A Study Of Visual Evoked Potential Changes in Diabetes Mellitus

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ABSTRACT

Recording visual evoked potentials in response to pattern reversal stimuli is a very sensitive test for detecting any abnormality of anterior visual pathways. Peripheral neuropathy occurring in diabetes mellitus is a well-documented and extensively studied entity. In order to assess whether such a process affects the optic nerves also, we studied 25 diabetic patients and 15 age and sex-matched controls. This included both NIDDM and IDDM patients with duration of diabetes less than 15 years. All patients underwent detailed neurological examination and ophthalmological workup to rule out any ophthalmological pathologies which may effect the visual evoked responses. Patients with reduced visual acuity not correctable by glasses and those with diabetic retinopathy were excluded from study. P_{100} latencies and amplitudes as well as N_{75} latencies and amplitudes were recorded. The P_{100} latencies in diabetic patients were significantly prolonged with a mean ± SD of 107.32 ± 4.14 in diabetics and 102.5 ± 3.77 in controls (P value = 0.001). Mean P_{100} amplitude was 7.64 ± 1.84 in diabetics with a control value of 8.03 ± 1.79 ($P > 0.05$). N_{75} latency was 71.50 ± 5.3 in diabetics with a control of 70.4 ± 4.8. The difference was not statistically significant. N_{75} amplitude in diabetics was 6.5 ± 2.58 with a control of 7.88 ± 3.33 ($P < 0.01$), denoting a significant reduction of N_{75} amplitude in diabetics. A positive correlation was documented between glycemic control and prolonged P_{100} latencies. There was no correlation between presence and absence of peripheral neuropathy and the delay in P_{100} latencies.

In conclusion, we observed that the anterior visual pathways get involved in diabetic patients before development of retinopathy and it shows no correlation with peripheral neuropathy.

INTRODUCTION

The nervous system frequently gets involved with the complications of diabetes as the duration of diabetes increases. The peripheral nerves suffer the major brunt of attack from the disease. The prevalence of peripheral neuropathy varies from 55% if based on signs. 62% based on subjective symptoms and as high as 100% if based on motor conduction velocities [1]. Similarly, cranial mononeuropathies are also commonly observed in diabetes. The 3rd, 4th and 6th nerves are involved commonly, either separately or in varying combination. Optic nerve affection manifested as optic atrophy, as a result of diabetes alone is estimated to occur in about 0.6% cases [2].

Recording visual evoked potentials from scalp is a highly sensitive, reliable and reproducible method for diagnosing conduction defects in the anterior visual pathways. The visual neurons respond selectively to visual patterns of progressively greater complexities [3]. Hence, the evoked potential recording in response to pattern reversal stimulation is even more sensitive for assessing visual pathways than the old flash method.

Various clinical conditions where delayed Visual Evoked Potential (VEP) latencies are of diagnostic importance include multiple sclerosis, retrobulbar neurities, papillitis, hereditary toxic and nutritional optic neuropathies [3]. Spuriously prolonged VEP latencies are observed with ocular causes like glaucoma or conditions affecting conducting media of eyes like cataract, vitreous opacities and retinal diseases.

There have been several anecdotal reports from Western countries showing alteration in VEP latencies in diabetic patients [4,6,7]. Such a study in the Indian population is lacking as far as the literature could be traced. We therefore performed an evaluation of visual evoked potential to pattern reversal stimulation (VEP-PR) in a group of subjects with NIDDM and IDDM without retinopathy and with normal visual acuity at baseline. The aim was to find whether the VEP-PR latencies are altered in diabetics or not and if altered, whether it shows any correlation with the fasting blood sugar level and other chronic complications of diabetes.

MATERIAL AND METHOD

25 patients with relatively short duration of diabetes (£ 10 years) (18 males and 7 females; mean age 46.2 years ± 9.2 years, Range: 20-60 years) and 15 healthy volunteers (12 males and 3 females, mean

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age: 38.2 years ± 10.2 years, Range: 20-58 years) were evaluated.

All patients were either NIDDM (21 cases) or IDDM (4 cases) proved by recent blood glucose studies. Fasting blood glucose level was again estimated prior to recording of VEP. All cases were clinically examined for evidence of chronic complications of diabetes. Patients with long-standing hypertension were excluded, as also those with past history of cerebrovascular accidents. Biochemical parameters of renal functions and ultrasound abdomen were studied to rule out chronic renal failure. Patients consuming more than 100 ml of alcohol daily and those with peripheral nervous system disease unrelated to diabetes were excluded from the study.

