Early Diagnosis Of Diabetic Retinopathy By Visual Evoked Potential

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Abstract

The visual evoked potential is an electrophysiological study used to assess the visual pathway to detect the occipital response to a light stimulus. The aim **of the study is:** early diagnosis of diabetic retinopathy by VEP study in patients who were newly diagnosed with diabetes mellitus (DM), with assessment of visual pathway impairment due to diabetic retinopathy.

Methods: This study was conducted as a case-control study that was carried out on ninety (90) patients presented with a new diagnosis of type II diabetes mellitus (within 3 years from the time of diagnosis) who attended the medical departments of Alazher University Hospital during the period from December 2020 to the end of October 2021, and twenty healthy persons of the same age and sex were used as a control group. Each participant has undergone a battery of neurological and ophthalmological tests, including visual-evoked potentials. The patients have received reverse-patterned VEP through a single eye.

Results: There were statistically significant differences in latency of N 75 and P 100 and amplitude of N 75 to P 100 between patients and the control group. Also, there was a statistically significant difference in latency between P 100 and N 75. There was no significant difference between the results of VEP and the age of patients, sex, or in between both sides of the eye.

Conclusions: This study diagnoses diabetic retinopathy early and analyzes its prognosis by observing changes in VEP pathway latency and P100 wave amplitude in group A patients.

Keywords: diabetes, retinopathy, visual evoked potential

Introduction

Diabetes is a metabolic disorder represented by abnormal glucose metabolism, insulin resistance, and relative insulin deficiency. It may eventually lead to diabetic retinopathy, the leading cause of blindness and visual impairment in diabetic patients. Diabetic neuropathy (DR) is an unpleasant long-term complication of diabetes mellitus that results in vasculopathy and metabolic abnormalities that impair the small blood vessels of the retina, optic nerve, and visual pathway. Diabetic retinopathy can be considered a retinal vascular abnormalties , and it is also regarded as a neurosensory disorder. Transmission of the impulses through the optic nerve and tract could be affected by the vascular neuropathy (1).

Diabetic retinopathy is the leading cause of visual morbidity and blindness in people with diabetes and is the most common microvascular consequence of the disease. In the first five years after the diagnosis of diabetes, DR typically shows few to no symptoms. The worsening of DR and the delay in treatment are both associated with this pervasive lack of retinal symptoms over time. Although they are commonly used for screening for DR and macular edema, fluorescein fundus angiography and optical coherence tomography are typically unable to identify the early microangiopathy and neuropathy that occur in the disease. As a result, numerous methods have been explored with the hope of identifying early anatomical and functional problems in diabetic retinopathy. Optical, VEP, , EOG, and corneal confocal microscopy are all useful tools for spotting the alterations brought on by DR in its earliest stages (1, 2, 3).

The anatomical and functional problems in the central nervous system and especially their relationship with visual disabilities were not well investigated. The neuronal retina is affected first by diabetes mellitus before the onset of microvascular pathology and retinal pathology caused by diabetes , at which there is no or minimal affection of the visual acuity and no signs of retinal diseases can be detected by ophthalmic examination, so early diagnossi of the central nervous system damage in diabetes is a very important step for the diagnosis and follow-up of patients with diabetes mellitus (2).

VEP is an objective noninvasive electrophysiological test that is used in ophthalmology for measuring how long the visual impulse needs to travel from the retina to the occipital cortex and evaluating the functions of the visual pathway. VEP reflects the function of the central visual field at all levels of the visual pathway. It generally reflects the function of the macula relatively. When the optic nerve sheath may be affected by many diseases, the electrical stimuli take long time to reach the occipital cortex, resulting in abnormal VEP. When there is a structural damage to the optic nerve sheath and fibers, prolonged latency of the P100 wave can be registered. There are many pathogenic metabolic and vascular mechanisms in diabetes mellitus can lead to axonal loss and abnormal VEP (3) that may be detected long before the retinopathy manifestations become clinically diagnosed in diabetic patients , so these anomalies may be detected by this objective and non-invasive electrophysiological technique. (4)

Pattern-reversal VEP is a noninvasive test used for early detection of diabetic changes in the retina and optic nerve. It is a sensitive test that provides subclinical evidence of visual abnormalities, that could enable us to prevent or delay the development and progression of diabetic retinopathy through strict glycemic control. Also, the prognosis of the condition can be determined during the follow-up and treatment period. (5)

The aim of the study

The aim of this study was to evaluate central nerve conduction changes in newly diagnosed diabetes mellitus patients by using a pattern-reversal VEP test.

