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Correlation of Duration Between Type 2 Diabetes Mellitus and Central Neuropathy in Type 2 Diabetics: A Cross Sectional Analytical Study

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ABSTRACT

Type 2 Diabetes Mellitus (DM) Diabetes Mellitus (DM) has detrimental effects on the various organs of our body including central and peripheral nervous system which is widely accepted. However, not much research is done on understanding the central nervous system abnormalities of DM. Visual evoked potential (VEP) is a non-invasive Neuro-physiological examination that detects early diabetic retinopathy changes which is important in preventing loss of vision. The study was conducted in Type 2 diabetic patients with 20 cases with duration of more than 2 years and 20 controls were taken. Visual evoked potential (VEP) was done in both groups. Patient having complications of diabetes, cataracts, reduced vision were excluded from the study. Aim of the study was to evaluate the correlation of VEP in detecting retinal ganglion cell damage in diabetics and to study the correlation between P 100 latency and duration of Diabetes. There was Significant prolongation of P100 latencies (msec) in type 2 diabetics with mean±SD of (110.90±6.11 msec) in right eye compared to controls (101.07±1.92 msec) and Left eye 110±5.97 compared to controls 101±1.29 with p value <0.001. It can be concluded that the prolongation of P 100 latencies observed in diabetics could be a manifestation of structural damage before development of diabetic retinopathy and P 100 latencies showed significant positive correlation with duration of diabetes.

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Key Words
Diabetes mellitus type 2, diabetic retinopathy, evoked potentials, visual

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INTRODUCTION

Diabetes mellitus (DM) is a global pandemic raising serious challenges to health care system. Nearly 150 million people throughout the world are affected and the incidence increases with time as sedentary lifestyle and obesity is on rise. Major complications of DM are due to atherosclerosis and it can affect any organ in body especially eyes, peripheral nerves, kidney and heart. These are categorized into micro vascular and macro vascular complications.

The peripheral nervous system involvement in DM has been studied extensively in various studies but central nervous system involvement in DM has not been studied in detail. The term "central neuropathy" has been unknown until recently. The term central neuropathy was recognized only after identification of subclinical optic nerve involvement in DM by electrophysiological studies in few western studies. Just like subclinical peripheral neuropathy, asymptomatic optic neuropathy or central neuropathy can occur and is evaluated by visual evoked potentials. Although in diabetic the most common cause for blindness is diabetic retinopathy asymptomatic optic nerve dysfunction can occur as proved in various studies.

Visual evoked potential (VEP) is non-invasive, sensitive tool which measures the impulse conducted along the central nervous pathway. VEP measures the P 100 latency which reflects the functional abnormalities of optic pathway even on early stages.

Adam and Brown[1]. in their study included 12 diabetic patients both type 1 and type 2. They subjected all patients to VEP and found that diabetic patients had P 100 prolongation more than of controls. The mean increase in P 100 latency was 116.8+/-4.5 with p-value<0.01. After 3 days of intensive blood sugar control the repeat P 100 latency was slightly prolonged compared to controls but there was significant reduction. Dolu *et al.*[2] studied electrophysiological characteristics of 51 patients with type 2 DM and compared with 30 age sex matched controls. They did VEP, BAEP (brainstem stem auditory evoked potentials) SEP for all patients and concluded that there was significant latency prolongation suggestive of central neuropathy in diabetic patients compared to controls. The latency prolongation in SEP, VEP and BAEP correlated well with duration of diabetes and not with glycaemic control of disease.

Comi *et al.*[3] also studied multifocal evoked potential in type 2 diabetic patients using VEP, BAEP, and SEP. They found that central neuropathy due to cortical latency prolongation was more common in diabetic patients with peripheral neuropathy. Isolated abnormalities in VEP or BAEP nor SEP was more common than all three getting affected together. They concluded that central neuropathy may occur due to hyperglycaemia or hypoglycaemia but exact cause unknown. Algan *et al.*[4] studied VEP in 50 type 1 diabetes and 19 type 2 diabetes. They found significant prolongation of P 100 in diabetic patients with p-value less than 0.001. But on further analysis they concluded that P 100 prolongation did not correlate with duration of DM or glycaemic control of disease. Their findings are contradictory to previous studies[5-10].

Aim of the Study:

- To find out any abnormality in visual evoked potential in diabetics even before diabetic retinopathy sets in
- To find out any positive correlation with duration of diabetes and VEP prolongation.

MATERIALS AND METHODS

A cross-sectional comparative study was conducted among 20 type 2 DM patients of more than 2 year's duration and without any clinical complications. in the department of medicine of PIMS and RC Thiruvalla and 20 age and sex matched controls formed the comparative group With an expected odds ratio of 10 and the control arm prevalence as 10% the sample size required for the study is 20 in each group.

