both ear , it is clear that mean absolute latencies is higher in diabetic patient. (Table2)

Table 3: Comparison of Inter peak latencies (in msec) in two groups in right and left Ear

		Control Group (n=50)	Diabetic Group (n= 50)	t-value	p-value
BEAP Inter peak latencies					
Left Ear Mean±SD	I-III	1.86±0.33	2.06±0.26	3.37	0.0001,**S**
	I-V	3.70±0.25	3.87±0.39	2.69	0.008,**S**
	III-V	1.72±0.19	1.81±0.28	1.94	0.043,**S**
RightEar Mean±SD	I-III	1.89±0.30	2.33±0.30	7.22	0.0001,**S**
	I-V	3.64±0.25	4.13±0.38	7.50	0.0001,**S**
	III-V	1.74±0.15	2.10±0.35	6.39	0.0001,**S**

BEAP: Brainstem auditory evoked potential, n: Number of subjects , **S:** Significant (p< 0.05) SD: Standard deviation.

Similarly it was seen that all measures of inter peak latencies were significantly higher in diabetics. A comparison between the mean values of the various absolute wave latencies done separately for both, in diabetics and controls. Statistically significant differences between the mean absolute latencies of waves I, II, III, IV and mean IPL III-V were statistically significant between both the groups ($P > 0.05$), with either ear stimulation.

Discussion

Both central and peripheral nerve damage in diabetes mellitus may lead to the microangiopathy of diabetes. Diabetic neuropathies are nerve damaging disorders that result from diabetic microvascular injury affecting small blood vessels supplying the nerves (vasa nervosum). As small precapillaries and capillaries develop thickened basement membranes they may interfere with their function in diabetes. Accumulation of alcohol sugars sorbitol and fructose is the the second major metabolic derangement that may lead to the development of diabetic neuropathy. Possibly, an excessive accumulation of alcohol sugar in the nerves in similar fashion damage nerve structures.[11] Diabetic neuropathy can occur due to a deficiency of myoinositol in the nerve . Capillary dysfunction, tissue

Volume - 7 | Issue - 2 | February - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

hypoxia, oxidative stress, tissue inflammation, aldose reductase activity, and glucose clearance from blood are the probable mechanism for diabetic neuropathy. [12,13]

There are lots of studies which support the incidence of palsy in the third, sixth and seventh cranial nerves in diabetic patients but little was known regarding the involvement of eighth nerve. Function of 8th nerve is hearing and equilibrium. Makashima and Tanaka in their studies have also observed cochlear atrophy and related demyelination of the 8th cranial nerve.[13]

Electrophysiological investigations are sensitive in determining peripheral and central neuropathy in diabetic patients. Decrease of nerve conduction velocity was found in many patients having normal clinical examination. A latency delay in evoked potentials is found in central demyelinating diseases. Evoked potentials are useful as an investigational method in establishing neuropathy developing in the central nervous system.[14] BAEP study relies on the measurement of latencies of waves which arise after giving a sound higher than the hearing threshold15. An auditory stimulus when delivered to the ear , it evokes consecutive stimulation of brainstem structures like the cochlear nucleus and tracts of the lateral lemniscus and inferior colliculus. Consecutive waves on a BAEP pattern from I to V reflect the electrical activity of the acoustic nerve, cochlea, superior olives, lateral lemniscus, and inferior colliculus respectively[15].

Lengthening in the first wave latency indicates that the disorder is peripheral (distal to the nucleus), whereas, lengthening in the Vth wave latency is specific for brainstem involvement. If the lengthening in I-III inter peak latency occurs together with I-V inter peak latency, this refers to upper or lower brainstem pathology. Lengthening in I-III inter peak latency with normal III-V inter peak latency indicates that the pathology is in the lower brainstem or pons.[15,16]

In our study, inter peak latencies of I-V and I-III were most significantly longer in diabetic group as compared to control group ($p<0.05$) this was in accordance to study conducted by Chaudhary Shatdal et al found latency and inter peak latency of I-III, III-V, I-V of BAEP waveform were prolonged in diabetic patients. Similar findings were observed by Arrthy S et al., 2015, (8) i.e a prolongation of inter peak latencies of I-III IPL,III-V IPL & I-V IPL in diabetic [4]. According to our findings, prolonged inter peak latencies shows that the pathology affected both the peripheral and the central nervous system structures. Some previous studies indicate similar results, and the main affected item is reported to be BAEP inter peak latencies[18].

Due to the high metabolic demands of the inner ear and the auditory pathway making them a target of the disease, even before evidence of other micro vascular complications are occured. In patients of diabetes mellitus main pathological findings are atrophy of spiral ganglion in the cochlea, demyelination and beading of the myelin sheaths of the VIIIth cranial nerve.[19,20]

Conclusion

BAEP is a most helpful technique for an early diagnosis of central and cranial nerve abnormalities in diabetic patients. It is an non-invasive technique which provides data that cannot be obtained through clinical examination. Patients with type 2 diabetes mellitus had the findings of delay absolute latency I, II, III, IV, V and inter peak latencies I–III, III–V, I–V when compared to control groups. This indicates that there is an abnormality in neural conduction in type 2 diabetes mellitus .

