Original article:

Study of brainstem auditory evoked potentials in type 2 diabetic patients

Dr.K.Kannan M.D.

Assistant Professor in Physiology, Govt Kilpauk Medical College, Chennai, Tamilnadu

Corresponding author*

ABSTRACT

Introduction: Diabetes mellitus (DM) is a metabolic disorder of several aetiology, characterised by long lasting hyperglycaemia resulting in deranged metabolism of carbohydrate, fat and protein resulting due to loss of insulin secretion, resistance to insulin action, or both. The long-term complications of diabetes include hypertension, end-stage chronic renal disease, diabetic retinopathy, autonomic and peripheral neuropathy, diminished blood flow to lower extremities, myocardial ischemia, cerebrovascular accidents, dysfunction and damage of various organs. Central diabetic neuropathy is a newer and emerging concept and it can be detected by simple and non-invasive methods. One of these methods is brainstem auditory evoked potentials (BAEP) and interpretations of them.

Methods: Brainstem auditory evoked potentials (BAEP) were measured from both the ears in diabetic cases and healthy controls. Forty type 2 diabetes mellitus patients of both sexes in the age group between 35 and 55 were included in the study. Age and gender matched healthy subjects were used as controls. Results were analysed by student's independent t-test. P-Value <0.05 was considered significant.

Result: Brainstem auditory evoked potentials of diabetic patients showed a significant increase in the absolute latencies of wave III and V and significant increase in interpeak latencies of I-III, I-V and III-V when compared with controls.

Conclusion: Periodic assessment of latency delay in BAEP will provide an insight about the effects of DM on central nervous system.

Keywords: DM –Diabetes mellitus, BAEP -Brainstem auditory evoked potential

INTRODUCTION

Diabetes mellitus is a global epidemic, it was estimated that the global number of adults suffering from any form of diabetes was about 285 million in 2010 and will further increase to 439 million by 2030, most of them non insulin dependent diabetes mellitus cases[3,4]. Globally, type 2 diabetes mellitus has become one of the most important chronic public health problems[5]. The metabolic deregulation associated with DM leads to secondary pathophysiologic changes in various organ systems that produce a huge burden on the individual with diabetes and on the health care system. DM is the leading cause of end-stage renal disease (ESRD), peripheral neuropathy, non traumatic lower limb amputations, and loss of vision in adults. The ever increasing incidence of DM worldwide will make this disorder to be one of the leading causes of morbidity and mortality in the near future. The involvement of central nervous system (CNS) in DM is recent concept. Woltman and Wilder[6] concluded from pathological material that diabetic neuropathy is a disease of peripheral nerves and that degeneration in the CNS is unimportant. However, it is reasonable to question whether such a universal metabolic derangement and diffuse angiopathy might involve any part of the nervous system. Recent studies[7] showed the involvement of brain parenchyma in patients with long standing diabetes mellitus. In diabetic patients,

deficits have been reported in neuropsychological, neuroradiological and neurophysiologic studies[8,9]. Neuropsychological studies report deficits in cognitive functions, in particular learning and memory and complex information processing[10]. Neuroradiological studies report modest cerebral atrophy and an increased occurrence of sub cortical and brainstem lesions[11,12]. Neurophysiological studies of the CNS in diabetic patients have mostly involved measurements of evoked potential latencies. Increases in the latencies of evoked potentials of different modalities, including brainstem auditory evoked potentials, visual evoked potentials, and somatosensory evoked potentials, have often been reported[13]. Neurophysiologic alterations have also been described in animal models of diabetes, in particular in rats. Neurophysiologic alterations have been reported in the CNS of diabetic rats[14, 15, 16, 17] by various studies.

AIM AND OBJECTIVES

1. To measure the latency of various waves in BAEP in type 2 diabetic patients and comparing them with healthy controls.

2. To study the involvement of Central nervous system in type 2 diabetic patients by using brainstem auditory evoked potentials as a tool.

MATERIALS AND METHODS

The study was conducted in the Institute of Physiology and Experimental Medicine, Madras Medical College- Chennai, after getting permission from the Institutional Ethical Committee. Type 2 diabetes mellitus patients of both sexes in the age group between 35 and 55 years, were included in the study. They were selected from the Diabetology outpatient department, Government General Hospital, Chennai. Tests were conducted using RMS – EMG MEDICARE SYSTEMS. Age and gender matched healthy subjects were used as controls.

