Original Article

Visual Evoked Potential in Patients of Type 2 Diabetes Mellitus with and without Diabetic Retinopathy

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Abstract

Introduction: Diabetes mellitus is a leading public health care problem, with increasing incidence and its long term complications. Diabetic retinopathy is a common complication of DM that affects retinal blood vessels. Unfortunately, in many cases the patient is asymptomatic until it is too late for effective treatment. VEPs are produced by electrical activity of the visual cortex in response to light or pattern stimulation of the eye. It can detect functional loss in the visual pathway from retina to the visual cortex.

Aims and Objectives: The aim of the study is to compare latencies and amplitudes of P100 waveform of VEP in diabetic and control subjects and to determine whether changes in VEP response occur before clinically evident diabetic retinopathy on fundus examination.

Method: PRVEP was recorded in 60 diabetic patients including 30 patients without any retinopathy and 30 others with non-proliferative diabetic retinopathy (NPDR), and compared to 60 age and sex matched normal non diabetic healthy controls. VEP was recorded using pattern reversal stimulation with RMS EMG MARK II machine. P100 wave latencies and amplitudes were obtained in all the subjects.

Results: Our results show significantly prolonged P100 latencies of VEP’s in Type 2 DM patients and DR patients when compared to controls. The difference between diabetics with retinopathy and controls were significant in terms of P100 amplitude. However, there was no significant difference observed in the P100 amplitudes of VEP’s in Type 2 DM patients without retinopathy when compared to controls.

Conclusion: The present study clearly shows that changes in VEP may be detected in diabetics before the onset of retinopathy. Thus, a routine VEP assessment should be recommended to all the diabetic patients, for the early identification of visual defects and for early and proper management of the disease.

Keywords: Visual Evoked Potential, Type 2 Diabetes mellitus, Diabetic retinopathy

Introduction

Diabetes mellitus is a leading public health care problem, with increasing incidence and its long term complications.¹ Chronic hyperglycemia of diabetes is associated with dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels.²

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It is well known that patients with diabetes over a course of time, develop peripheral and autonomic neuropathy. Studies have suggested that they may also suffer from central neuropathy or the degeneration of higher nervous system. The advent of advanced electro neurophysiological techniques to assess cerebral functions such as the measurement of electrical evoked potential like the visual evoked potential (VEP), have increased our understanding of the normal visual function and the possible effects that diabetes may exert.³ VEP’s are electrical potential differences occurring in the visual areas of the occipital cortex, in response to visual stimuli.
and are recorded from the scalp. 

Diabetic retinopathy is a common complication of DM that affects retinal blood vessels. Growth of new blood vessels, known as proliferative retinopathy, may lead to blindness through hemorrhage and scarring. One of the primary goals of management in diabetic patients is to avoid the risk of diabetic retinopathy and early diagnosis and management. Before the onset of microvascular lesions, the neural retina of diabetic eye undergoes subtle functional changes that are not detectable by fundus examination.

The present study includes evaluation of VEP waveforms, such as latency and amplitude of P100, occurring in patients of type 2 diabetes mellitus, and in patients with Diabetic retinopathy. This study was aimed to determine whether changes in VEP response occur before clinically evident diabetic retinopathy by fundus examination.

Materials and Method

Study design: A Hospital based case control study.

Study setting: The study was carried out in the Neurophysiology lab of Department of Physiology, Gandhi Medical College, Bhopal.

The study was approved by the Ethical Committee of Gandhi Medical College, Bhopal. Informed consent was taken from all the participants before enrolling in the study. Patient was provided the information about the procedure of test to be performed on him with plausible adverse effect in detail before performing the test.

Sample size:

The study was carried out on 120 subjects, 60 Type 2 diabetes mellitus patients and 60 non diabetic healthy subjects.

Test group: Diabetes mellitus type 2 patients were grouped as follows:

Group 1: Included 30 cases of type 2 diabetes mellitus without diabetic retinopathy.

Group 2: Included of 30 cases of type 2 diabetes mellitus with non proliferative diabetic retinopathy (NPDR).