Inclusion criteria for cases:

- Who criteria was used for diagnosing DM:
- Random plasma glucose of $\geq$11 1 mmol L^{-1}
- Fasting plasma glucose $\geq$7.0 mmol L^{-1}
- Two-hour plasma glucose concentration $\geq$11.1 mmol L^{-1} 2 hrs after 75 g anhydrous glucose in oral glucose tolerance test(OGTT)

Inclusion criteria for controls:

- Random plasma glucose of $\leq$11/1 mmol L^{-1}
- Fasting plasma glucose $\leq$7.0 mmol L^{-1}
- Two-hour plasma glucose concentration $\leq$11.1 mmol L^{-1} 2 hrs after 75 g anhydrous

Exclusion criteria for cases and controls:

- Patients with long standing history of hypertension and with the past history of CVA
- Evidence of optic atrophy
- Past history of optic neuritis
- Visual acuity less than 6/18
- Patients consuming >100 mL of alcohol daily
- Patients with peripheral nervous system disease unrelated to diabetes mellitus
- Patient with diabetic retinopathy, cataract, glaucoma and vitreous haemorrhage
- Patients with type 1 diabetes mellitus

VEP was recorded using pattern reversal stimulation with EMG RMS MARK II machine. Detailed clinical examination, peripheral nervous system and ophthalmic evaluation including visual acuity, fundus examination was performed in all subjects. Later all patients were subjected to visual evoked potential.

Recording technique: Visual evoked potentials were recorded using pattern reversal stimulation. Patients were advised to come without applying oil to scalp. They were further instructed to shampoo and dry their hair. The skin was prepared by abrading and degreasing. Monocular, pattern-reversal checkerboard stimulation of 1.8 Hz frequency was used. The distance between the TV screen and each subject was 100 cm. The patient was instructed to fix his gaze at the centre of the screen. An average of 200 sweeps of stimuli was given to each eye and the visual function was assessed with the help of P 100 wave latency[16-20].

The bioelectrical signals were recorded by silver or silver chloride disc electrodes placed at 1) Grounding (FPZ) 2) Active (OZ), 3) Reference (Fz) using electrode paste according to 10-20 international system of EEG electrode placement as shown in Fig. 1. Uniform illumination was maintained in the laboratory and the electrode impedance was kept below 5k. The evoked responses were averaged and analysed by the Evoked Potential Recorder (EMG RMS MARK II machine). The peak P 100 latencies were recorded and correlated with duration of diabetes.

Statistical analysis: Two tailed independent student t-test was used to find the significance in P100 latencies of VEP waveforms between the diabetic and control groups. The correlation between duration of diabetes and P100 latency of diabetics was done using Pearson correlation co-efficient. The statistical software namely SPSS 19.0 was used to analyse data and to generate tables Microsoft word and Excel was used. $p<0.05$ was considered as statistically significant.

The mean P100 wave latencies were significantly prolonged in diabetics compared to the control group. Mean SD of cases 110.8 units (5.14) and controls is 101.07 (1.07). The difference is stastically significant with $t = 8$ with $p<0.001$ (Table 1-3) (Fig. 2 and 3).

Table 1: Group statistics

Mean P100 latency	Mean	SD	t	p-value
Cases-20	110.8	5.14	8.271	<0.001
Controls-20	101.07	1.07		

Table 2

Eye	Cases mean (SD)	Controls mean (SD)	t value	p-value
P100 latency	110.8(5.14)	101.07(1.07)	8	P<0.001

Table 3: Correlation between duration of diabetes and P100 latency

	Correlations		
Duration	Duration	P100 RE	P100 LE
Pearson Correlation	1	0.167	0.220
Sig. (2-tailed)		0.480	0.352
N	20	20	20

*: Correlation is significant at the 0.05 level (2-tailed)

RESULTS

There was Significant prolongation of P100 latencies (msec) in diabetics with Mean±SD of (110.90±6.11 msec) in right eye compared to controls (101±1.92 msec) and Left eye 110±5.97 compared to controls 101±1.29 with $p<0.001$. The results shows that diabetes have caused significant change in latency potential of both eyes when compared to non-diabetics and the difference in values between cases and controls are also significant. The duration of type 2 diabetes there had a positive correlation for P_{100} latencies with ($p>0.05$).

