DOI Number: 10.5958/2320-608X.2019.00006.4

Visual Evoked Potential in Diabetics – A Non-invasive Study

Harini S [1], Bhagya V[2]

[1]Assistant Professor, Physiology, The Oxford Medical College Hospital & Research Centre, Bangalore, Karnataka, [2]Professor, Physiology, JJM Medical College, Davangere, Karnataka, (Rajiv Gandhi University of Health Sciences, Bangalore, India)

ABSTRACT

Background: Prevalence of diabetes mellitus is increasing worldwide, more commonly due to improved lifestyle changes. It is particularly more common in developing countries. Involvement of peripheral, central & autonomic nervous systems are frequently encountered. Diabetes is associated with visual impairment, which if not detected early, can lead to early disability in patients. Visual evoked potential (VEP) is a non invasive method to assess visual pathway. Present study was done to evaluate impact of diabetes on central nervous system, particularly visual functions.

Aims and Objectives: To analyse visual evoked potential in diabetes and age matched controls.

Materials and Method: 60 diabetics (NIDDM and IDDM) attending medical out patient department of Bapuji & Chigateri hospital, Davngere and 60 age matched controls selected randomly from general population were subjected to visual evoked potential. Parameters such as latencies of N^{70}, P^{100} and N^{155}, peak to peak amplitude of waves N^{70}-P^{100} and P^{100}-N^{155} were assessed and analyzed by using unpaired student T test for comparison between cases and controls and one way ANOVA for multiple group comparisons within diabetics based on duration of diabetes and fasting blood sugar levels.

Results: patients with diabetes mellitus have subclinical visual impairment as revealed by impaired visual evoked potential. Diabetics showed delayed latencies and reduced amplitude of various parameters of VEP. There was a positive correlation between prolongation of latencies and duration of diabetes and FBS levels.

Conclusion: present study correlates with earlier findings that visual pathway gets involved in diabetics even before the development of retinopathy which can be detected using VEP. Meticulous control of blood sugar levels is a must to prevent complications of diabetes, so that further damage can be prevented.

Keywords: *Diabetes mellitus; vision; visual evoked potential (VEP); VEP & duration of diabetes mellitus; VEP & FBS levels; waves N70 & P100;*

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia , caused by complex interaction of genetics and environmental factors. Factors causing hyperglycemia include, reduced insulin secretion, decreased glucose utilization and increased glucose production.

Worldwide prevelance of diabetes has risen dramatically over the past two decades from an estimated 30million cases in 1985 to 285 million in 2010 .[1] Prevalence in adults is found to be 2.4% in rural and 4-11.6% in urban dwellers.[2] According to latest 2016 data from world health organisation , globally an estimated 422 million adults are living with diabetes mellitus. In India, diabetes currently affects more than

Corresponding Author:
Dr. Harini S
Assistant Professor, Department of Physiology,
The Oxford Medical College Hospital & Research Centre, Bangalore, Karnataka -562107. (Rajiv Gandhi University of Health Sciences, Bangalore, India)
Phone: 9986910541, Email: drharini87@gmail.com,

62 million Indians, which is more than 7.1% of adult population.[15] Based on current trends, more than 360 million individuals will have diabetes by the year 2030. Diabetes mellitus increases with aging. Worldwide estimates project that, in 2030 the greatest number of individuals with diabetes will be 45-64 years of age.[1] It is a set of clinical syndromes that affect distinct regions of the nervous system, singly or combined, encompasses wide range of abnormalities affecting proximal and distal peripheral sensory and motor nerves and autonomic nervous system[3] .

Cranial nerve mononeuropathies are commonly observed in diabetes. The 3rd, 4th and 6th nerves are involved, separately or in varying combination. Optic nerve affection manifested as optic atrophy, as a result of diabetes alone is estimated to occur in 0.6% cases[7]. The significance of these changes has proved to be difficult to be investigated, as for many years, electroencephalography (EEG) was the only technique available to study the electrophysiological activity of the brain. However, the information provided by this method is limited, particularly in assessment of deeper brain structures. The advent of advanced electro-neurophysiological techniques to assess cerebral function, such as measurement of electrical evoked potentials like visual evoked potential (VEPs), have increased our understanding of normal visual function and possible effects that diabetes may exert[6].

AIMS AND OBJECTIVES

The present study was conducted to evaluate visual evoked potential to pattern reversal stimulation in a group of subjects with type I and type II diabetes mellitus. The aim was to find whether the VEP latencies are altered or not, and if altered, whether it shows any correlation with fasting blood sugar (FBS) and duration of diabetes mellitus.