Patients and methods

This study was conducted as a case-control study that was carried out on ninety (90) patients (180 eyes) who presented with a new diagnosis of type II diabetes mellitus (within 3 years from the time of diagnosis) and attended the medical departments of Alazher University Hospital during the period from December 2020 to the end of October 2021. Twenty healthy persons (40 eyes) of the same age and sex were used as a control group.

Both patients and controls received an explanatory note explaining the aim of the study with written medical consent and the right to deny participation in the study.

Exclusion criteria included those with established diabetic retinopathy and diabetic macular edema, diabetic papillopathy, ocular surgery, macular diseases, glaucoma , cataracts, multiple sclerosis, or a past history of optic neuritis or papilledema.

A personal history of all the patients was taken, such as name, age, sex, residence, occupational and relevant medical history, including duration of diabetes mellitus, HBA1C at the time of diagnosis, and other medical diseases.

A retinal examination for all patients was done using a direct and indirect ophthalmoscope after dilatation of the pupils, fluorescein fundus angiography and ocular coherence tomography to document the absence of DR.

Visual acuity was measured, and best corrected visual acuity was assessed by decimal and log MAR for all patients, and intraocular pressure was measured by applanation tonometry for all patients.

Random blood sugar was measured for all patients at the time of the VEP test to exclude hyper- or hypoglycemia, which could affect the test, and it was corrected before the test.

Each patient's VEPs were recorded using the Neurowark EMG 17-NWEMG-5960 equipment (Sigma, Medzin, Technik, Germany) per ISCEV standards (6). Patients were informed of the test and its instructions. All patients were instructed to wash their hair and not use lubricant the night before the test. The patient would have worn glasses during the VEP test if he had a refraction error. A semi-dark, acoustically isolated room was used for 10 minutes before the test. The subject was told to avoid meiotic or mydriatic eye drops and systemic drugs 12–16 hours before the test. A checkerboard was used to record VEPs during pattern-reversal stimulation with mid-size checks (24–32). Silver/silver-chloride cup-shaped electrodes were fixed in the Oz (active electrode), Cz (reference), and Fpz (ground) positions. A 90-cm distance separated the patient from the TV. Patients were instructed to fixate their eyes throughout the test. The goal was maximal foveal and parafoveal fibre stimulation at 75% contrast and 1.2 Hz reversal. Laboratory illumination was uniform, and electrode impedance was below 5 kΩ. Each eye had 100 stimulus sweeps on average. To prove reproducibility, this was done twice and the average superimposed. Any trial latency difference over 3 msec was excluded from the study. Normal VEPs had several waves with three peaks after 75–100 and 145 ms. Polarity peaks were negative (N75), positive (P100), and negative (N145). Each wave's peak latency and amplitude were accurately measured on the displayed records using two cursors. Visual function was assessed by the latency of the first major positive component of the evoked response (P100) and the peak-to-peak amplitude of N75 to P100. P100 latencies over 110.85 ms in any eye indicated abnormal responses (6, 7).

This study's patients gave informed consent after the local ethical committee approved the protocol.

Statical analysis:

SPSS 11.5 (SPSS, Chicago, USA) was used to analyze the data using Spearman's correlation coefficient, t-test, and Mann-Whitney test. The significance level was set at $P<0.05$.

Results

Table 1: Demographic data of both groups

Variable	Group A		Group B		P value
	Number	Percent	Number	Percent	
Sex					
Male	39	43.33%	9	45%	0.465
Female	51	56.66%	11	55%	
Age (years) (Mean ± SD)	49.08 ± 6.20		45.9 ± 7.14		0.116
HbA1c (Mean ± SD)	6.9 ± 1.17		5.6 ± 1.25		0.001**

This table showed that there is a significant relationship between two groups according to the presence of DM, while there is no significant relationship between age and sex in between.

Table 2: Comparison results of VEP between the two groups

Variable	Patients (Mean ± SD)	Controls (Mean ± SD)	P value
N 75	71.58 ± 1.22	64.04 ± 2.12	0.001**
P 100	106.20 ± 12.11	95.66 ± 5.99	0.002**
N 145	139.77 ± 20.01	135.4 ± 12.34	0.12

Amplitude	4.67 ± 3.55	7.7 ± 5.66	0.002**

This table showed a statistically significant difference in delayed N75 and P100 latency and diminished amplitude of visual evoked potenials between the studied groups.

