Original Research Article

EVALUATION OF RETINAL GANGLION CELL ACTIVITY BY PATTERN VISUAL EVOKED POTENTIALS IN TYPE 2 DIABETES MELLITUS

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Abstract

Background: Visual evoked potentials VEP is used for extracting the electroencephalographic activity in visual cortex that can detect the optic nerves,retinal ganglion cells,chiasmal and retrochiasmal dysfunction which includes optic radiations and occipital cortex. As diabetes causes diabetic retinopathy due to neuropathy and microangiopathy involving metabolic disturbances and intraneural blood flow disorders, diabetic patients are screened for non functional changes which occurs much more earlier than clinically detectable changes like early identification of diabetic retinopathy This study was conducted among the 80 Diabetic patients both male and female attending Diabetic OP at Chenagalpet Medical College and 40 healthy individuals were selected for the study for a period of one year from March 2015 to February 2016. Based on the inclusion and the exclusion criteria the study participants were recruited. The final attained sample is 120. The study participants were grouped into three groups .Routine investigations like anthropometric measurements (height,weight),Blood pressure measurements and Fasting and 2 hr postprandial blood sugar level were done. Ophthalmic investigations like visual acuity ,intra ocular pressure and fundoscopy was also done. On the day of recording the subjects were asked to come with oil free hair after the last hair wash and to avoid any miotic or mydriatic 12 hours before the procedure. Those wearing glasses recording of VEP done with glasses and without glasses .The data collected was entered in excel sheet and analysis was done by SPSS 23, P value <0.05 is considered as statistically significant. **Result:** The baseline characteristics like age, height and weight were not found to be statistically significant. Fasting blood sugar, postprandial blood sugar levels and duration were found to be clinically significant. P100 latency prolongation was observed in both right and left eye of DM and DR group compared to control group and it is highly significant. There is no significant difference in mean amplitudes between study group and control group in both right eye and left eye. P100 latency was delayed in rt eye in males and in left eye in females.P100 correlates with duration of DM. **Conclusion:** Our study concludes by stating the relevance in P100 latency prolongation which indicates the possibility of CNS involvement subclinically.P100 latency also had association with FBS and duration of Diabetes. Thus by using PVEP we can detect the retinal dysfunction earlier and it can be used as a screening tool to avert the morbidity.

INTRODUCTION

The most serious challenge in our health care is Type II Diabetes Mellitus.[1] Among diabetic patients the chronic hyperglycemia tends to damage, and cause dysfunction and malfunction various organs like eyes, kidneys, heart and blood vessels. continuously. It is also well known to us that the

Diabetic patients tends to develop Autonomic and peripheral neuropathy.[2] Many studies have been done in Diabetes patients regarding peripheral nervous system there is paucity of studies on central nervous system involvement. Many reviews done recently state that diabetic patients also suffer from central neuropathy or degeneration of central nervous system.

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The chronic progressive sight threatening complication of diabetes is Diabetic retinopathy. It is a progressive disease of retinal vasculature.The clinical feature are vascular occlusion,increased vascular permeability and retinal ischemia.Diabetic retinopathy is the leading cause of blindness in both developed and developing countries.In India it is the sixth leading cause of blindness and by good metabolic control we can significantly reduce the development and progression of ocular and visual complications.The number people with diabetic retinopathy tends to increase from 126 million to 191 million.[3]

Visual dysfunction in Diabetes mellitus is multifactorial and has pathophysiological factors in various stages of disease.[4] In managing the Diabetic patients the primary goal is to maintain blood glucose level in normal range.[5] Even before the onset of microvascular lesions,the subtle functional changes occurs in retina which are not detected by fundus photography.[6] Clinical neurophysiology helps in functional evaluation of the nervous system through evoked potentials which is a new method.This non invasive method gives much information about the functional state of the the central nervous systems. This is helpful particularly when the clinical signs and the neuroimaging methods results are non informative and non conclusive.[7] Visual evoked potentials (VEP) is a non invasive,sensitive test which can identify the central demyelination of the optic nerve.[8] With the help of pattern VEP we can diagnose the early diabetic changes and can determine the prognosis with treatment. Any defect from the optic nerve to the occipital cortex is also detected by Pattern VEP.

VEP recording from scalp is found to be highly reliable, sensitive in finding the conduction defects in the anterior pathways. The visual neurons selectively responds to the visual patterns with progressively greater complexities.[9] Delayed VEP is also found in various clinical conditions like retrobulbar neuritis, papillitis, hereditary toxic and nutritional optic neuropathies and multiple sclerosis.In diseases like glaucoma, conducting media diseases of eyes like vitreous opacities, cataract and retinal diseases prolonged VEP latencies are observed.[10]

As the duration of the Diabetes mellitus increases there is a progressive decrease in amplitude and increase in latency values. In Retinal ganglion cell damage there is a progressive delay in VEP latency and this damage occurs even before the first opthalmoscopically noticeable signs of diabetes retinopathy occurs. The structural damage at the level of myelinated optic nerve fibres is indicated by the prolongation of P100 latencies. The aim of the study is to detect retinal ganglion cell activity in diabetes mellitus patients type 2 and compare the VEP among diabetes mellitus patients with non proliferative diabetic retinopathy and diabetes mellitus patients without non proliferative diabetic retinopathy.

