Visual Evoked Potentials (VEPs) in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background

Type 2 diabetes constitutes about 85-95% of all diabetes in developed countries, and accounts for an even higher percentage in developing countries. Diabetic retinopathy is probable the most characteristic, easily identifiable and treatable complication of diabetes, but remains an important cause of visual loss.

Objective

To study P100 latencies and inter ocular latency difference in diabetic group and compared it with a control group and study the correlation between P100 and inter ocular latency difference with the duration of disease in diabetic group.

Method

A comparative, cross sectional study was done from September 2016 to January 2018 in Neurophysiology Lab, Basic and Clinical Physiology, BP Koirala Institute of Health Sciences. The sample size was 64 and random sampling technique was used. Subjects were divided into three groups according to the duration of disease. Anthropometric and visual evoked potentials were recorded. Descriptive analysis, analysis of covariance and Post Hoc multiple comparison analyses were done using SPSS 11.5. Pearson's correlation was applied between P100 latency and inter ocular latency difference with the duration of disease.

Result

On using analysis of covariance, P100 latencies were significantly prolonged in diabetic as compared to healthy controls ($p < 0.001$). Post Hoc multiple comparison showed significant differences in both left and right P100 latencies within diabetic groups and between diabetic groups and healthy controls. Left inter ocular latency difference showed positive correlation with the duration of disease.

Conclusion

P100 latencies are significantly prolonged in diabetes patients and is positively correlated with duration of disease. Visual evoked potential test can be useful for detecting retinal dysfunction before the appearance of symptoms of retinopathy.

KEY WORDS

P100 latencies, Type 2 diabetes, Visual evoked potentials

INTRODUCTION

Diabetes mellitus and lesser forms of glucose intolerance, particularly impaired glucose tolerance can now be found almost every population in the world and epidemiological evidence suggests that without effective prevention and control programs, diabetes will likely to continue to increase globally.[1]

Type 2 diabetes mellitus (DM) constitutes about 85-95% of all diabetes in developed countries, and accounts for an even higher percentage in developing countries. Type 2 DM is now a common and serious global health problem.

Diabetic retinopathy is probable the most characteristic, easily identifiable and treatable complication of diabetes, but remains an important cause of visual loss in the developed world.[1]

Visual evoked potentials (VEPs), a simple, sensitive, non invasive tool is effective in detecting retinal dysfunction in diabetes.[2] VEPs are visually evoked electrophysiological signals extracted from the electroencephalographic activity in the visual cortical areas 17, 18 and 19 recorded from the overlying scalp to visual stimulation.[3]

Diabetic retinopathy is the central neuropathy. Changes in the central nervous system and particularly their correlation with visual function, have received much less attention. VEPs can be used to evaluate the disturbance in the central nervous system with a simple, sensitive and non invasive methodology.[4] Most of the studies showed significant changes in VEP variables in diabetic patients along with positive correlation with duration of the disease.[5,6]

Thus, we aim to study if P100 latency is altered in type 2 diabetes and its correlation with the duration of the disease.

METHODS

A comparative, cross sectional study was done in a period of September 2016 to January 2018 in Neurophysiology Lab, Basic and Clinical Physiology Department, at BP Koirala Institute of Health Sciences. Type 2 diabetes patients were divided into three groups according to the duration of the disease: (group 1: < or =2 years; group 2: 3-10 years; group 3: > 10 years) and age and sex matched healthy controls (group 4) were enrolled. Sample size was calculated using Power/Sample size calculator, 2016 and the estimated sample size was 64. Random sampling technique was used. Diabetic patients referred from the diabetic clinic from Department of Internal Medicine were enrolled. Those diabetic patients with history of cataract, glaucoma, vitreous opacities or diabetic patients with history of alcohol intake or smoking were excluded. The recording procedure was explained in detail to the subjects and informed written consent was taken before the recording. Ethical clearance was taken from the Institute's Review Committee (IRC), BPKIHS. VEP recording was done using a standard technique with a Nihon Kohden machine (NM-420s, H636, Japan). Data obtained were entered into MS Excel sheet and analyzed using SPSS 11.5 version. Descriptive analysis was done for anthropometric and VEP variables in all groups. ANOVA (analysis of covariance) and Post Hoc multiple comparison analyses were done. Pearson's correlation was applied to find the association between P100 latency and inter ocular latency difference (IOLD) with the duration of disease in diabetic subjects.