Table 3: Comparison results of the visual-evoked responses of diabetic patients with age

Variable	**Patients (Mean ± SD)**	**Age (Mean ± SD)**	**P value**
N 75	70.99 ± 1.40	49.08 ± 6.20	0.089
P 100	108.24 ± 15.11	49.08 ± 6.20	0.451
N 145	139.69 ± 22.87	49.08 ± 6.20	0.857
Amplitude	4.62 ± 3.20	49.08 ± 6.20	0.090

This table showed no significant relationship between all parameters of visual evoked response and the age of patients.

Table 4: Comparison results of visual evoked response with sex of patient groups.

Variable	**Male (Mean ± SD)**	**Female (Mean ± SD)**	**P value**
N 75	71.94 ± 1.25	72.00 ± 1.33	0.980
P 100	106.55 ± 14.22	108.91 ± 17.58	0.602
N 145	140.84 ± 23.21	143.68 ± 24.20	0.598
Amplitude	4.78 ± 3.06	4.5 ± 2.59	0.620

This table showed no significant relationship between all parameters of the visual evoked response and the sex of the patients.

Figure 1: Normal FFA and OCT but delayed latency and reduced amplitude of the P wave by VEP

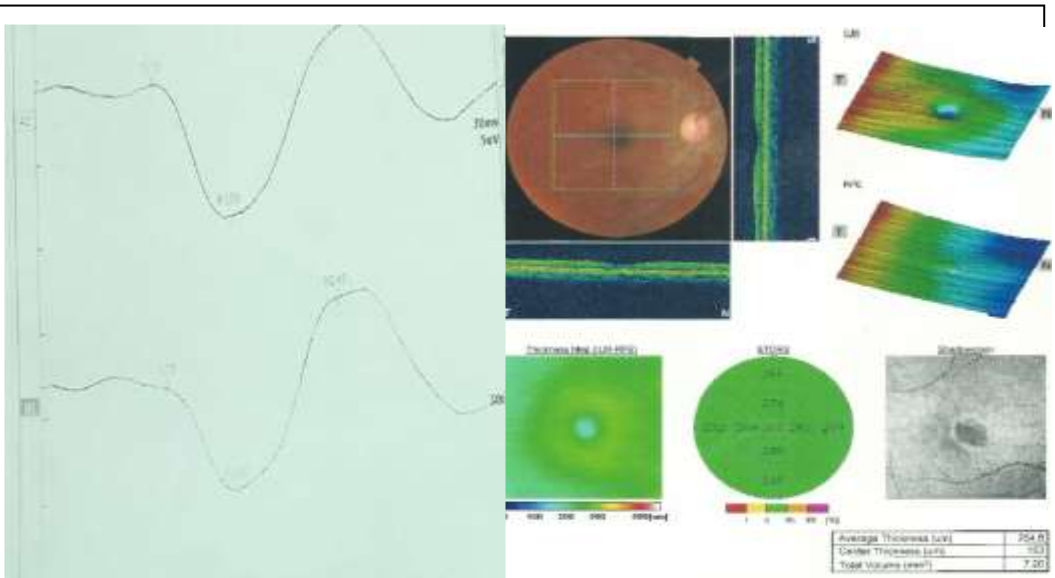
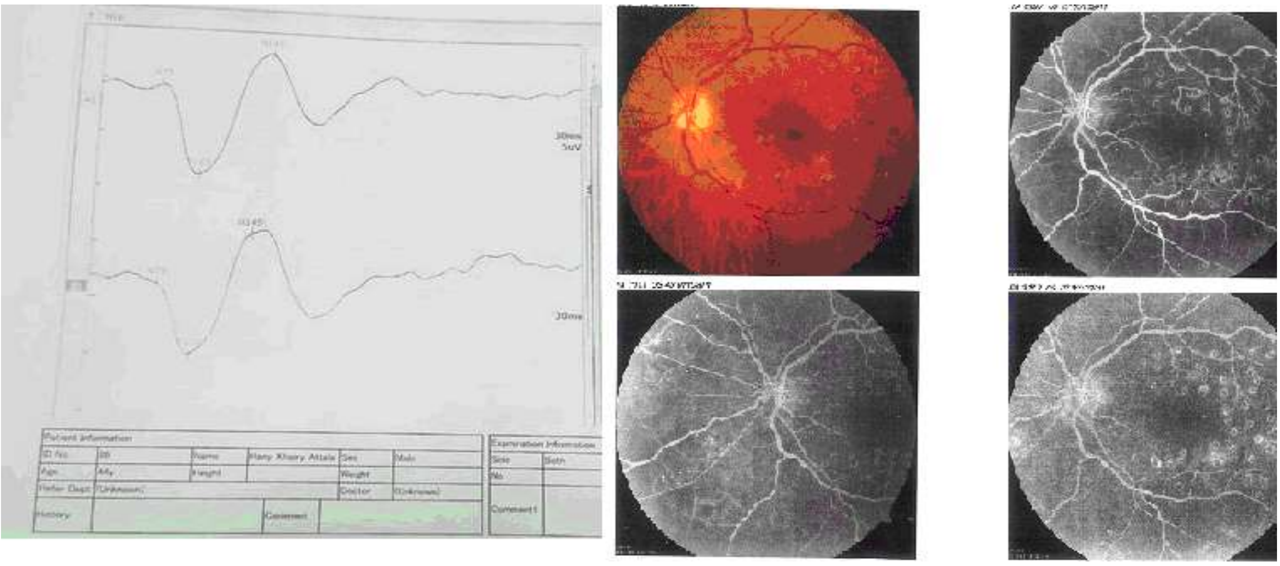


