Visual evoked potential changes in pre-diabetics, type 2 diabetics and normal subjects

Zaahid Naseer[1], Arun Kumar M[2,*], Roopakala M S[3], Pramila Kalra[4]

[1]Intern, [2]Assistant Professor, [3,4]Professor, [1,2,4]Dept. of Physiology, [3]Dept. of Endocrinology, Ramaiah Medical College, Bangalore, Karnataka, India

***Corresponding Author:**
Email: drarunkm@gmail.com

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Abstract

Introduction: Diabetes mellitus type 2 is the most common metabolic disorder and diabetic retinopathy is the leading cause of blindness. Persistent hyperglycemia leads to damage of microvasculature supplying the retina and optic pathway. Visual evoked potential is the most commonly used test to evaluate the integrity of visual pathway. The purpose of the study is to compare the visual evoked potential latency and amplitude between the pre-diabetes, diabetes and normal controls.

Materials and Methods: There were three groups in the study with 23 patients in each group; pre-diabetic group, diabetic group and controls. Group was made based on fasting blood sugar levels. Pattern visual evoked potential was measured in all the groups by connecting scalp electrodes according to 10-20 International electrode placement system. Latency and amplitude of N75, P100 and N145 were measured and used for statistical analysis.

Results: All the parameters individually were compared between three groups using ANOVA test. There was no statistical difference between latencies and amplitude all the three parameters N75, P100, N145 in all the three channels O1-NE, O2- NE, Oz-NE in all the three groups.

Conclusion: There is no differences in the visual evoked potential latency and amplitude in the between pre-diabetics, diabetes and controls.

Keywords: Visual evoked Potential, Diabetic retinopathy, Pre-diabetes, P100, N75, N145.

Introduction

Diabetes mellitus (DM) is most common metabolic disorder in the world. Diabetes mellitus currently affects more than 62 million Indians, which is more than 7.1% of the adult population.[1] It is a metabolic disorder which occurs due to defect in insulin secretion or insulin action or both. Lack of insulin leads to persistent hyperglycemia and other related complications. Chronic hyperglycemia is central to the pathophysiology of chronic complications such as cardiovascular and peripheral vascular disease, retinopathy, nephropathy, and neuropathy.[2]

Pre-diabetes is defined as elevated blood sugar that does not reach the criterion accepted for an outright diagnosis of diabetes. Pre-diabetics have an elevated risk for development of frank diabetes. Approximately 77 million adults are pre-diabetic in India. Diabetes is the leading cause of blindness between the ages of 20 and 74 across the globe. It is a serious problem because individuals with diabetes mellitus are 25 times more likely to get blindness. Blindness is primarily the result of progressive diabetic retinopathy and clinically significant macular edema. Duration of diabetes and degree of glycemic control are the best predictors of the development of retinopathy and subsequent optic nerve damage.[3]

Visual evoked potential (VEP) is the commonly used neurophysiological test for evaluating the functions and integrity of the visual pathway. Clinically, the VEP is used in the testing of diseases related to the areas of refraction, infant acuity, diseases of the optic nerve, color blindness, amblyopia and field defects.[4] Evoked potential are the tests wherein the stimulus of particular type are given and electrical response to the stimuli are recorded using appropriate instrument. In VEP the visual stimulus is given and responses are captured by placing electrodes on the occipital region. Two types of VEP are available based on the stimuli that are given. There are three types of standardized visual stimuli that are described in standards and guidelines for clinical electrophysiology of vision 2016 (ISCEV 2016).[5] There are pattern reversal, pattern onset and flash. Pattern VEP and flash VEP wherein responses that are evoked by pattern stimuli and flash stimuli respectively. Pattern VEP testing is known to detect minor visual pathway abnormality with much greater sensitivity and accuracy. Checkerboard pattern reversal stimulation is the gold standard.[6]

VEP is described using different waves, its latency and amplitude. The most common wave that is used in the VEP is P100 (first positive wave) and other uncommon waves are N75and N145 (negative waves). These N75, P100 and N145 actually means the wave occur around 75 ms, 100 ms and 145ms respectively with deviation on either side. The P100 waveform of VEP is generated in the visual areas occipital cortex and also thalamocortical volleys.[7,8]

There are studies that have described the changes of VEP in diabetes mellitus, and have found that there

is impaired VEP latency.[9] VEP studies have been done in several condition related to diabetes and its complications.[10] There are no studies which have considered done comparing VEP latency changes between diabetic and pre-diabetic condition. There could be a possibility of optic nerve/pathway damage that could occur as a result of hyperglycemia in pre-diabetes. The aim of the study was to detect the latency and amplitude changes in pre-diabetics and diabetic patients and compare them with normal subjects.