Control group:

Group 3: 60 non diabetic healthy volunteers matched for age and gender were included in the study to serve as control.

Inclusion criterion:

The study included following type 2 diabetes mellitus patients within age group of 40-60 years:

- Type 2 DM patients without retinopathy with duration of DM <10 years.
- Type 2 DM patients with non proliferative diabetic retinopathy (NPDR) with duration of DM <10 years.

Exclusion criterion:

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 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.

A complete clinical examination of each subject was done after obtaining a written informed consent and detailed clinical history. Ocular examination findings were noted which include determination of visual acuity by Snellen’s chart and near vision chart, ocular movements, pupil reactions, confrontational visual field screening. Direct ophthalmoscopy was done for the initial evaluation of fundus.

Visual Evoked Potential (VEP) Test-

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

3. Subjects were explained about the procedure in detail to ensure full co-operation and avoid apprehension

Electrodes and Electrode Placement -

Standard surface electrodes were placed according to the international 10/20 system of electrode placement (ISCEV standards, 2009). This system specifies the position of scalp electrodes as percentage of distances between definitive landmarks such as nasion, inion and ear tragus (Figure 1).

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

VEP Recording-

A montage consisting of one channel (Oz-Fz) was used for VEP recording. The video-monitor presented a black and white checkerboard pattern with a fixation spot in the centre of the screen (mean luminance 50 candela/m2 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. Subjects were instructed to fix the gaze on a small red coloured block at the centre of the screen of video monitor (Figure 2). Monocular stimulation was done with an eye-patch covering the other eye.

PVEP waveform and markings --PVEP recording parameters

The waveforms were labeled for the peaks N75, P100 and N145. The first major positive peak (P100) was measured after stimulation of each eye. The parameters taken for the study were P100 latency of the waveform measured in milliseconds (ms), and N75-P100 amplitude measured in microvolts (μV) in both eyes.

Statistical Analysis

The parameters for the study were peak P100 latencies, N75- P100 amplitudes. All the data was expressed as mean ± S.D.

The significance of difference between groups was calculated using one way ANOVA and multiple comparisons were done using post hoc Tukey multiple comparison tests to compare variables between the three study groups. The analysis was done at 5% level of significance.

Results

PRVEP was recorded in the diabetic groups as well as the control group and P100 latency and N75-P100 amplitude were analysed.

Mean values of PRVEP parameters (P100 latency and N75-P100) were obtained for both right and left eyes in all the subjects. As there was no significant difference in the mean values of both the parameters between the right and left eyes, hence, for comparison between different groups, mean values of both eyes was obtained in both controls and diabetics. There was no statistically significant difference between age in different study groups.

The results are shown in Table 1. There was significant difference between different groups in terms of P100 latency (p<0.01) by using one-way ANOVA. Significant differences between each paired groups were then evaluated by post hoc Tukey test. Differences between diabetics with and without retinopathy was statistically significant in terms of P100 latency and amplitude (p<0.01). Differences between diabetics without retinopathy and controls were also significant regarding P100 latency but there was no significant difference regarding P100 amplitude. The difference
between diabetics with retinopathy and controls were significant in terms of P100 latency and amplitude.

**TABLE 1: COMPARISON OF VEP TEST (MEAN P100 LATENCY AND AMPLITUDE) BETWEEN DIFFERENT GROUPS. (Mean ± SD)**

<table>
<thead>
<tr>
<th>Test parameter</th>
<th>No Ret (1)</th>
<th>NPDR (2)</th>
<th>Control (3)</th>
<th>P value</th>
<th>Inter group comparison*</th>
</tr>
</thead>
<tbody>
<tr>
<td>P100 latency (ms)</td>
<td>112.09±5.709</td>
<td>116.43±7.12</td>
<td>98.79±5.75</td>
<td>&lt;0.01</td>
<td>(1,2) (1,3) (2,3)</td>
</tr>
<tr>
<td>P100 amplitude(μV)</td>
<td>6.94±0.92</td>
<td>4.648±0.75</td>
<td>7.45±1.142</td>
<td>&lt;0.01</td>
<td>(1,2) (2,3)</td>
</tr>
</tbody>
</table>

*shows that significant p value is contributed by the pairs mentioned in the column.