Acknowledgement

We are thankful to the staff of Department of Physiology, Mahatma Gandhi Institute of Medical Sciences, Sewagram, Wardha, Maharashtra, India for helping us in conducting this study smoothly.

References

1. Joshi SR, Parikh RM. India - Diabetes capital of the world: Now heading towards hypertension. J Assoc Physicians India. 2007 May;55 :323–4.
2. Kumar A, Goel MK, Jain RB, Khanna P, Chaudhary V. India towards diabetes control: Key issues. Australas Med J. 2013;6(10):524–31.
3. Alberti KGMM, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. Diabet Med. John Wiley & Sons, Ltd.; 1998 Jul;15(7):539–53.
4. Arrthy S, Vinodha R, Saravanan S. Evaluation of optic and vestibulocochlear nerve involvement in type 2 diabetes mellitus patients by using evoked potential. Int J. 2015;4(4):865–7.
5. Siddiqi SS, Gupta R, Aslam M, Abrar Hasan S, Ahmad Khan S, Gandhi R. Type-2 diabetes mellitus and auditory brainstem response. Indian J Endocrinol Metab. Medknow Publications; 2013 Nov;17(6):1073–7.
6. Baweja P, Gupta S, Mittal S, Kumar A, Singh KD, Sharma R. Changes in brainstem auditory evoked potentials among North Indian females with Type 2 diabetes mellitus. Indian J Endocrinol Metab. 2013 Nov;17(6):1018–23.
7. Chalak S, Khatib N, Waghmare T. Binaural recordings of auditory brainstem response for establishment of normative data and its application in screening patients with symmetrical hearing loss. Natl J Physiol Pharm Pharmacol. 2014;4(1):51–6.
8. Ren J, Zhao P, Chen L, Xu A, Brown SN, Xiao X. Hearing Loss in Middle-aged Subjects with Type 2 Diabetes Mellitus. Arch Med Res. 2009;40(1):18–23.
9. Das T, Kundu S, Mazumdar AK, Mukhopadhyay SC. Studies on central nervous system function in diabetes mellitus. J Indian Med Assoc. 2001 Feb;99(2):84,86-87,89.
10. Glantz S. Primer of biostatistics. 2005.
11. Abdülkadiro Z, Kaya A, Gönen S. Brainstem Auditory Evoked Potentials in Patients with Type 2 Diabetes Mellitus. Turkish J. 1999;19(1):29–32.
12. Østergaard L, Finnerup NB, Terkelsen AJ, Olesen RA, Drasbek KR, Knudsen L, et al. The effects of capillary dysfunction on oxygen and glucose extraction in diabetic neuropathy. Diabetologia. Springer; 2015 Apr;58(4):666–77.
13. Reske-Nielsen E, Lundbeak K. Pathological changes in the central and peripheral nervous system of young long-term diabetics. Diabetologia. 1968 Jan;4(1):34–43.
14. Dolu H, Ulas UH, Bolu E, Ozkardes A, Odabasi Z, Ozata M, et al. Evaluation of central neuropathy in type II diabetes mellitus by multimodal evoked potentials. Acta Neurol Belg. 2003;103(4):206–11.
15. Chiappa KH, Ropper AH. Evoked potentials in clinical medicine (second of two parts). N Engl J Med. Massachusetts Medical Society; 1982 May 20;306(20):1205–11.
16. Kikuchi S, Kaga K, Yamasoba T, Higo R, O'uchi T, Tokumaru A. Slow Blood Flow of the Vertebrobasilar System in Patients with Dizziness and Vertigo. Acta Otolaryngol. Taylor & Francis; 1993 Jan 8;113(3):257–60.
17. Shatdal C, Prahlad K, Kumar BB, Sushila P. Evaluation of Brainstem Auditory Evoked Potential. J Univers Coll Med Sci. 2013 Aug 9;1(2):8–12.
18. Brookler K, Rubin W. Practical method of reporting test results in neurotologic disorders. Am J Otol. 1991;12(5):347.
19. De León-Morales LVD, Jáuregui-Renaud K, Garay-Sevilla ME, Hernández-Prado J, Malacara-Hernández JM. Auditory impairment in patients with type 2 diabetes mellitus. Arch Med Res. 2005;36(5):507–10.
20. Huang, C. R., Lu, C. H., Chang, H. W., Tsai, N. W., & Chang WN. Brainstem auditory evoked potentials study in patients with diabetes mellitus. Acta Neurol Taiwan. 2010; 19(1):3340.