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Visual evoked potentials in non insulin dependent diabetes mellitus without retinopathy: A pilot study.

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Abstract

Diabetes Mellitus (DM) has detrimental effects on the various organs of our body including peripheral nervous system, which are widely accepted. However, not much research is done on understanding the central nervous system (CNS) abnormalities in DM. Visual evoked potential (VEP) is a non-invasive neurophysiological examination that detects early diabetic retinopathy changes, which is important in preventing loss of vision. Aim was to evaluate the efficacy of VEP in detecting retinal ganglion cell damage in diabetics and to correlate between P_{100} latency in milliseconds (ms) and duration of diabetes. This study included 20 diagnosed DM type II patients of more than 2 years duration and without any clinical complications. 20 age and sex matched subjects were taken as controls. VEP was recorded using pattern reversal stimulation with EMG RMS MARK II machine. P_{100} latencies (ms) was significantly prolonged in diabetics with mean ± SD of (110.14 ± 5.30 ms) as compared to controls (100.17 ± 0.75 ms) with p value <0.001. Significant positive correlation was found between duration of diabetes and P_{100} latencies (r =0.63; p=0.003). It can be concluded that the prolongation of P_{100} latencies observed in diabetics could be a manifestation of structural damage at the level of the myelinated optic nerve fibres or retinal ganglion cell damage before development of diabetic retinopathy and P_{100} latencies showed significant positive correlation with duration of diabetes.

Key-words: Diabetes Mellitus type II, diabetic retinopathy, evoked potentials, visual

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Key Messages

Diabetic retinopathy is a leading complication of diabetes. Often, the patient is ignorant of any symptoms until it is too late to manage effectively. Through visual evoked potentials, diabetic retinopathy can be diagnosed early and this could lead to better prognosis during treatment.

Introduction

In diabetics, the most common cause of blindness is retinopathy. The abnormalities of central nervous system (CNS) and predominantly their relevance to optical function, have not received much attention [1].

Diabetes mellitus (DM) causes vascular and metabolic abnormalities resulting in visual deficit [2]. Visual evoked potential (VEP) is effective in detecting retinal dysfunction in diabetics with normal visual acuity [2].

The present study is therefore carried out with the aim of establishing the role of VEP in the assessment of retinal ganglion cell damage, which is a sign of diabetic preretinopathy and to correlate between P_{100} latency in milliseconds (ms) and duration of diabetes.

Subjects and Methods

Study included 20 patients with more than 2 years of duration of diabetes (17 males and 3 females; mean age: 57.5 ± 9.7 years, range: 42-70 years) and the control group included 20 subjects matched for their age and sex.

All patients had Non-Insulin Dependent Diabetes Mellitus (NIDDM) proved by recent blood glucose studies (fasting blood glucose levels). All cases were clinically examined for chronic complications of diabetes for exclusion. Patients with long standing hypertension and with past history of cerebrovascular accidents were excluded. Patients consuming more than 100ml of alcohol daily and those with peripheral nervous system abnormalities not related to diabetes were excluded from the study.

The ophthalmological examination carried out on all patients included visual acuity, recording of intraocular tension and fundus examination under full mydriasis. The patient was instructed to avoid any miotic or mydriatic drugs 12 hours before the test. The study included only those patients with normal visual acuity. Patients with diabetic retinopathy, cataract, glaucoma, vitreous opacities or any evidence of optic atrophy were excluded from the study. The institutional ethical clearance was obtained for the study. The informed consent was taken from selected subjects.

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 100cms.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.

The bioelectrical signals were recorded by silver or silver chloride disc electrodes placed at: 1) Grounding (F_{PZ}), 2) Active (O_Z), 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 5kΩ. The evoked responses were averaged and analysed by the Evoked Potential Recorder (EMG RMS MARK II machine). The peak P_{100} latencies (Fig.2) were recorded and correlated with duration of diabetes.

Statistical analysis

Two tailed independent student t-test was used to find the significance in P_{100} latencies of VEP waveforms between the diabetic and control groups. Significance was also assessed at 1% level of significance. The correlation between duration of diabetes and P_{100} latency of diabetics was done using Pearson correlation co-efficient.

Statistical software

The statistical software namely SPSS 19.0 was used to analyse data and to generate tables Microsoft word and Excel was used.

Results

There was no significant difference in P_{100} latency between the right and left eyes in both control and diabetic groups as shown in Table: 1.

Regarding results, the mean values for both eyes were taken. The mean P_{100} wave latencies were significantly prolonged in diabetics compared to the control group (110.14± 5.30 ms Vs. 100.17± 0.75 ms, $p < 0.001$) (Fig. 3).

Significant positive correlation was found between mean P_{100} wave latency and duration of diabetes mellitus ($r = 0.63$; $p = 0.003$) (Fig. 4).