DISCUSSION

Diabetes affects both central as well as peripheral nerves Diabetic retinopathy is a micro vascular complication of diabetes. The term central neuropathy means studies have shown electrophysiological changes in brainstem evoked potential and auditory evoked potentials in diabetic patients .However identifying central retinopathy which leads on to visual loss need much importance[21-22]. Early

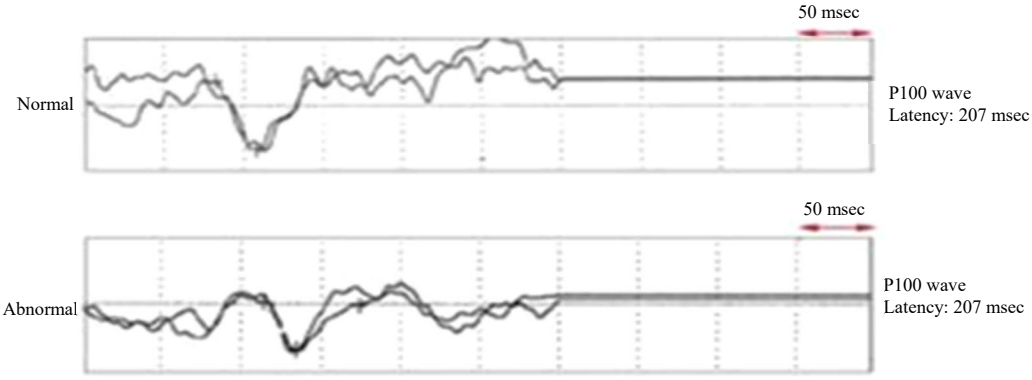

Fig. 1: Showing tracing of normal and abnormal Visual evoked potential

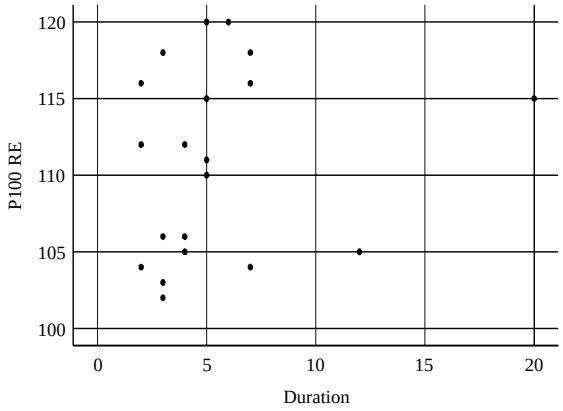

Fig. 2: Duration of diabetes and P100 Right eye

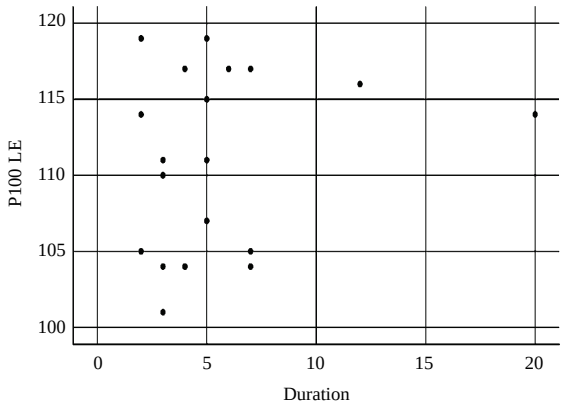

Fig. 3: Duration of diabetes and P100 left eye

identification of diabetic retinopathy or optic neuropathy is the key factor in preventing sudden onset vision loss in diabetes. Since VEP is a non-invasive sensitive tool for diagnosing retinal ganglion cell damage. Limitations of this tests is that any visual obscuration in the form of cataract, advanced retinopathy can alter the results. Studies have shown that better glycemic control have a reversal effect of the retina damage demonstrated by reduction of p100 latency prolongation. However the onset of the changes in retinal cell ganglion need to be found out in future studies.

The VEP are electrical potential differences recorded from scalp in response to visual stimuli and can also be used to assess the visual path which runs from retinal ganglion cells to the visual cortex[23]. In the present study, the differences in P100 wave latencies between the Diabetics and the control group indicate that VEP detected damage in retinal ganglion cell in diabetics. This ganglion cell damage can be considered as a sign of preclinical diabetic retinopathy as no signs of diabetic retinopathy were detected in the patients on ophthalmoscope examination It is already established that the intervention is most effective when done at the onset of first sign of diabetic retinopathy.

CONCLUSION

In conclusion, the present study showed the importance of VEP in detecting diabetic preretinopathy in diabetics which has a positive correlation with duration of diabetes. Further work is required to evaluate the time taken for the first detectable abnormal neurophysiological variations to appear and for retinal changes to be appreciated on ophthalmoscope examination in diabetics.

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