Detailed ophthalmological checkup of all patients was done which included, visual acuity, recording of ocular tension and fundus examination under full mydriasis. Only those patients with normal visual acuity at baseline were included in the study. Patients with diabetic retinopathy, cataract, glaucoma, vitreous opacities or any evidence of optic atrophy were excluded from the study. Clinical evidence for peripheral neuropathy was sought for by means of pinprick testing, cottons touch and vibration testing. Motor power and reflexes were studied for evidence of motor neuropathy.

Urine examination for protein was preformed for detecting overt diabetic nephropathy. ECG with QTC recording Valsalva ratio was studied for detecting autonomic neuropathy. Glycosylated Hemoglobin (HBA_{1c}) was estimated in 11 cases. (Bio-Rad HBA_{1c} microcolumn test protocol).

RESULTS:

Patients were grouped into 3 categories based as fasting blood glucose levels:

Good Control : FBG < 130 mg%

Fair Control : FBG between 130 – 145 mg%

Poor Control : FBG > 145 mg%

Visual evoked potentials were recorded using pattern reversal stimulation. Binocular stimulation was done with small checks and large checks using a checkerboard. 3 scalp electrodes were used: (1) Frontal (FP_2), (2) Occipital (O_2), (3) Grounding (C_2) electrodes.Patients were advised to come without applying oil to scalp and to shampoo the hair and make it dry. Preparations of scalp skin were done with omniprep. The distance between the TV screen and each subject was kept at a constant distance of 100 cms. The aim was to achieve maximal stimulation of the foveal and parafoveal fibers at 75% contrast and a reversal rate of 1.2 Hz. Uniform illumination was maintained in the laboratory and the electrode impedance was kept less than 2 ohms. An average of 100 sweeps of stimuli was given to each eye per pattern used. This was repeated twice and the averages of the two were superimposed to demonstrate reproducibility. Any difference of more than 3 m secs. In the latencies between trials was not included in the study. The peak P_{100} latencies and amplitudes as well as peak N_{75} latencies and amplitudes were studied.

The patients whose HBA_{1c} was studied; were divided into 2 groups; one with HBA_{1c} 7-8% and second with > 8%, in order to assess the relation between long term glycemic control and altered VEPs.

All data is expressed as mean ± S.D. student ‘t’ test was used to assess the statistical significance. P value < 0.005 was considered significant

Table 1

Incidence of complications with duration of diabetes in study group.

Duration	No. of Diabetic Patients	Distal Symmetric Polyneuropathy	Autonomic Neuropathy	Nephropathy	CAD / PVD
05- years	9	7 (78%)	5 (56 %)	5 (56 %)	2 (23 %)
5-10 years	14	11 (78%)	9 (64%)	9 (64%)	3 (21%)
10-15 years	2	Nil	Nil	Nil	Nil

Table 2
Mean P_{100} Latencies / Amplitudes and N_{75} Latencies / Amplitudes in diabetic and controls.

Subject	No. of Cases	P_{100} Latency	S.D.	P_{100} amplitude	S.D.	N_{75} Latency	S.D.	N_{75} amplitude	S.D.
Diabetic	25	107.32	4.14	7.64	1.84	71.56	5.3	6.5	2.58
Controls	15	102.5	3.77	8.03	1.79	70.4	4.8	7.88	3.31

Table3
Relating the mean P_{100} amplitudes and Latencies in Test Groups with the Duration of Diabetes.

Duration of Diabetes	No. of Patients	Percentage	Mean P_{100} Latency	S.D.	Mean Amplitude	S.D
Total	25	100	107.32	4.14	8.03	1.79
0-5 years	9	36	105.66	4.91	7.97	0.82
5-10 years	14	56	107.67	2.95	7.49	1.76
10-15	2	8	112.3	4.91	8.65	2.61

Table 4
Relation between metabolic control of diabetes and P_{100} Latencies / Amplitudes in Test Group.

Metabolic Control	No. of Patients	Percentage	Mean P_{100} Latency	S.D.	Mean P_{100} Amplitude	S.D
Good Control PBG < 130mg %	8	32	105.93	5.3	7.9	2.74
Fair Control FBG (130-145mg %)	6	24	107.0	0.89	0.86	1.03
Poor Control FBG > 145mg%	11	44	108.5	4.23	8.13	1.78

Table 5
Relationship between P_{100} Latencies / Amplitudes and Nephropathy in Test Group.

Nephropathy	No. of Patients	Percentage	Mean P_{100} Latency	S.D.	Mean P_{100} Amplitude	S.D.
Present	9	36	107.83	3.50	6.62	1.19
Absent	16	64	107.83	4.5	8.31	1.83

Table 6
Metabolic control of diabetes as determined by HBA_{1C} and P_{100} Latencies / Amplitudes in Test Group.