Table: 1. *P_{100} wave latency in diabetic patients and control subjects.*

	Diabetic patients	**Control subjects**
Total number of subjects	20	20
P_{100} latency of Right eye	109.63±5.18(102-119)*	99.69±0.94(98-101)
P_{100} latency of Left eye	110.65±5.49(101-119)*	100.65±0.74(98-101)
Mean P_{100} latency of both eyes	110.14±5.30(101-119)*	100.17±0.75(98-101)

Values (in milliseconds) are mean ± SD (ranges in parentheses)
**p<0.001, diabetic Vs. control subjects*

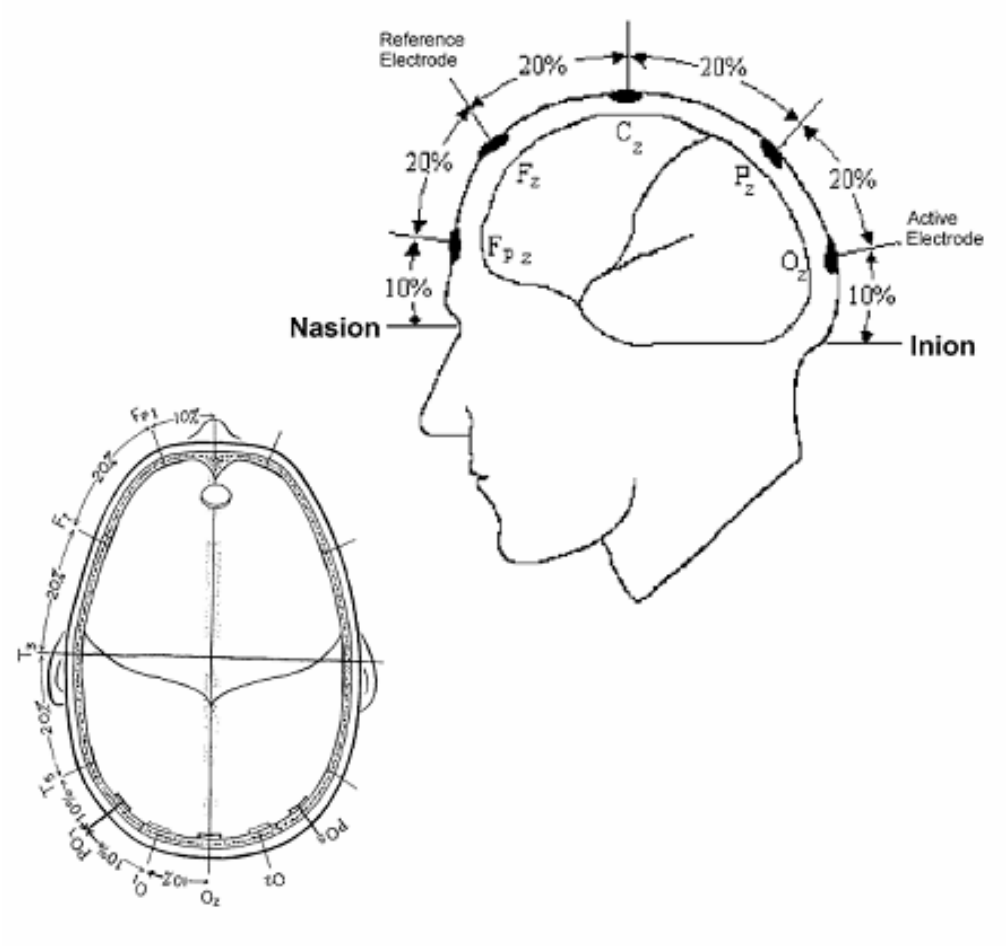

Figure 1. *Electrode locations [10].*
a)Location of active, reference and ground electrodes for standard responses. The active electrode is located at Oz. The reference electrode is located at Fz. The ground electrode is located at F_{PZ}.The subscript z indicates a midline position [10].