Patients with following conditions were excluded from the study 1.hypertension, 2.smoking and alcoholism, 3.history of head injury, 4.drug intake (ototoxic drugs), 5.ear surgery 6. External ear / middle ear pathologies, 7.conductive / mixed hearing loss. Patients with metabolic abnormalities causing neuropathy, history of cerebral ischemia, and those with cochlear implant were also excluded from the study.

Results were analysed by student's independent t-test. P-value was calculated to test the statistical significance. P- Value <0.05 was considered significant.

BRAINSTEM AUDITORY EVOKED POTENTIALS [18].

Brainstem auditory evoked potentials are the potentials recorded from the ear and vertex in response to a brief auditory stimulation to assess the conduction through the auditory pathway up to midbrain. Brainstem auditory evoked potentials comprise 5 or more waves each comprising a peak within 10 ms of the stimulus. The auditory nerve and brainstem auditory potentials are volume conduction to surface electrodes. At the vertex and earlobe, these form vertex positive and vertex negative waves which are known as brainstem auditory evoked potentials. The peak to peak amplitude of these waves recorded from the scalp are only about 1/00 the amplitude of ongoing spontaneous EEG activity. Absolute amplitudes are measured from the peak to the trough of a wave. The absolute amplitudes are too variable to be of any clinical use and interpretation. There are 5 or more distinct waveforms recorded within 10 ms of the auditory stimulus. Origin of brainstem auditory evoked potentials (I) VIII NERVE (II) COCHLEAR NUCLEUS (III) SUPERIOR OLIVORY NUCLEUS (IV) LATERAL LEMNISCUS (V) INFERIOR COLLICULI.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

INSTRUMENT SETTINGS FOR RECORDING BAEPs: ELECTRODES - Surface electrodes were used to record electrophysiological signals produced in the auditory pathway in response to auditory stimulus. The electrodes were standard cup type silver – silver chloride electrodes of 10mm diameter.

MONTAGE SETTINGS

Active electrode – ipsilateral mastoid.

Reference electrode – vertex (Cz).

Ground electrode - contra lateral mastoid.

AMPLIFIER AND AVERAGER. BAEPs are recorded using an amplification of 200000 - 500000. A 10 ms epoch after the stimulus is averaged for BAEP recording and about 2000 trials are averaged to get a good quality recording. Two repetitions are done and superimposed to get a good quality recording. FILTER SETTINGS Low frequency filter – 100 Hz, electrical activity with frequencies lower than 100 Hz like electroencephalogram activity or other low frequency electrical noise are filtered. High frequency filter – 3000 Hz.

AUDITORY STIMULATION.

Auditory stimulation is produced via headphones fitted to the person's ear. The BAEPs are produced by a brief click stimulus which is a square wave pulse of 0.1 ms duration. Click rate – 11 Hz. Click intensity – 80 Db. Masking – white noise at 60 db intensity.

PROCEDURE Using electrode paste, the recording electrode was placed at ipsilateral mastoid (the ear to which click stimulus is to be given) the reference electrode was placed at Cz midline in the vertex. The ground electrode was placed in the contra lateral mastoid. The electrodes were connected to the pre–amplifier. The subject is asked not to move his/her head during the test.

RESULTS

Chart -1, Comparison of absolute latencies of BAEP between diabetics and controls – RIGHT EAR;

BAEP LATENCY (ms)	GROUP	NO OF SUBJECTS	MEAN ± SD	P -value
Wave -I	diabetic	40	1.49 ± 0.05	0.539
	control	40	1.48 ± 0.05	
Wave -II	diabetic	40	2.73 ± 0.10	0.088
	control	40	2.77 ± 0.09	
Wave -III	diabetic	40	3.79 ± 0.14	<0.05
	control	40	3.56 ± 0.05	
Wave-IV	diabetic	40	4.95 ± 0.10	0.404

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

	control	40	4.93 ± 0.06	
Wave-V	diabetic	40	6.24 ± 0.42	<0.05
	control	40	5.69 ± 0.06	

