

# Correlation of Visual Evoked Potentials with Duration of Diabetes in Type 2 Diabetes Mellitus Patients

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## Abstract

**Introduction:** Chronic hyperglycemia of diabetes is associated with dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels. Visual evoked potential (VEP) test evaluates how the visual system responds to light. As it tests the function of the visual pathway from the retina to the occipital cortex, VEP is a useful clinical tool in the diagnosis and documentation of visual impairment in many ophthalmological disorders.

Analysis of pattern reversal VEPs may provide early diagnosis of diabetic changes and determine prognosis during treatment. The visual evoked potential is suggested to be a sensitive indicator of functional changes in the visual processing pathway.

**Aims and Objectives:** The objective of this study was to establish whether duration of DM has an effect on the VEP measurements, P100 wave latency.

**Material and methods:** VEP was recorded in 60 type 2 diabetic patients and compared to 60 age and sex matched normal healthy non-diabetic controls. The patients were divided into three groups based on the duration of diabetes. VEP was recorded with a pc based, two channel, RMS EMG EP MK II machine. Comparison between two groups were done using independent Students' 't' test. One way ANOVA (Analysis of Variance) and multiple comparisons were done using post hoc Tukey Multiple Comparison Test to compare the variables between the three study groups. To determine correlation between variables, Pearson's correlation coefficient was used. The mean difference was statistically significant at  $p < 0.05$

**Result:** P100 wave latency was significantly longer in diabetic patients as compared to normal controls ( $P < 0.001$ ); There was significant reduction in N75- P100 amplitudes in diabetic subjects ( $p < 0.01$ ). Duration of diabetes was found to influence the VEP parameters as statistically significant increase in the mean P100 latency with the duration of the disease. (110.2 ± 6.51 ms in group < 3 yrs duration of DM, 113.4 ± 5.00 ms in 4-6 yrs duration group, 118.2 ± 4.23 ms in 7-10 years duration group) ( $p < 0.01$ ). On applying, Pearson's correlation coefficient test, significant positive correlation was observed between P100 latency and duration of diabetes. ( $r = 0.5803$ ;  $p < 0.001$ ).

**Conclusion:** It is concluded that diabetes has effect on the visual pathway and changes in VEP response in diabetic patients are correlated with duration of disease. So, VEP can be used for early diagnosis of diabetic changes of the visual pathway.

**Keywords:** Visual Evoked Potential, Type 2 Diabetes Mellitus, P100 wave latency.

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## Introduction

Diabetes mellitus is one the most serious challenges to healthcare, primarily because of the increase in the prevalence of sedentary lifestyles and obesity.<sup>1</sup>

Chronic hyperglycemia of diabetes is associated with dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels.<sup>2</sup>

Visual evoked potential (VEP) test evaluates how the visual system responds to light. As it tests the function of the visual pathway from the retina to the occipital cortex, VEP is a useful clinical tool in the diagnosis and documentation of visual impairment in many ophthalmological disorders.<sup>3</sup>

Functional exploration of the optic pathways with pattern reversal visual evoked potentials (PRVEPs) had been accepted as a non-invasive method of investigation of diabetics. Analysis of pattern reversal VEPs may provide early diagnosis of such diabetic changes and determine prognosis during treatment.<sup>4</sup> The visual evoked potential is suggested to be a sensitive indicator of functional changes in the visual processing pathway.<sup>5</sup>

### **Aim and Objective**

The objective of this study was to establish whether duration of DM has an effect on the VEP measurements.

### **Material and Method**

The study was carried out in the Neurophysiology lab of Department of Physiology, Gandhi Medical College, Bhopal, in collaboration with the Department of Medicine and Department of Ophthalmology, Gandhi Medical College & associated Hamidia Hospital, Bhopal.

The study was carried out on 120 subjects, 60 Type 2 diabetes mellitus patients and 60 non diabetic healthy volunteers matched for age and gender were included in the study to serve as control.

The study included Type 2 diabetes mellitus patients within age group of 40-60 years with duration of DM <10 years.

Following patients were excluded from the study:

Type 2 diabetes mellitus patients with proliferative retinopathy.

Patients with significant ocular disorders including cataract, glaucoma, optic nerve disease, best corrected visual acuity <6/9 for distance, amblyopia, vitreous opacities.

Patients suffering from any cardiovascular illness or cardiac autonomic neuronal dysfunction of non-diabetic origin like hypertension.

Patients with prior history of head injury, cerebrovascular accident, h/o migraine, epilepsy.

Medical conditions such as multiple sclerosis and other demyelinating disorders led to exclusion from the study.

Subjects with history of smoking, alcoholism, chronic drug intake.

The patients who satisfied the inclusion and exclusion criterion, and gave written consent were included in the study.

Detailed systemic clinical examination was done on the patient to rule out any other systemic diseases which might lead to effect on VEP and cardiac autonomic functions.