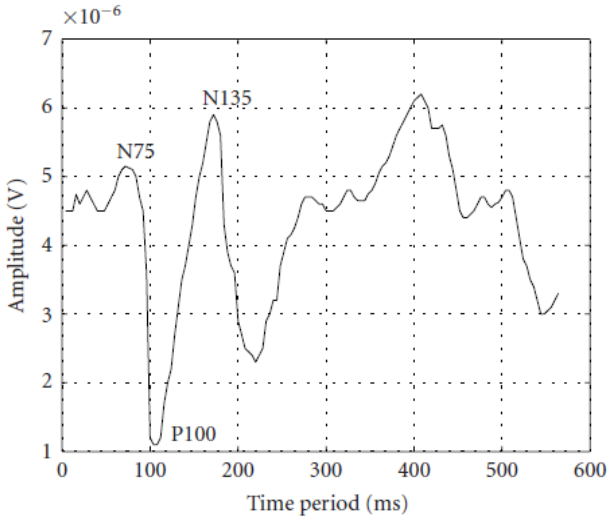

Figure 2*. Normal subject VEP waveform [10].*

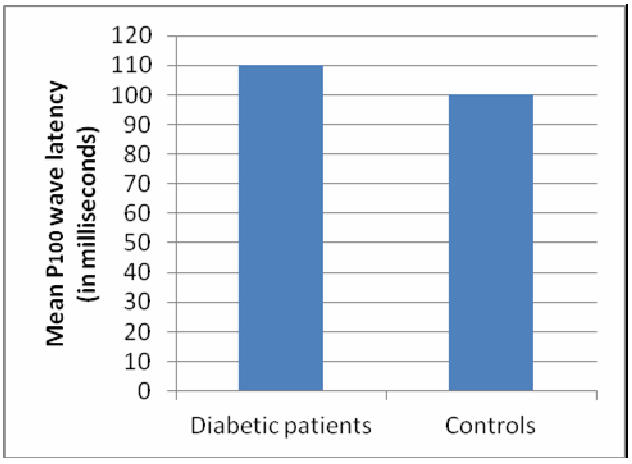

Figure 3*. P_{100} wave latency in diabetic patients and control subjects*

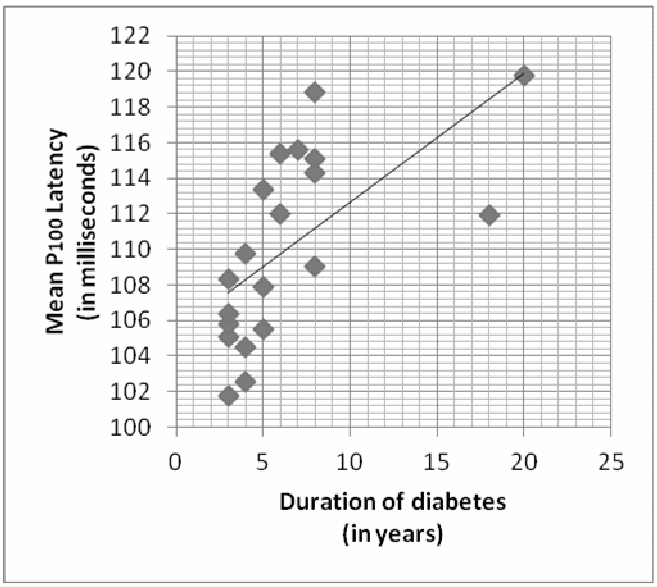

***Figure 4**. Correlation between duration of diabetes and Mean P_{100} wave Latency*

Discussion

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 [2]. In the present study, the differences in P_{100} wave latencies between the diabetics and the control group as shown in Table:1 and Fig.3 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 ophthalmoscopic examination [2].

Damage in retinal ganglion cell in diabetics can be due to extracellular glutamate accumulation leading to functional and anatomical changes, which arise even before vascular damage. Oxidative stress, apart from microvascular abnormalities and consequences of glucose metabolism, play a great role in the pathological development of diabetic retinopathy. Oxidative stress might be attributed to either rise in free radical and oxidant production or reduced activity of antioxidative mechanisms [2].

The most ideal parameter of VEP is Latency. As amplitude has greater variability, it is considered to be less reliable. In diabetics, the latency values have a tendency to prolong with time, which could be due to damage to ganglion cell. Therefore, this paper focussed more on the correlation of latency values and the duration of diabetes. The present study showed statistically significant positive correlation between mean P_{100} latency values and the duration of diabetes ($r=0.63$; $p=0.003$) as shown in Fig.4. indicating that the neurophysiologic variations are caused by ischemic neuronal and other retinal structural damage caused by microvascular abnormalities [2].

Vascular damage in diabetic retinopathy is due to non-enzymatic advanced glycosylation products [2]. Visual evoked potentials (VEP) showed that P_{100} latency was significantly prolonged in diabetics compared to control subjects. The abnormal basal VEPs are suggestive of a premature involvement of the optic nerve [3].

A study found prolongation of P_{100} latencies in 50 DM patients of which 6 of them had diabetic retinopathy [4]. Another study found prolongation of P_{100} latencies in 35 diabetic patients, but they did not have retinopathy [5].The correlation was found to be positive between VEP latencies and duration of diabetes [5,6]. Prolongation of VEP latencies were reported in 50 asymptomatic insulin dependent diabetic patients without retinopathy [6, 7, 8]. VEP measurement seems to be a simple method for detecting premature alterations in anterior visual pathways in diabetics [5].

A study has shown that P_{100} wave latency was significantly lengthened during hypoglycaemic episodes [9]. None of the patients in our study had any signs and symptoms of hypo-glycaemia during VEP recording.

It is already established that the intervention is most effective when done at the onset of first sign of diabetic retinopathy.

In conclusion, the present study showed the importance of VEP in detecting diabetic preretinopathy in diabetics. 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 ophthalmoscopic examination in diabetics.

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