Table -1, Comparison of absolute latencies of BAEP between diabetics and controls – RIGHT EAR;

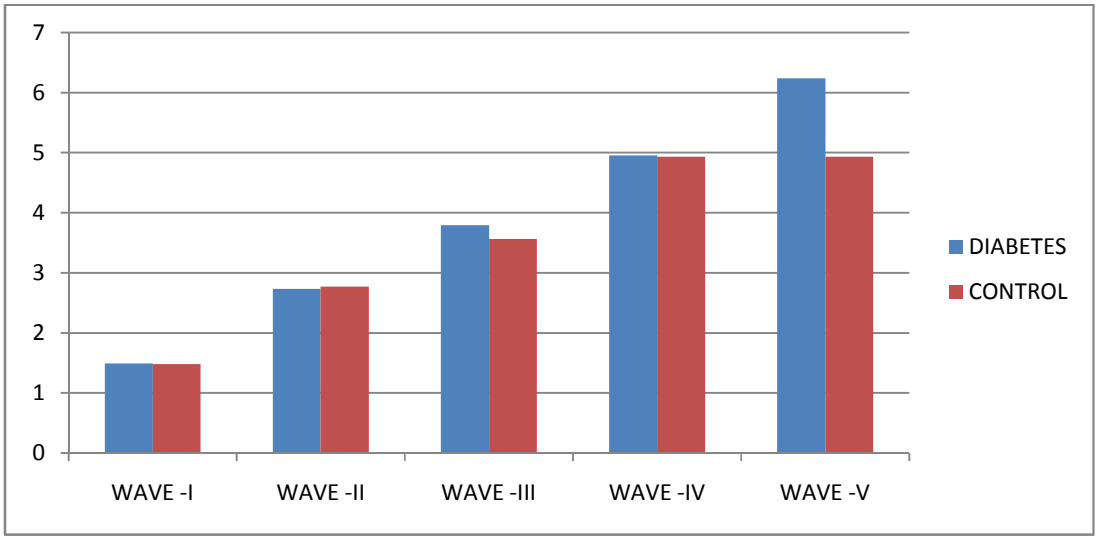
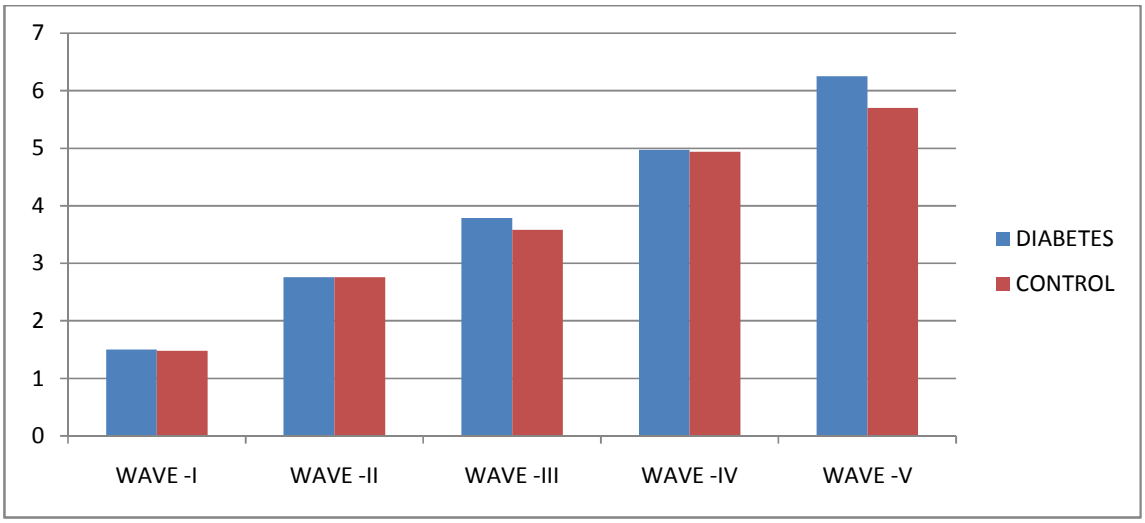