RESULTS

Descriptive analysis was done for anthropometric and VEP variables (table 1). Further, ANOVA was done between diabetic groups and healthy controls. On ANOVA, age and BMI were comparable between the groups while VEP variables were statistically significant ($p < 0.001$) (table 2). Post Hoc Multiple Comparison analysis showed significant difference between P100 latency in diabetics and controls and also, there was significant difference in P100 latencies within diabetic groups and diabetic groups and controls while IOLD was not statistically significant (table 3). Pearson's correlation showed a positive correlation between left P100 latency and duration of disease while there was no any significant correlation between IOLD and duration of disease (table 4).

Table 1. Descriptive analysis of anthropometric and VEP variables

Groups	Variables	Mean ± S.D
Group 1 (< or = 2 years)	Age (years)	49.71±14.66
(n=12)	BMI (kg/m^2)	25.31±5.71
	Left P100 latency (ms)	111.75±9.21
	Right P100 latency (ms)	109.24±8.45
Group 2 (3-10 years)	Age (years)	60.60±5.59
(n= 16)	BMI (kg/m^2)	24.26±4.08
	Left P100 latency (ms)	118.88±7.28
	Right P100 latency (ms)	115.96±5.55
Group 3 (>10 years)	Age (years)	55.60±7.50
(n=20)	BMI (kg/m^2)	23.68±2.10
	Left P100 latency (ms)	122.44±5.60
	Right P100 latency (ms)	124.36±5.55
Group 4 (controls)	Age (years)	50.18±9.08
(n=16)	BMI (kg/m^2)	23.40±2.61
	Left P100 latency (ms)	101.30±5.87
	Right P100 latency (ms)	100.87±3.26

BMI- body mass index, ms- millisecond

Table 2. **ANOVA within groups**

Variables	Group 1 (n=12) Mean ± SD	Group 2 (n=16) Mean ± SD	Group 3 (n= 20) Mean ± SD	Group 4 (n=16) Mean ± SD	P value
Age (years)	49.71 ± 14.66	60.60 ± 5.59	55.60 ± 7.57	50.18 ± 9.08	0.22
BMI (kg/m^2)	25.31 ± 5.71	24.26 ± 4.08	23.68 ± 2.10	24.08 ± 0.69	0.76
Left P100 latency (ms)	111.75 ± 9.21	118.88 ± 7.28	122.44 ± 5.60	101.30 ± 5.87	<0.001
Right P100 latency (ms)	109.24 ± 8.45	109.24 ± 8.45	124.36 ± 5.55	100.87 ± 3.26	<0.001
IOLD (ms)	5±3.71	4.12 ± 3.65	4.24 ± 0.90	3.47 ± 2.95	0.87

Table 3. **Post Hoc Multiple Comparison Analyses of VEP variables within groups**

Variables	Groups	P value
Left P100 latency	1 and 2 (P1)	0.33
	1 and 3 (P2)	0.07
	1 and 4 (P3)	**0.02**
	2 and 3 (P4)	0.85
	2 and 4 (P5)	**0.001**
	3 and 4 (P6)	**< 0.001**
Right P100 latency	1 and 2 (P1)	0.21
	1 and 3 (P2)	**0.001**
	1 and 4 (P3)	**0.02**
	2 and 3 (P4)	0.12
	2 and 4 (P5)	**< 0.001**
	3 and 4 (P6)	**< 0.001**

Table 4. **Pearson's Correlation between duration of disease and P100 latency and IOLD in diabetic groups**

Diabetic Groups	Left P100 latency (ms)	Right P100 latency (ms)	IOLD (ms)
1	r= -.155	r = -0.32	r =- 0.77
	P = 0.074	P = 0.48	P = 0.15
2	r = -0.757	r = -0.523	r = -0.819
	P = 0.13	P =0.36	P = 0.09
3	**r = 0.962**	r = 0.699	r = 0.067
	P = 0.009	P = 0.18	P = 0.91

DISCUSSION

Our results showed P100 latency is prolonged in diabetic subjects as compared to healthy controls. Also, left P100 latency was positively correlated with duration of disease. However, IOLD was not statistically significant within the groups and did not show any correlation with the duration of disease in diabetic subjects.