Relevant information was collected using a detailed questionnaire covering all the relevant symptoms and signs pertaining to Diabetes mellitus and autonomic disturbances. On the basis of response obtained the study group was selected.

Detailed history was obtained and recorded from the control and the diabetic groups in the prescribed proforma. It included personal details, habit of smoking, alcohol, family h/o diabetes and hypertension, all types of medications taken, h/o being diagnosed or being treated for diabetes including age of onset, duration, treatment, associated risk factors.

Patients were subjected to VEP test on RMS EMG EP MK-II machine in the Neurophysiology unit of Department of Physiology, Gandhi Medical College, Bhopal.

### **Pre test evaluation - Participant preparation for PRVEP test**

1. The subjects were advised to come without oil or any hair chemical to the scalp.

2. Subjects were also instructed to avoid any mydriatic or miotic drug 12 hours before the test as altered pupil size may change the stimulus luminance thereby affecting the PVEP parameters.

3 Patients were asked to put on their usual glasses during the test.

4. They were instructed to have an adequate sleep the previous night to prevent the effect of drowsiness on the responses.

### **VEP instrumentation room set-up**

#### **Equipment –**

VEP was recorded with a pc based, two channel, RMS EMG EP MK II machine -equipped with pattern-shift stimulator television screen, signal amplifier with filters, computer system for averaging.

VEP was performed in a specially equipped electro diagnostic procedure room, made dark and sound attenuated for the test. Subjects were seated comfortably about 100 cm away from a video monitor.

#### **VEP Recording-**

A montage consisting of one channel (Oz-Fz) was used for VEP recording. The subjects were made to sit comfortably approximately 100 cm away from the video- monitor which presented a black and white checkerboard pattern with a fixation spot in the centre of the screen (mean luminance 50 candela/m<sup>2</sup> and contrast 70%). At the viewing distance of 100 cm, the check edges subtend a visual angle of 15 minutes with video monitor screen subtending an angle of 12.5°. The checks / pattern elements reversed alternately at a rate of twice per second. The bioelectric signal was amplified (gain 20,000), filtered (band-pass, 1-100 Hz), and 150 events free from artifacts were averaged for every trial. Every time the pattern alternates, the subject's visual system generates an electrical response that was detected and recorded by surface electrodes, which were placed on the scalp overlying the occipital and parietal regions with reference electrodes on the midline of frontal region (Fz). Subjects were instructed to fix the gaze on a small red coloured square at the centre of the screen of video monitor. Monocular stimulation was done with an eye- patch covering the other eye.

#### **Electrodes and Electrode Placement -**

The recording electrodes were placed on the scalp at the following reference points:

Oz (Occipital region) = Active or recording electrode

Cz (Vertex) = Ground electrode

Fz (Frontal region or forehead) = Reference electrode

Head size measurements were taken from nasion toinion prior to the electrodes placement. To apply the electrodes, conductive electrode paste was applied on the marked electrode locations to make sure a good, stable electrical connection between the scalp and the electrodes was made. Each electrode was pressed firmly onto the scalp with the help of contact paste .Micropore gauze was placed on top of the electrodes to ensure their contact was maintained. The electrode impedance was kept below 5 k $\Omega$ .

#### **PRVEP instructions given to participants :**

The participants were requested to remain comfortable and relax when viewing the checkerboard screen. They were instructed to maintain a normal blink rate to ensure a clear optical image. Also, if the subject experienced any discomfort he or she was asked to mention it.

The participants were instructed to maintain their focus on the central red coloured block in the centre of the display screen VEP test was started only when the participant confirmed that he or she was comfortable to begin the test.

PVEP waveform and markings --PVEP recording parameters

With the preset stimulus and recording conditions as mentioned above and keeping the electrode impedance <5 k $\Omega$ , the recording procedure was started. To verify the reproducibility of the waveform, two responses were recorded and superimposed. Trials were repeated if there was inconsistency of the response.

#### **Statistical methods applied:**

Comparison between two groups were done using independent Students' 't' test.. One way ANOVA (Analysis of Variance) and multiple comparisons were done using post hoc Tukey Multiple Comparison Test to compare the variables between the three study groups. To determine correlation between variables, Pearson's correlation coefficient was used.The mean difference was statistically significant at  $p < 0.05$  and non significant at  $p > 0.05$ .

## Results

As compared to control group, values of peak latencies of P100 waves were found to be delayed in diabetic groups.

It was observed that mean P100 latency was  $114.27 \pm 6.76$  ms in diabetic group and  $98.79 \pm 5.75$  ms in control group. The difference was significant between different groups ( $p < 0.001$ ).

The mean N75-P100 amplitude was decreased in the diabetic groups  $5.80 \pm 1.42 \mu V$  in diabetic group, while in control group it was  $7.45 \pm 1.14 \mu V$ .