Chart -2 Comparison of absolute latencies of BAEP between diabetics and controls –LEFT EAR:

BAEP LATENCY (ms)	GROUP	NO OF SUBJECTS	MEAN ± SD	P -value
Wave -I	diabetic	40	1.50 ± 0.06	0.315
	control	40	1.48 ± 0.05	
Wave -II	diabetic	40	2.76 ± 0.11	0.935
	control	40	2.76 ± 0.15	
Wave -III	diabetic	40	3.79 ± 0.21	<0.05

	control	40	3.58 ± 0.06	
Wave-IV	diabetic	40	4.97 ± 0.12	0.125
	control	40	4.94 ± 0.06	
Wave-V	diabetic	40	6.25 ± 0.44	<0.05
	control	40	5.70 ± 0.07	

Table -2 Comparison of absolute latencies of BAEP between diabetics and controls –LEFT EAR:



www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

Chart-3 Comparison of interpeak latencies of BAEP between diabetics and controls - RIGHT EAR:

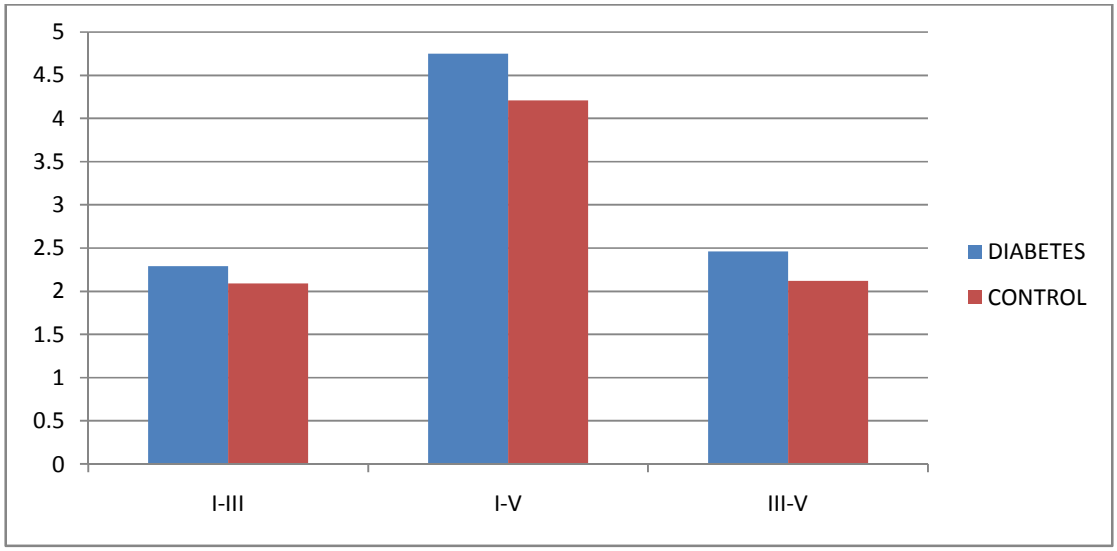
BAEP LATENCY (ms)	GROUP	NO OF SUBJECTS	MEAN ± SD(ms)	P - value
I-III INTERPEAK LATENCY	Diabetic	40	2.30 ± 0.17	
	Control	40	2.08 ± 0.07	<0.05
I-V INTERPEAK LATENCY	Diabetic	40	4.75 ± 0.46	
	Control	40	4.20± 0.08	<0.05
III-V INTERPEAK LATENCY	Diabetic	40	2.45 ± 0.32	
	Control	40	2.12 ± 0.09	<0.05

Chart-4 Comparison of interpeak latencies of BAEP between diabetics and controls - LEFT EAR:

BAEP LATENCY (ms)	**GROUP**	**NO OF SUBJECTS**	**MEAN ± SD(ms)**	**P - value**
I-III INTERPEAK LATENCY	Diabetic	40	2.29 ± 0.25	
	Control	40	2.09 ± 0.08	<0.05
I-V INTERPEAK LATENCY	Diabetic	40	4.75 ± 0.48	
	Control	40	4.21 ± 0.09	<0.05
III-V INTERPEAK LATENCY	Diabetic	40	2.46 ± 0.35	
	Control	40	2.12 ± 0.09	<0.05