PR VEP done in 25 diabetic subjects showed that P100 and N70 latencies were prolonged in diabetes and positively correlated with duration of disease in diabetic subjects.[5]

Studies done by Chopra et al. and Bhanu et al. also showed significantly prolonged P100 latencies in diabetic subjects and also, a positive correlation of P100 latency with the duration of disease in diabetic subjects.[4,7]

A study done on 51 subjects (29 females and 22 males) with duration of diabetes from 2-21 years and none of the patients had diabetic retinopathy. The study showed that there was bilateral increase in VEP latency and also, concluded that central neuropathy in diabetes is related to the duration of disease and not to the level of glycemia and metabolic control.[8]

Puvanendran et al. studied VEPs in sixteen diabetic patients compared with 35 healthy controls and concluded that the P100 latency was significantly increased in diabetics along with marked inter ocular latency difference (> 7 ms) in 5 diabetic patients.[9]

Gupta et al. studied pattern reversal VEP in 64 diabetics without retinopathy and 52 controls.[10] P100 latency, N75-P100 amplitude and inter ocular latency difference were compared between diabetics and controls. The study demonstrated significant prolongation of mean P100 latency, reduction of N75- P100 amplitude and increased inter ocular latency difference in the diabetics as compared to controls. The duration of illness was found to alter the mean P100 latency while the glycemic status of the diabetes was not found to be correlated with the pattern reversal VEP abnormalities.[10] All these findings are similar to our findings.

Meanwhile, a study done on 20 type 1 and 20 type 2 diabetes patients showed a significantly prolonged P100 latency as compared to controls. However, a positive correlation was reported with fasting plasma glucose level and prolonged P100 latencies but not with type and duration of disease, age and sex of diabetic patients.[11]

A cross sectional study done on 100 type 2 diabetes and 100 healthy controls showed significant prolongation of P100 latency in type 2 diabetes and a significant positive correlation between duration of diabetes with P100 latency but not with amplitude of P100.[12]

VEP was done on 111 subjects, aged 40-70 years of both sexes. Subjects were divided into 3 groups; patients with type 2 diabetes, patients with diabetic retinopathy and normal subjects and total number of subjects in each group was 37. The results showed significant prolongation of P100 latencies in type 2 diabetes and diabetic retinopathy patients as compared to controls.[13]

Similarly, pattern reversal VEP recorded on 100 subjects with 50 patients with type 2 diabetes and 50 healthy controls showed a statistically significant increase in mean P100 latency and inter ocular latency difference along with reduction in N75-P100 amplitude in diabetics as compared to controls.[14]

Many of the literatures showed significantly prolonged P100 latencies in diabetic subjects as compared to healthy controls. Also, P100 latencies were positively correlated with the duration of disease in diabetic subjects. And these findings comply with our findings. But, fewer studies showed a positive correlation of P100 latency with the glycemia and not with the duration of the disease.

This study if done in a larger sample size could have helped us for better understanding of the neurophysiological variations in type 2 diabetic patients. Also, if fasting and post prandial blood glucose could be estimated at the time of recording of VEP, these parameters could also be correlated with the VEP variables. But due to limitation of the budget, blood parameters could not be estimated.

CONCLUSION

P100 latency is significantly prolonged in type 2 diabetes patients as compared to controls. Left P100 latency is positively correlated with the duration of the disease. VEP study can be a reliable, simple, non invasive tool for assessing diabetic patients to rule out pre retinopathic changes. Thus, VEP can be used as a screening tool for an early assessment of central neurological involvement in diabetes patients.

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