HBA_{1C}	No. of Patients	Percentage	Mean P_{100} Latency	S.D.	Mean P_{100} Amplitude	S.D.
7-8%	5	45	108	7.85	9.11	2.47
> 8%	6	55	107.75	5.14	7.56	2.56

Table 7
N_{75} and P_{100} Latencies in (RT) and (LT) eyes and the Interlatency difference in diabetics and controls.

	Mean P_{100} Latency	S.D	Mean N_{75} Latency	S.D	Mean P_{100} Latency	S.D.	Mean N_{75} Latency	S.D.	Inter latency diff. P_{100}	S.D.	Inter latency diff. N_{75}	S.D.
Diabetic	106.36	5.44	72.08	6.12	108.36	6.77	71.08	6.25	4.08	3.09	5.12	4.23
Controls	101.0	4.08	69.33	6.36	103.06	3.63	71.46	3.56	2.86	1.55	3.33	2.59

The mean P_{100} latencies in diabetic patients were significantly prolonged compared to controls (Table 2) i.e. 107.32 ± 4.14 Vs 102.5 ± 3.77 – P value < 0.001. Similarly the P_{100} latencies recorded for individual eyes were also significantly delayed in diabetics (Table 7). The interlatency difference in P_{100} latencies was also more in diabetics (4.08 ± 3.09 Vs 2.86 ± 1.55. P < 0.005). Three of the 25 patients (12%) had P_{100} latencies greater than 3 S.D. and 5 (20%) had greater than 2 S.D. of the mean of the control subjects.

The P_{100} amplitudes in test groups had a mean value, which was lower than the mean of controls. (7.64 ± 1.84 Vs 8.03 ± 1.79). P value was not significant for this observation (Table 2).

The N_{75} latencies in diabetic patients were also prolonged in diabetics, but the statistical significance could not be demonstrated (P value > 0.5). Similarly, as evident from Table 2, the N_{75} amplitudes in diabetics had a lower mean value compared to controls (6.55 ± 2.58 Vs 7.88 ± 3.3, P value 0.1).

When we analysed peripheral neuropathy and nephropathy in the test group, 18 patients showed evidence of peripheral neuropathy (72%) and 14 had proteinuria (56%). These complications occurred as the duration of diabetes increased (Table 1).

As illustrated Table 3, the delayed P_{100} latencies showed a positive correlation with the duration of disease (P value 0.5). The P_{100} latencies also showed a correlation with the metabolic control of diabetes. In patients with fasting blood sugar more than 145 mg%, the mean P_{100} latency was 108.5 ± 4.23 while in those with good control (FBS < 130 mg%), corresponding value was 105.43 ± 5.3 (P value 0.1) (Table 4).

As evident from Table 5, the P_{100} latencies were prolonged in diabetic patients with nephropathy compared to those without nephropathy (107.8 ± 3.5 Vs 107.03 ± 4.5). This is not significant statistically. The P_{100} amplitude was decreased in diabetics with nephropathy (6.62 ± 1. /19 vs. 8.31 ± 1.83 P < 0.05).

The P_{100} latencies and amplitude in diabetic patients did not show any correlation with clinical evidence of peripheral neuropathy. Latencies were equally prolonged in those with and without retinopathy.

Glycosylated Hb estimation was done in 11 cases and the analysis of P_{100} latencies in them (Table 6) showed that the prolongation was more in those with a poor long term diabetic control (HbA_{1c} > 8%).

DISCUSSION:

In conformity with other authors [4.5,6,7] significant differences in VEP latencies and amplitudes were demonstrated in our study group. These delayed latencies which were recorded in the absence of retinopathy or any ocular pathology are

indicative of anterior visual pathway affection in diabetes of even relatively shorter duration. Such alterations in visual pathways are little studied including the histopathological changes in the optic nerves. Kamijoet al [8] have demonstrated from animal studies that axonal atrophy and axonal dysfunction are the two structural lesions that occur in optic neuropathy of diabetes which are similar to the lesions of diabetic peripheral neuropathy. These changes are responsible for the changes in latency of optic nerve responses and are probably related to polyol pathway. These authors also demonstrated that axoglial dysjunction is completely prevented by treatment with aldose reductase inhibitors whereas axonal atrophy is not. This is in contrast to the situation in peripheral nerves, where the above drug prevented axonal atrophy also.

The prolongation of P_{100} latencies, which are observed in diabetics, is thus an expression of structural damage at the level of the myelinated optic nerve fibers. The delayed responses did not show any correlation with clinical evidence of peripheral neuropathy. This may be because of different pathogenetic mechanisms operating behind peripheral nerve involvement and optic pathway affection. P_{100} latencies were observed to be more prolonged in those poor glycemic control as a result of more prolonged exposure to the toxic metabolites.

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