Objectives of the Study

- To detect retinal ganglion cell activity in diabetes mellitus patients using pattern reversal VEP
- To compare the latencies among diabetes and non diabetes.

MATERIALS AND METHODS

Study Setting
This study was conducted among the 80 Diabetic patients both male and female attending Diabetic OP at Chenagalpet Medical College .40 healthy individuals were selected for the study for a period of one year from March 2015 to February 2016

Study Design
Case control study

Sample Size
The study participants fulfilling the inclusion and the exclusion criteria were included in the study throughout the study period. The final attained sample is 120. The study participants were grouped into three .
Group I-Control group
Group II-Diabetic without retinopathy
Group III-Diabetic with non proliferative retinopathy

Inclusion Criteria
- Age group 30-60 years
- Both sex
- Diabetic retinopathy cases(Early Treatment Diabetic retinopathy study)
- Normal visual acuity
- Abnormal blood glucose(ADA criteria)

Exclusion Criteria
- Known Hypertensive /evidence of cardiovascular illness
- Past H/O CVA demyelinating diseases (multiple sclerosis)
- Cataract
- Glaucoma
- Evidence of optic atrophy
- Known Smoker/Alcoholic/Tobacco chewing/Any medications affecting optic nerve (ATT ,Chloroquine etc)
- Proliferative diabetic retinopathy
- Body mass index >40

Data Collection Method
After obtaining the Institutional Ethical Committee clearance, the study was started after obtaining patients informed consent. The study participants recruited during the study period i.e 120 underwent the routine investigations like anthropometric measurements (height,weight),Blood pressure measurements and Fasting and 2 hr postprandial blood sugar level. Ophthalmic investigations like visual acuity ,intra ocular pressure and fundoscopy was also done.

On the day of recording the VEP the patients were asked to come with oil free hair after the last hair wash and to avoid any miotic or mydriatic 12 hours

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before the procedure. The usual glasses used by the subjects were worn by during VEP recording

VEP Recording

During the procedure the study participants were asked to be seated at a distance of 1 metre from the VEP monitor screen. They were explained about the procedure and the electrodes were fixed in the following positions after preparing the skin by abrading and degreasing.

- Recording electrode-just above the inion as per 10-20 international system
- Ground electrode-at forehead
- Reference electrode -places 12 cm above nasion
- Electrodes were connected to the Physiopac.
- Pattern of reversal stimulus (black and white checks)
- The study participants were instructed to look at the centre red square on the VEP monitor screen
- In each recording 200 sweeps averaged
- Each eye tested separately .When one eye is test the other eye was patched.

- Recordings were done in a dark room and VEP was recorded using Physiopac (Neuroperfect EMG 2000)

Statistics

The obtained data was entered in MS Excel Windows 10.Statistical analysis was done with the help of SPSS 23.Continuous data was expressed in terms of mean and standard deviation. Categorical data was expressed in terms of Numbers and Percentages. Test of association for Categorical data was Chi square test and for Continuous data was t test and Anova test.p values <0.05 is considered as statistically significant.

RESULTS

The baseline characteristics like age,height and weight are found to be not statistically significant (Table-1).Fasting blood sugar,duration and postprandial blood sugar levels are found to be clinically significant between the study group and the control group(Table -2).

Table 1: Baseline characteristics of the study participants

Baseline characteristics	Group I (N=40)	Group II (N=40)	Group III (N=40)
Age	42.44±6.74	46.95±7.44	48.60±8.24
Height	156.68±3.08	156.75±3.08	156.68±3.49
Weight	60.65±4.95	65.30±12.75	64.22±7.12

Table 2: Laboratory values of the study participants

Variables	Group I (N=40)	Group II (N=40)	Group III (N=40)
FBS	89.25±12.68	133.38±4.95**	164.45±45.39**
PPBS	137.52±27.18	201.65±84.51**	284.28±95.93**
SBP	115.95±8.08	115.00±9.60	116.50±11.44
DBP	75±5.54	72.50±4.83	73.75±5.40
Duration	NA	4.85±2.61**	6.55±3.25**

Table 3: Mean latency of VEP in Right and Left Eye

	Group I		Group II		Group III	
	Right Eye	Left Eye	Right Eye	Left Eye	Right Eye	Left Eye
P100 latency	96.79±5.93	98.28±5.31	104.98±5.09**	103.09±17.48**	109.26±6.67**	108.46±5.83**
N75 latency	72.48±8.21	72.86±8.54	75.43±10.83	74.59±11.70	76.11±10.20	77.24±9.52
N145 latency	137.76±17.35	139.52±17.56	140.42±13**	140.76±22.21	143.16±13.27	143.16±12.32

P<0.01 is highly significant
P<=0.001 very highly significant
P100 latency prolongation was observed in both right and left eye of DM and DR group compared to control group and it is highly significant.