Materials and Methods

The study was conducted at M S Ramaiah Medical College and Memorial Hospitals. It was a case control study with 23 subjects in each of three groups: pre-diabetic, diabetic and control group. The sample size was calculated based on the study conducted on the Visual evoked potential in non-insulin dependent diabetes retinopathy it was found that mean P100 latency of both eyes in diabetes patient was 110.14± 5.30 ms(mean ± SD).[1] In controls 100.17 ±0.75 ms, so with a power of 95% and confidence level of 95% it was proposed to include 23 patients of diabetes, 23 subjects of pre-diabetes and 23 controls in present study with an effect size of 1.32. The study was approved by institutional ethical committee.

The groups were made based on the fasting blood sugar (FBS) levels according to WHO Criteria.[5] Fasting blood sugar level less than 100 gm/dl, more than 125 mg/dl are considered to be normal and diabetic group respectively. FBS levels between 100-125 mg/dl in considered in pre-diabetes group. Patients were in the age group of group was 30-60 years were included in the study. Alcoholics, smokers and patients with local eye disorders and abnormal fundoscopy were excluded from study. The FBS was determined by hexokinase method using the early morning samples collected from the after overnight fasting.

The study participants were explained about procedure of the visual evoked potential (VEP) and consent was obtained. If the patient had applied oil to head, they were asked to come on another day after taking head bath. If the participants were using spectacles they were asked to wear them during test procedure. The pattern VEP was measured and analyzed in all the groups by using Galileo NT instrument and software. The skin is prepared by abrading and degreasing. Five surface EEG electrodes were used and placed according to 10-20 international system. The recording electrodes were placed at Oz, O1 and O2 using conducting jelly. Oz is a point 5 cm above the inion in the occipital region, 5 cm to the left of it O1 and 5 cm right to that is O2. The reference electrode (NE) is placed at Fpz or 12cm above the nasion. The ground electrode is placed at the vertex, i.e. at Cz. Resistance of less than 5 ohms was considered acceptable. Stimuli used is a standard checkerboard pattern which alternates at the frequency of 10/sec and is projected on the computer screen. Subjects were asked to focus at the center regions of screen with one eye at the time, the other eye was covered. Average of 200 responses was taken for interpreting the latencies and amplitudes. Latencies marked were N75, P100 and P145 by stimulus giving to both the eyes separately. Latency and amplitudes of first negative wave (N75), first positive wave (P100) and second negative wave (N145) was determined for all three leads i.e., O1-NE, O2-NE and OZ-NE.

Data was tabulated and analyzed using MS-Excel and SPSS software version 17. The statistical test used was descriptive analysis with mean and SD for baseline parameters. The latency and amplitude were compared using ANOVA analysis.

Results

The study consists of 23 subjects in each of 3 groups i.e., pre-diabetes group, diabetes group and control group. The mean and SD values of VEP latencies of N75, P100 and N145 in the three leads i.e., O1-NE, O2-NE and OZ-NE measured from right eye stimulus and left eye stimulus are depicted in table 1 and 2 respectively. Mean values of latencies of N75, P100 and N145 is more in diabetes group when compared to the pre-diabetic group which is more when compared to the control group. On application of one way analysis of variance (ANOVA) there was no significant difference in all the parameters.

Table 1: Comparison VEP latencies in the groups with right eye stimulus

Channel	Latency	Prediabetic group	Diabetic group	Control group	P value
O1-NE	N75	76.47 ± 4.513	75.93 ± 6.772	71.99 ± 9.831	0.107
	P100	103.59 ± 4.703	105.25 ± 12.714	100.16 ± 11.791	0.270
	N145	140.32 ± 19.671	154.98 ± 37.361	143.84 ± 34.488	0.314
O2-NE	N75	74.15 ± 4.293	76.74 ± 9.921	73.82 ± 7.367	0.401
	P100	103.86 ± 6.198	106.28 ± 11.94	100.04 ± 20.699	0.375
	N145	143.92 ± 13.335	157.02 ± 38.337	141.48 ± 21.656	0.133
Oz-NE	N75	76.83 ± 7.591	74.06 ± 6.512	73.1 ± 7.171	0.220
	P100	104.38 ± 7.942	101.77 ± 4.338	101.44 ± 5.089	0.229
	N145	144.41 ± 15.716	143.65 ± 10.51	142.96 ± 20.419	0.959

p value < 0.05 was considered statistical difference.

Comparison of amplitudes of P100 in all the channels, O1-NE, O2- NE and Oz-NE was done with stimulus on right and left eye. The Mean values of amplitudes of P100 are almost same in the diabetes group when compared to the pre-diabetic group and control group. On application of one way analysis of variance (ANOVA) there was no significant difference in between the parameters in all the 3 groups. The values are mentioned in table 3.