MATERIALS AND METHOD

Methodology:

The study was conducted in the department of Physiology, J.J.M. medical college, Davangere. In this study, diabetics (total 60) between 25 to 55years attending medical outpatient department of Bapuji hospital and Chigateri General hospital attached to J.J.M. medical college were selected and 60 normal age matched subjects were selected randomly from the general population. Inclusion criteria:Age group between 25 – 55 years, patients who are biochemically proved diabetes mellitus, Patients of type I and type II diabetes mellitus, Normal healthy age matched controls between 25-55 years.

The groups are divided as follows, Group 1→ 60 controls, age matched healthy individuals, Group 2→ 20 diabetics with duration less than 10 years, Group 3→ 20 diabetics with duration 10-15 years, Group 4→ 20 diabetics with duration more than 15 years. Based on FBS (Fasting blood sugar) levels, Good control→ less than130mg/dl, Fair control→ 130-145mg/dl, Poor control→ more than 145mg/dl.

Age group below 25 years and above 55 years, Patients with visual acuity less than 6/18 even with corrected lenses, Patients with acute complication of diabetes like, diabetic ketoacidosis, recurrent ketonuria, non ketotic hyper- osmolar coma and hypoglycaemia, Patients with diabetic retinopathy, cataract, glaucoma, vitreous opacities, optic atrophy, maculopathy, Patients taking psychoactive drugs or drug addiction, H/O Hypertension, anaemia, stroke, dementia, Smokers, Alcoholics, H/O cardiovascular or neurological disorders were excluded from the study. Written and informed consent were taken for the study after explaining the procedure and its significance in their vernacular language. The ethical committee clearance was taken. A brief personal history was taken and a clinical examination of all the systems was done to exclude medical problems and to prevent confounding of results. Detailed ophthalmological check up of all patients was done which includes visual acuity, ocular tension and fundus examination.

After selecting the subjects, they were subjected to VEP testing on PC based, 2 channel, RMS EMG. EP MARK II machine manufactured by RMS RECORDERS and MEDICARE SYSTEM, Chandigarh. Procedure in brief: Recording was carried out in a quiet and dimly lit room. Subjects were asked to come without applying oil to scalp and to shampoo hair and make it dry.

VEP RECORDING: VEPs were recorded using the RMS machine and standard silver- silver chloride disc electrodes. A VEP monitor displaying checker board is used to give the pattern reversal stimulus. A montage consisting of one channel is used for the VEP recording. The subject is asked to sit comfortably in front

of the checkerboard pattern at an eye screen distance of 100cm. An amplification which ranged between 20,000 and 1,00,000 was used to record the VEPs. The electrode impedance was kept below 5KΩ. The recording was performed in a dark and sound attenuated room. Uniocular stimulation was given to both eyes separately with black and white checks which changed phase (black to white and white to black) abruptly and repeatedly at a specified number of reversals per second, by using a checkerboard.

The usual glasses (if any) were allowed to be put on during the test. The subject is instructed to avoid the usage of meiotic or mydriatic drugs, 12 hours before the test. The electrodes were placed with an electrode paste after cleaning the site with a spirit swab. The scalp electrodes were placed relative to bony landmarks. The anterior/posterior midline measurements were based on the distance between nasion and inion over the vertex. The active electrode was placed in the middle of the variation zone of the calcarine fissure at Oz, which is the highest point on the occiput. The reference electrode was placed at Fz or 12cm above the inion. The ground electrode was placed over the forehead Cz.

RESULTS

TABLE 1: Comparison of VEP parameters between Diabetics and Healthy controls in left eye.

LATENCIES LEFT EYE (ms)	Cases (N=60)		Controls (N=60)		Unpaired t Test	
	Mean	Std. Deviation	Mean	Std. Deviation	t Value	P Value
N_{70}	74.09	4.39	68.04	1.47	10.11	P<0.001
P_{100}	105.69	6.15	96.93	1.33	10.76	P<0.001
N_{155}	139.10	4.76	131.62	3.18	10.12	P<0.001
AMPLITUDE LEFT EYE(μv)						
N_{70}-P_{100}	3.59	1.47	6.61	0.85	-13.81	P<0.001
P_{100}-N_{155}	6.28	2.06	8.91	1.05	-8.79	P<0.001

TABLE 2: Comparison of VEP parameters and Duration of Diabetes in left eye.