Table 4: Mean amplitudes of VEP in Right and Left Eye

	Group I		Group II		Group III	
	Right Eye	Left Eye	Right Eye	Left Eye	Right Eye	Left Eye
P100 latency	2.15±1.49	2.65±1.45	2.32±1.24	2.36±1.09	2.49±1.30	2.93±1.46
N75 latency	0.89±0.52	1.13±0.68	6.93±0.43	0.87±0.42	0.92±0.54	1.01±0.56

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	Group I					
N145 latency	**2.97±1.62**	**3.72±2.13**	**3.12±1.46**	**3.25±1.22**	**7.87±2.76**	**3.69±1.77**

There is no significant difference in mean amplitudes between study group and control group in both right eye and left eye.

Table 4: Gender variation

	Group I		Group II		Group III	
	P100RT	**P100LT**	**P100RT**	**P100LT**	**P100RT**	**P100LT**
Male	95.15±1.49	95.67±1.45	106.69±5.92	101.24±25.8	111.85±6.81	109.9±6.14
Female	97.50±0.52	99.39±0.68	103.58±3.90	104.6±4.65	106.3±5.35	106.7±5.13

P100 latency was delayed in right eye in males and in left eye in females

DISCUSSION

Both vascular and metabolic abnormalities in Diabetes Mellitus will affect the retina and visual pathways which leads to visual insufficiency.The integrity of the neural pathways are examined through visual evoked potential (VEP) which is a non invasive neuro physiological examination.[11] The loss of vision can be prevented by detecting diabetic retinopathy at it earliest. Peak amplitudes and latencies are used to quantify the visual evoked responses. Attention, distribution of sulci brain ,size of the brain and cranial shape will modify the VEP amplitude.[12] The ganglion cells damage is observed in the form of prolonged latency values.[13]

In our study the mean age of Group I was found to be 42.44±6.74,Group II 46.95±7.44 and in Group III 48.60±8.24.In contrast to our results study done by Raghda et al[14] showed that the mean age was found to be more ranging from (50.5 -65.7)in the three groups. The fasting blood sugar level in our study was found to be less than Raghda et al study.

The Sysolic BP of Group 1 is 115.95±8.08, Group II is 115.00±9.60 and Group III is 116.50±11.44 in our study. The Diastolic BP of Group 1 is 75±5.54,Group II is 72.50±4.83 and Group III is 73.75±5.40 in our study. Similar results was also seen in Rahda et al[14] study. The mean duration of Diabetes in Group II was found to be 4.85±2.61and in Group III was 6.55±3.25 which was lesser than the duration of Raghda et al where Group II had 7.7 and Group III was 9.7 years. Females were more in Diabetic Retinopathy group and Males are more in Diabetes group without retinopathy.

P100 latency prolongation was observed in both right and left eye of DM and DR group compared to control group and it is highly significant in our study.In A.A .Alidani et al[15] study the mean P100 latency was found to be increased in Diabetes and there is statistically significant difference observed with control group.The mean P100 wave latency in males were found to be prolonged in right eye in both Diabetic and Diabetic retinopathy group. Similarly in female the mean P100 value was increased in left eye which is not statistically significant. Sangeetha gupta et al[16] showed in her study that gender influence was observed among males and the P100 latency was increased.Similar findings were observed in males in

Ruby sharma et al study also.In contrast to the results Phuralitpam et al[17] doesn't observed any significant difference in gender.

The P100 latency in patients with Diabetes Mellitus with retinopathy and without retinopathy showed delay when compared with the controls .This was similar to studies done by Gayathri et al[18], Omer azal et al.[19] The mean value of FBS and PPBS was more in DR group compared to DM group. New England journal states that there is a relationship between the glycemic control and development of DR are indirectly related. There is no significant difference in mean amplitudes between study group and control group in both right eye and left eye in our study.

CONCLUSION

Diabetes mellitus is a disease which affects millions of people and leads to both acute and chronic complications and eventually death if uncontrolled.Our study concludes by stating the relevance in P100 latency which indicates the possibility of CNS involvement subclinically . P100 latency also had association with FBS and duration of Diabetes.Thus by using PVEP we can detect the retinal dysfunction earlier and it can be used as a screening tool to avert the morbidity.

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