Fig. 1: electrode placement

Fig. 2: Checkerboard pattern for PR – VEP

**Discussion**

In the present study, mean P100 latency of diabetics was found to be significantly prolonged (p<0.01) when compared with those of controls. These findings are consistent with the observations of Gayathri V et al. (2012), Heravian J et al. (2012), Szabela DA et al. (2005), Varkonyi TT et al. (2002), and Azal O et al. (1998). Mean P100 latency delay was more in group 2 followed by group 1. On comparing mean P100 latency between different groups, statistically significant delay was noted between the two diabetic groups (p < 0.01) and also between diabetic groups and controls (p < 0.01).

The result of the present study are consistent with earlier studies that have shown abnormalities as an increase in latencies of P100 in patients with Type 2 DM with and without retinopathy. Algan M et al. (1989) reported prolonged P100 latency in 50 DM patients, six of whom had diabetic retinopathy. MarianiE et al. (1990) observed prolongation of P100 latency in 35 diabetic patients who did not have retinopathy. YaltkayaK et al. (1988) found increased P100 latency. They explained these findings by the presence of retrochiasmal involvement. Millinger KS et al. (1987) reported similar findings. They reported that abnormal VEP could reflect papillomacular bundle or optic nerve involvement. Bortek L et al. (1989) found PVEP abnormalities in diabetic patients and reported that abnormalities did not correlate with level of retinopathy.

While majority of the published studies have reported prolongation of P100 latency, few studies show no significant prolongation. (Collier A et al., 1988; Ismail GM, 2014).

In the present study, we found significantly longer P100 wave latencies in diabetic patients as compared to controls. Two factors may contribute to the delay in P100 latency: the first related to the innermost retinal layers and the second related to an impairment of the neural conduction at post retinal level. Both these factors may
contribute in parallel to increased P100 latency. (Parisi V et al., 1997)\(^2\). In diabetes mellitus, damage occurs to ganglion cell layer which can be due to extracellular glutamate accumulation, leading to functional and anatomical changes, which rise even before the vascular damage. Oxidative stress, besides micro vascular abnormalities and consequences of glucose metabolism, play a great role in the pathological progress of diabetic retinopathy. That might be due to either an increase in free radical and oxidant production or reduced activity of anti-oxidative mechanisms, considered as a sign of preclinical diabetic retinopathy. (Karlica D et al., 2010)\(^3\).

The VEP P100 amplitudes were reduced in diabetics. The mean amplitudes show greater reduction in group 2 as compared to controls. The difference in decrease in amplitude was significant between group 1\& 2 (p <0 .01) and also between group 2 and group 3 (p< 0.01).However, difference between group 1 & 3 was not significant (p >0.05). Heravian J et al. (2012)\(^10\) studied VEP in diabetic patients with NPDR and without any retinopathy and found significant difference between diabetics with retinopathy and controls in terms of P100 amplitude. Differences in P100 amplitude was also statistically significant between diabetics with and without retinopathy. Decrease in amplitude of P100 in diabetics was observed by Chopra D et al (2011)\(^23\). No significant difference in amplitude variation was reported by Parisi V et al. (1997)\(^21\), Raman PG et al. (1997)\(^24\), Verrotti A et al. (2000)\(^25\). The findings of the present study are in accordance with the observations of Ismail GM et al. (2014).\(^20\) They reported that amplitudes of the VEP are affected in the presence of diabetic retinopathy.

**Conclusion**

It is evident that diabetes has an effect on visual functions. The present study has highlighted the importance of VEP as a valuable non-invasive test to detect early neuronal changes in the pre-retinopathy stage. It can be proposed that the impairment of Visual Evoked Potential should be regarded as early central manifestation of diabetic neuropathy. Thus, a routine VEP assessment should be recommended to all the diabetic patients, for the early identification of visual defects.

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

**Source of Funding:** None

**Conflicts of Interest:** Nil

**References**


10. J. Heravian, A. Ehyaei, N. Shooibi et al., “Pattern visual evoked potentials in patients with type II