LATENCIES LEFT EYE(ms)	DURATION			ANOVA	
	<10 =20)	10-15 (N=20)	>15 (N=20)	F Value	P Value
N_{70}	71.86 ± 3.3	74.7 ± 4.18	75.72 ± 4.81	4.61	P<0.01
P_{100}	98.87 ± 1.5	106.5 ±4.40	111.84 ± 3.06	77.7	P<0.001
N_{155}	137.9 ±4.87	139.31 ± 3.19	140.1 ± 5.92	1.05	0.35
AMPLITUDE LEFT EYE(μv)					
N_{70}-P_{100}	5.2 ±0.65	3.48 ±0.81	2.01 ± 0.64	102.3	P<0.001
P_{100}-N_{155}	8.48± 0.57	6.44 ±1.12	3.78 ±0.45	174.8	P<0.001

TABLE 3: Comparison of VEP parameters and FBS levels in left eye.

LATENCIES LEFT EYE(ms)	FBS			ANOVA	
	< 130 (N =47)	130-145 (N=6)	>145 (N=7)	F Value	P Value
N_{70}	70.5 ± 1.81	72.5 ±4.0	74.8 ±4.4	3.73	0.03
P_{100}	98.23 ± 1.1	99.12 ±0.99	107.6 ±5.5	16.22	P<0.001
N_{155}	139.5 ± 4.8	139.5 ± 3.16	136.99 ± 5.17	0.78	0.46
AMPLITUDE LEFT EYE(μv)					
N_{70}-P_{100}	5.14 ± 0.61	5.06 ± 1.08	3.17 ±1.3	12.25	P<0.001
P_{100}-N_{155}	8.91 ±0.43	7.83± 1.42	5.69 ± 1.86	13.14	P<0.001

DISCUSSION

Central diabetic neuropathy is a newer concept and it can be detected by simple and non- invasive methods. The methods used in the present study are visual evoked potential (VEP) and Event related potential P_{300} (ERP P_{300}). Visual evoked potential relies on measurement of latencies and amplitude of waves arising after giving uniocular visual stimulus in the form of black and white checks which changed phase, by using a checkerboard. Consecutive waves N_{70}, P_{100} and N_{155} reflect the electrical activity of primary visual cortex and visual association areas. They are also used to assess the visual pathway, which runs from retinal ganglion cells to visual cortex.

In our study we found that there was prolongation of latencies of waves N_{70}, P_{100} and N_{155} ($p<0.001$) and reduced amplitude of N_{70}-P_{100} and P_{100}-N_{155} ($p<0.001$) in diabetics compared to controls in both eyes. The P_{100} waveform is generated in the striate and peristriate occipital cortex, N_{70} reflects activity of the fovea and primary visual cortex while N_{155} reflects activity of visual association areas.[6]The delayed latencies and reduced amplitude which were recorded even in the absence of retinopathy or any ocular pathology is indicative of anterior visual pathway affection.[7] Also VEP detected damage in retinal ganglion cell in diabetics. This ganglion cell damage is considered as a sign of preclinical diabetic retinopathy, as no signs of diabetic retinopathy were detected in patients on ophthalmoscopic examination.[8,9] similar findings were reported earlier by Chopra D et al [6], Essam M Ebrahim et al[10].

Comparison of VEP parameters with duration of diabetes mellitus

In our study, we found that the latencies of N_{70} and P_{100} were significantly prolonged in diabetics with duration of illness between 10-15years and more than 15 years compared to duration of less than 10 years ($p<0.01$, $p<0.001$) respectively. There was also significant reduction in amplitude of N_{70}-P_{100} and P_{100}-N_{155} ($p<0.001$) in diabetics of longer duration in both eyes. The present study concurs with findings of V. Gayathri et al., studies have shown that alterations in VEP latency are not present at the onset of diabetes, but occur only after the disease has been present for a mean of atleast 3.3 years. Retinal, macular and visual pathway function is differently impaired in diabetes patients with different duration of disease, having no signs of retinopathy. The impairment starts in the nerve conduction of the visual pathways with an early involvement. It is carried on into the innermost retinal layers and in the macula and ends in the middle and outer retinal layers.[5] Similar findings were reported in Siedl R et al[11] .

Comparison of VEP parameters with FBS levels.

In our study, we found, significant prolonged

latencies of N_{70} and P_{100} in diabetics with FBS 130-145mg/dl (fair control) and more than 145mg/dl (poor control) compared to diabetics with less than 130mg/dl (good control) ($p<0.03$, $p<0.001$). Also, there was significant decrease in amplitude of N_{70}-P_{100} and P_{100}-N_{155} in diabetics with poor glycemic control ($p<0.001$) in both eyes respectively. Similar findings were found in Kumar R et al[12].