Table 2: Comparison VEP latencies in the groups with left eye stimulus

Channel	Latency	Prediabetic group	Diabetic group	Control group	P value
O1-NE	N75	74.77 ± 5.989	75.47 ± 6.78	72.88 ± 7.194	0.423
	P100	104.86 ± 10.91	103.17 ± 8.819	102.85 ± 6.222	0.729
	N145	144.86 ± 9.133	147.2 ± 17.062	138.24 ± 14.803	0.103
O2-NE	N75	75.04 ± 9.056	75.65 ± 6.394	74.02 ± 8.646	0.401
	P100	105 ± 6.263	109.84 ± 13.436	103.24 ± 6.39	0.375
	N145	149.07 ± 38.996	150.24 ± 18.798	142.06 ± 15.84	0.133
Oz-NE	N75	77.9 ± 9.728	76.01 ± 8.764	74.12 ± 7.208	0.358
	P100	104.4 ± 7.951	102.67 ± 7.228	100.52 ± 6.403	0.214
	N145	145.59 ± 7.38	146.84 ± 19.278	140.22 ± 8.153	0.192

p value < 0.05 was considered statistical difference.

Table 3: Comparison VEP amplitudes in all the groups with both eye stimulus

Channel	Stimulus Side and Wave	Control Group (Mean ± SD)			Prediabetic Group (Mean ± SD)			Diabetic Group (Mean ± SD)			p value
O1-NE	Right P100	3.69	±	2.32	4.12	±	2.09	4.51	±	2.61	0.78
	Left P100	3.38	±	1.89	4.53	±	2.02	5.12	±	3.1	0.378
O2-NE	Right P100	4.1	±	2.4	4.57	±	2.97	4.48	±	2.28	0.93
	Left P100	3.89	±	2.42	4.27	±	2.68	4.79	±	2.36	0.755
Oz-NE	Right P100	2.23	±	3.4	4.94	±	5.55	6.55	±	2.78	0.115
	Left P100	1.97	±	2.49	4.8	±	5.45	6.84	±	2.97	0.055

p< 0.05 is considered significant

Discussion

Diabetes is the most common disease and its complication is life threatening. As the duration of diabetes increases and the occurrence of complications also increases. Most often patient reaches the hospital during the stage wherein the disease and its complication had made the patient morbid. Management of such conditions is difficult and challenging. It becomes important to detect such complications in the early stage given an indication to the patient about its impending danger. In this study an attempt was made to identify if it is possible to detect if there was any early damage to the optic nerve and its pathway in patients with Prediabetic condition.

Visual evoked potential is the one of the commonly used test in the assessment of the integrity of optic nerve pathway. When the stimulus is given the light gets processed from the retina enters the optic nerve, optic chaisma, and then enters in the visual area in the occipital area. Electrodes on the scalp is placed on the O1 and O2, these areas corresponds to the scalp region above left and right occipital cortex respectively whereas as Oz corresponds to the center of these to waves.[11,12]

In all the channels, i.e., O1-NE, O2-NE and Oz-NE, the N75, P100 and N145 did not show any significant change between the three groups. There is no significant delay in the latencies of these waves in the diabetic or prediabetic group. This is in contrary to the studies like Brian et al 2010 who has reported that there is increase in the latency in the subjects with diabetes.[13] In another study conducted by Karlica[14] et al it is had been reported that latencies of P100 is significantly delayed in diabetes mellitus type I subjects. There are other studies which have studied the effect the blood glucose on VEP recordings in the normal individuals and patient with diabetic retinopathy.[15,16]

Diabetes mellitus and its complication are better studied by understanding the pathophysiological process involved in development of such complications. Anticipation of complication in the pre-diabetic stage seems to be too early to get the overt effects of retina or optic nerve damage. However few studies are suggestive of increased macular choroidal thickness as the earliest determiner to detect the onset of diabetic retinopathy in pre-diabetes.[17] In a cohort study, it was found that the prevalence of pre-diabetes was 22.4%, and of diabetic retinopathy was 8.1% with majority of participants having mild Diabetic retinopathy (7.2%).[18] Diabetic retinopathy is classified into two stages: non-proliferative and proliferative. The pathophysiological mechanisms invoked in non-proliferative retinopathy

include loss of retinal pericyctes, increased retinal vascular permeability, alterations in retinal blood flow, and abnormal retinal microvasculature, all of which lead to retinal ischemia. The appearance of neovascularization in response to retinal hypoxemia is hallmark of proliferative diabetic retinopathy. These newly formed vessels appear near the optic nerve and/or macula and rupture easily, leading to vitreous hemorrhage, fibrosis, and ultimately retinal detachment.[19,20] On prediabetic condition there are several clinical observations recognizing that diabetes-specific microangiopathic complications such as diabetic retinopathy and others might be observed due to persistent hyperglycemia.[21,22]

Duration of diabetes, in an individual, is important factor which affects the latencies of VEP. As the person spends more time with uncontrolled status or increased blood sugar it has an adverse effect on the microvasculature of various systems.[23] Circumference of the head is one of the major factors which could affect the latencies in visual evoked potential. It said that the length of optic nerve increases as the head circumference increases and correspondingly there is increase in the latency of these waves. These factors have been ignored in the study and add to the limitation of the study.[24]

It can be concluded that the there is significant changes in the latencies and amplitude of VEP measurements between diabetes, prediabetes and the study group. The future studies with larger sample size have to be considered to evaluate the possibility of using pattern VEP in the early detection of complications in diabetes.

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