Figure 2: VEP at Patient underwent grid laser photocoagulation



After grid laser photocoagulation in non-proliferative diabetic retinopathy with macular edema, the VEP amplitude decreased in 60% of eyes with prolonged latency in them.

Table 6: Comparison results of VEP between both eyes

Variable	Right eye (Mean ± SD)	Left eye (Mean ± SD)	P value
N 75	73.20 ± 1.35	72.66 ± 1.33	0.77
P 100	108.22 ± 16.05	106.05 ± 15.02	0.325
N 145	142.60 ± 22.93	138.42 ± 22.90	0.509
Amplitude	4.22 ± 3.33	4.23 ± 3.58	0.987

This table showed no significant relationship between the results of visual evoked potentials at both eyes.

Discussion

Diabetes mellitus, a prevalent metabolic condition, causes chronic metabolic and vascular consequences like diabetic retinopathy and significant morbidity (7).

Early diagnosis of abnormalities in visual function is useful to identify and treat diabetic retinopathy, which can cause irreversible blindness (8).

The neuronal layers of the retina of diabetic eyes suffer functional alterations not detectable by fluorescein fundus angiography before microvascular abnormalities develop (9).

The present study included ninety newly diagnosed type 2 diabetes mellitus patients and twenty healthy volunteers as a control group. The results of VEP showed that the mean N 75 and P 100 latency in the diabetic group, as shown in the tables, was significantly prolonged when compared with those in the control group. Also, a statistically significant reduction in the mean N75-P100 amplitude was observed in the diabetic group as compared with the control group. This agrees with the results reported by many studies, including Parisi et al., 1998 (22); Puvanendran, 1983 (10); Pozzessere et al., 1991 (11); Lee, 2017 (12)); and other studies (7, 13, 14, 15), who found a statistically significant reduction in the mean N75-P100 amplitude in diabetics compared to controls. These findings show that VEP delay may be more sensitive to early DM alterations in the inner retinal and optic nerve pathways than fundus inspection for ocular injury identification.

This study found that optic nerve involvement may develop in diabetic patients before the onset of symptoms. Latency of P100 is observed in those early diabetic patients due to structural damage to the myelinated optic nerve fibers. This may be due to different pathogenic vascular and metabolic mechanisms involving peripheral nerve versus optic pathway involvement.

Our findings may also indicate that diabetics have a neurological deficit in the occipital cortex and visual pathway at an earlier stage of diabetes, possibly due to metabolic and vascular factors. Chemical mediators may delay visual pathway conduction, causing diabetic latencies to be longer than healthy controls.

The current study's findings that there was no significant correlation between mean P100 latency and patient age or sex are consistent with those of Verrotti et al. (14) and Lee et al. (13), who studied the association between P100 latency and clinical factors like age, sex, and HbA1c levels in people who had recently been diagnosed with diabetes mellitus and found no such correlation.

Sixty percent of eyes treated with grid laser photocoagulation for non-proliferative DR with macular edema saw a decrease in VEP amplitude and an increase in latency. However, this work suggests that the impacts of the redistribution of neurochemicals in the visual cortex following laser photocoagulation may contribute to the VEP waveform changes seen.

Conclusions and recommendations

VEP, as a valuable, non-invasive, harmless, fast, and repeatable test, could be used as an objective method for the detection of early neuronal changes in the pre-retinopathy stage when there are no features of retinopathy. It may monitor the early effects of retinal dysfunction and visual impairment.

Therefore, VEP can be recommended as a preventative measure against blindness as an early examination prior to the development of retinopathy to track the earliest impacts of diabetes on visual function. Diabetics would benefit from a more thorough evaluation and an improved prognosis if PRVEPs were indicated.

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