According to Pozzessere G et al[13] , increasing evidence suggests that the accumulation of glucose susbstrate, as a consequence of relative lack of insulin, increases aldose reductase activity. The increased enzyme activity of alternate polyol pathway at different level, including vessel walls, retina and particularly nerve complex metabolism, may slowly and progressively impair neurologic functions. Ziegler O et al[14], in their study showed that, after 3 days of close blood glucose monitoring the mean latencies were significantly shorter but were still significantly longer than control values

CONCLUSION

Our study provides a glimpse about the effect of diabetes mellitus on vision, which brings about changes in VEP parameters. Although we understand to some extent these changes and also since only a few studies have been done on this aspect, further research is needed to study the effect of diabetes mellitus on the visual aspects. VEP abnormalities in diabetes initially seem to appear due to central impairment of visual pathway. Thus, VEP can be of clinical importance for diabetes, as it reflects the degree of neural affection and may alert patients for adequate glycemic control, which can resist neuropathic progression any further. Although from our study we can say that duration of illness and poor glycemic control are definitve risk factors for the development of central neuropathy, a larger sample size would have had a significant outcome. As diabetes is widespread in our country, it is necessary to consider "Visual impairment as a long term complication of diabetes". It is recommended to perform VEP initially on all diabetic patients and to keep this as an "initial record of visual examination of patients". Also, performing the test every year on a regular basis could help the physician to update record of visual status of the patients as well as to give necessary guidance in regard to the control of diabetes to them.

Limitations:

The present study may have included more number of subjects for better interpretation of results.

Conflict of Interest: NIL

Source of Funding: Self

REFERENCES

1. Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL. Harrison's Principles of Internal Medicine, 18th Ed. New York: McGraw-Hill; 2011: 2968-69.
2. Park K. Park's Textbook of preventive and social medicine, 21st ed. Jabalpur: Bhanarsidas Bhanot; 2011 : 362-63.
3. Vinik AI, Park TS, Stansberry KB, Pittenger GL. Diabetic neuropathies. Diabetologia 2000; 43: 957-973.
4. Puvanendran K, Devathasan G, Wong PK. Visual evoked responses in diabetes. Journal of neurology, neurosurgery and psychiatry 1983; 46: 643-647.
5. V. Gayathri, B.Vijayalakshmi,M. Chandrashekhar. Electrophysiological assessment of neuropathy in visual pathway in diabetes mellitus. Journal of diabetology 2012 Feb; 1-4.
6. Chopra D, Gupta M, Manchanda KC, Sharma RS, Sidhu RS. A study of visual evoked potentials in patients of type 2 diabetes mellitus. Journal of clinical and diagnostic research 2011 Jun; 5(3): 519-522.
7. Raman PG, Sodani A, George B. A study of visual evoked potential changes in diabetes mellitus. Int. Journ. Diab. Dev. Countries 1997; 17: 69-73.
8. Al-Idani MAA, Strak SK, Al-Maraj KA, Kathim LA. The study of visual evoked potential changes in patients with diabetes mellitus. The medical journal of Basrah university 2009; 27 (2): 55-65.
9. Karlica D, Galetovic D, Ivanisevic M, Skrabic V, Znaor L, Jurisic D. Visual evoked potential can be used to detect a prediabetic form of diabetic retinopathy in patients with diabetes mellitus type I. Coll. Antropol. 2010; 34(2): 525-529.
10. Ebrahim ME, Khallaf ME, Omar ME, Sobh MK, Seiam AR, Elgezery MM et al. Neurophysiological

assessment of subclinical central neuropathy in type II diabetic patients. AAMJ 2012 Sep; 10(3): 1-21.

11. Seidl R, Birnbacher R, Hauser E, Bernert G, Freilinger M, Schober E. Brainstem auditory evoked potentials and visually evoked potentials in young patients with IDDM. Diabetes care 1996 Nov; 19(11): 1220-1224.
12. Kumar R, Sundararajan D, Ponraj RS, Srinivasan M. A study of early detection of changes in visual pathway due to diabetes mellitus by visual evoked potential. International journal of medical research and health sciences 2014; 3(1): 161-164.
13. Pozzessere G, Rizzo PA, Valle E, Mollica MA, Meccia A, Morano S et al. Early detection of neurological involvement in IDDM and NIDDM. Multimodal evoked potential versus metabolic control. Diabetes care 1988 June; 11(6): 473-480.
14. Ziegler O, Guerci B, Algan M, Lonchamp P, Weber M, Drouin P. Improved visual evoked potential latencies in poorly controlled diabetic patients after short term strict metabolic control. Diabetes care 1994 Oct; 17(10): 1141-1147.
15. Epidemiology of diabetes mellitus. June 2013: https://en.m.wikipedia.org/wiki/Epidemiology_ of_ diabetes_ mellitus