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

Table-4 Comparison of interpeak latencies of BAEP between diabetics and controls - LEFT EAR:



DISCUSSION

BAEP LATENCIES IN TYPE 2 DIABETES:

Central diabetic neuropathy and involvement of brain in DM is a newer concept and it can be detected by simple and non-invasive methods. One of these methods is brainstem auditory evoked potentials (BAEP) and interpretations of them[1, 2]. Using this method, functional pathologies and physiological derangement from the acoustic nerve to the upper part of the brainstem can be detected at an early stage[1] in DM patients. Lesions at these levels result in changes in BAEP waves. Evaluation of these changes might help to determine early subclinical injuries restricted to the afore mentioned regions[19].In this study the absolute latencies of wave I to wave V and I-III,I-V and III-V absolute interpeak latencies were recorded and interpreted. In our study, the absolute latencies of wave III and wave V and the interpeak latencies of I-III, I-V and III-V were increased in DM group and showed a significant statistical difference when compared with the control group. The absolute latencies of wave I and wave II in diabetics did not show any significant statistical difference when compared with normal healthy subjects. The increase in wave III latency and interpeak latency I – III with no significant delay in wave I and II latency indicates that there may be a dysfunction in the lower brainstem. Involvement of brainstem is also evidenced by an increase in absolute latency of wave V, I-V and III-V interpeak latencies .The BAEP findings of this study indicates that there may be involvement of brain stem in diabetic patients as evidenced by previous studies[20,21,22]. Delayed auditory brainstem responses in diabetes Mellitus was reported by M.W Donald et al[23],they found that diabetic patients have longer interpeak latencies in the brainstem auditory evoked responses than age-matched controls and the delay is not related to clinical hearing loss or blood glucose level at the time of testing. M.W Donald et al[23] also found that waves I and II were normal in latency, the conduction velocity of the eighth nerve is not involved. The delay occurs between waves II and V, which would reflect altered transmission times in auditory brainstem and midbrain

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

structures, and suggests the presence of a central neuropathy in patients with diabetes. The observed delay in central transmission time in diabetics may be related to the pathological observations like degeneration of the ganglion cells and nerve fibres of the cerebrum, brainstem, and cerebellum-severe enough histological findings to justify the use of the term encephalopathy[7]. Olsson et al[24] and Reske-Nielsen et al[7] on the basis of detailed pathoanatomic studies concluded that brain involvement is common in longstanding diabetes. Biessels GJ[25] et al observed that, in streptozotocin diabetic rats, deficits in cerebral function develop gradually in the course of months and there is a significant deficit in nerve conduction velocity and evoked potential latencies.

This study thus reinforces previous findings that central neuropathy and brain involvement is a complication of DM.Hence involvement of central nervous system should be anticipated in diabetic patients and they should be subjected to evoked potential testing like BAEP.

CONCLUSION:

In this study we found out that in DM patients there was a delay in latency of waves III and V and interpeak latencies when compared with controls. Long standing metabolic derangements in type 2 diabetic patients will probably have an effect on central nervous system. Hence, diabetic patients can be periodically subjected to evoked potential (BAEP) testing to assess central nervous system dysfunction and referred for further screening if required. Diabetic patients with abnormal evoked potentials can be educated and motivated to maintain plasma glucose within normal levels for the normal functioning of central nervous system and normal quality of life.

REFERENCES:

1. Bergama chi R, Versino M, Callieco R. Multimodal evoked potentials in diabetics. Acta Neurol 13 (3): 228-235, 1991.

2. Chippa KH, Ropper HA. Evoked potentials in clinical medicine. N Eng Med 306: 1140-1150, 1982.

3. AJE, Sicree RA, Zimmet PZ: Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010, 87(1):4-14.

4. King H, Aubert RE, and Herman WH: Global burden of diabetes, 1995-2025: prevalence-numerical-estimates,-and-projections.-Diabetes-care-1998, 21 (9): 1414-1431.

5. International Diabetes Federation: Diabetes Atlas.2nd edition. Brussels: Gan D, Ed. Belgium; 2003.

6. Woltman HW, Wilder RM. Diabetes mellitus. Pathological changes in the spinal cord and peripheral nerves. Arch Intern Med 1929; 44:576-603.