Duration of diabetes was found to influence the VEP parameters as statistically significant increase in the mean P100 latency with the duration of the disease. ( $110.2 \pm 6.51$  ms in group  $< 3$  yrs duration of DM,  $113.4 \pm 5.00$  ms in 4-6 yrs duration group,  $118.2 \pm 4.23$  ms in 7-10 years duration group) ( $p < 0.01$ ).

On applying, **Pearson's correlation coefficient** test, significant positive correlation was observed between P100 latency and duration of diabetes. ( $r = 0.5803$ ;  $p < 0.001$ ).

**Table No. 1: Mean P<sub>100</sub> latencies and amplitudes in type 2 diabetics and controls**

groups	No. of subjects	P100 Latency (MEAN $\pm$ S.D.)	P100 AMPLITUDE (MEAN $\pm$ S.D.)
DIABETIC	60	$114.27 \pm 6.76$	$5.80 \pm 1.42$
CONTROL	60	$98.79 \pm 5.75$	$7.45 \pm 1.14$

**Table : 2: vep test(mean p100 latency) in relation to duration of Dm in study groups**

Duration of DM (Yrs)		No. of Cases	P 100 Latency (Mean $\pm$ SD)	Inference
A	< 3	17	$110.2 \pm 6.51$	F = 26.863
B	4-6	21	$113.4 \pm 5.00$	
C	7-10	22	$118.2 \pm 4.23$	P < 0.01
<b>Total</b>		<b>60</b>		

### INTERGROUP COMPARISON OF VEP TEST (MEAN P100 LATENCY) IN RELATION TO DURATION OF DM

	A VS B	A VS C	B VS C
P VALUE	<0.05	<0.01	<0.01

Comparison between two groups were done using independent Students' 't' test.. One way ANOVA (Analysis of Variance) and multiple comparisons were done using post hoc Tukey Multiple Comparison Test to compare the variables between the three study groups.

To determine correlation between variables, Pearson's correlation coefficient was used. The mean difference was statistically significant at  $p < 0.05$

**TABLE 3: PEARSON'S TEST FOR DETERMINING CORRELATION BETWEEN VEP P100 LATENCY AND DURATION OF DM**

Parameter	VEP P100 LATENCY
Duration of DM	r = 0.580
	p < 0.001

Significant positive correlation was observed between P 100 latency and duration of DM with r = 0.580.

### Discussion

The present study is conducted to assess and evaluate changes in Visual Evoked Potentials Type 2 Diabetes Mellitus patients in the Department of Physiology and Department of Medicine, Gandhi Medical College, Bhopal. Visual Evoked Potentials of diabetic patients were compared with the control group.

The study was carried out on 60 diabetic patients. The **control group** comprised of 60 healthy age and gender matched individuals. Involvement of optic nerve as an indicator of central neuropathy was assessed by **Visual Evoked Potential**.

The objective of this study was to establish whether duration of DM has an effect on the VEP measurements.

It was observed in the results of this study that duration of DM was associated with abnormalities in VEP P100 latency. Mean P100 latencies increased with duration of diabetes with statistically significant difference ( $p < 0.01$ ) between group with duration of DM < 3 years and > 7 years. Intergroup comparison between different groups based on duration of diabetes reveal significant difference in mean P100 wave latency. Pearson's correlation coefficient was applied to assess the correlation between P100 latency and duration of diabetes in diabetic patients. A significant positive correlation was found between duration of diabetes and P100 latency. ( $r = 0.5803$ ;  $p < 0.001$ ).

**Bhanu R et al. (2012)<sup>6</sup>, Chopra D et al. (2011)<sup>7</sup>, Dolu H et al. (2003)<sup>8</sup> and Azal O et al. (1998)<sup>9</sup>** indicated results similar to those of the present study in that they found a significant positive correlation between the duration of DM and increase in P100 latency.

On the other hand, in various other studies conducted by authors such as **Ismail GM (2014)<sup>10</sup>, Heravian J et al. (2012)<sup>11</sup>, Ziegler D et al. (1992)<sup>12</sup> and Algan M et al. (1989)<sup>13</sup>**, no correlation between P 100 latency prolongation and duration of DM was found.

In **contradiction** to the result of present study, **Rajewski P et al. (2007)<sup>14</sup>** reported no significant correlation between duration of DM and latency of P100.

### Conclusion

It is concluded that the changes in VEP response in diabetic patients are correlated with duration of disease. So, VEP can be used for early diagnosis of diabetic changes of the visual pathway. It can be used as noninvasive and valuable test for detecting changes in central visual pathways in diabetics.

**Ethical Clearance:** The study was approved by the Ethical Committee of Gandhi Medical College, Bhopal

**Source of Funding:** None

**Conflicts of Interest:** Nil

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