7. Reske-Nielsen E, Lundback K, Rafaelsen OJ. Pathological changes in the central and peripheral nervous system of young long term diabetics. Diabetic encephalopathy. Diabetologia 1966; 1: 233-41.k

8. Roy Freeman. The nervous system and Diabetes. In: Joslins Diabetes Mellitus, 14th Ed, A Wolters Kluwer Company, Philadelphia, 952.

9. Kent S. Geriatrics 1976; 31:140-51.

10. Tun PA, Nathan DM, Perlmuter LC. Cognitive and affective disorders in elderly diabetics. [Review]. Clin Geriatr Med 1990; 6:731–46.

11. Araki Y, Nomura M, Tanaka H, Yamamoto H, Yamamoto T,Tsukaguchi I, et al. MRI of the brain in diabetes mellitus.Neuroradiology 1994; 36: 101–3.

12. Dejgaard A, Gade A, Larsson H, Balle V, Parving A, Parving HH.Evidence for encephalopathy. Diabet Med 1991; 8: 162–7.

13. Di Mario U, Morano S, Valle E, Pozzessere G. Electrophysiological alterations of the central nervous system in diabetes mellitus. [Review]. Diabetes Metab Rev 1995; 11: 259–77.

14. Rubini R, Biasiolo F, Fogarolo F, Magnavita V, Martini A, Fiori MG.Brainstem auditory evoked potentials in rats with streptozotocin induced diabetes. Diabetes Res Clin Pract 1992; 16: 19–25.

15. Sima AA, Zhang WX, Cherian PV, Chakrabarti S. Impaired visual evoked potential and primary axonopathy of the optic nerve in the diabetic BB/W-rat. Diabetologia 1992; 35: 602–7.

16. Terada M, Yasuda H, Kikkawa R, Koyama N, Yokota T, ShigetaY. Electrophysiological study of dorsal column function in streptozotocin-induced diabetic rats: comparison with 2, 5-hexanedione intoxication. J Neurol Sci 1993; 115: 58–66

17. Carsten RE, Whalen LR, Ishii DN. Impairment of spinal cord conduction velocity in diabetic rats. Diabetes 1989; 38: 730–6.

18. UK Misra, J Kalita In: History of Clinical Neurophysiology. Clinical Neurophysiology, 1st Ed 2005, Elsevier, New Delhi 1-7.

19. Spehlman R. Evoked potential primer. Boston, Butterworth Publisher, 1987, 204-207.

20. Hikmet Dolu , Umit Hidir Ulas, Erol Bolu, Abdullah Ozkardes, Zeki Odabas, Metin Ozata and Okay Vural. Evaluation of central neuropathy in type II diabetes mellitus by multimodal evoked potentials Acta neurol. Belg., 2003, 103, 206-211

21. Khardori R., soler N. G., Good D. C., Devleschowarda. B., Broughton D. et al. Brainstemauditory and visual evoked potentials in type 1(insulin-dependent) diabetic patients. Diabetologia, 1986, 29 (6): 362-365.

22. Donald M. W., Erdahl D. L., Surridge D. H., Monga TN., Lawson J. S. et al. Functional correlates of reduced central conduction velocity in diabetic subjects. Diabetes, 1984, 33: 627-633.

23. M W Donald, C E Bird, J S Lawson, F J J Letemendia, T N Monga, D H C urridge, P Varette-Cerre, D L Williams, D M L Williams, and D L Wilson Delayed auditory brainstem responses in diabetes mellitus J Neurol Neurosurg Psychiatry. 1981 July; 44(7): 641–644

24. Olsson Y, Save-Soderberg Y, Sourander P, AmgervallL. A pathoanatomical study of the central andperipheral nervous system in diabetes of early onset and long duration. Pathol Eur 1968; 3:62-79.

25. Biessels GJ, Cristino NA, Rutten GJ, Hamers FP, Erkelens DW, Gispen WH. Neurophysiological changes in the central and peripheral nervous system ofstreptozotocin-diabetic rats. Course of development and effects of insulin treatment. Brain 1999; 122: 757-68