Original article

Visual evoked potentials in type 1 diabetes mellitus patients

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ABSTRACT:

INTRODUCTION: Type 1 diabetes mellitus (T1DM) is one of the most common pediatric endocrine illnesses. The incidence of T1DM continues to increase, and it has serious short-term and long term implications. Peripheral neuropathy is a frequent complication of diabetes mellitus. But the incidence of cranial neuropathies has not been studied in detail. Optic nerve affection manifested as optic atrophy, as a result of diabetes alone is estimated to occur in about 0.6% cases. Evaluation of the Visual Evoked potentials (VEP) furnishes a diagnostic tool for the assessment of functional anomalies of the optic pathway, even at an early stage of the pathogenetic process.

AIM OF THE STUDY: To detect subclinical optic neuropathy in type 1 diabetes mellitus patients, using Visual Evoked Potentials (VEP) as an investigative tool.

MATERIALS & METHODS: 30 type 1 diabetes mellitus patients were selected from the Diabetology OPD, Stanley Medical college. By using the standard RMS EMG EP MARK II machine, VEP recordings were done by using standard procedures. The results were compared with 30 age & gender matched normal healthy individuals. The data were statistically analyzed with Student independent unpaired 't' test using SPSS 11.5 version.

RESULTS: N75 latency in both eyes were significantly increased in cases ($p < 0.05$). There was a highly significant increase in P100 latency in the cases compared to controls($p < 0.01$).

The amplitude of P100-N75 of both eyes were significantly reduced in cases compared to controls

($p < 0.05$)

CONCLUSION: Our VEP data shows that there is a significant decrease in optic nerve conduction in Type 1 Diabetic patients. They showed a significant prolongation of the latency of P 100 and N 75 and a reduction in amplitude of the VEP wave form. Hence, all type 1 diabetic patients should be screened by neuro-electrophysiological tests like Visual Evoked potentials, so that the quality of life in these patients can be improved.

KEY WORDS: Type 1 Diabetes mellitus, Visual Evoked potentials.

INTRODUCTION

Type 1 Diabetes mellitus previously referred to as 'juvenile-onset' or 'insulin dependent' diabetes, most commonly develops in childhood and accounts for 5 to 15% of all cases of diabetes. Type 1 Diabetes is caused by an autoimmune, predominantly T-cell mediated process that selectively destroys the pancreatic β cells. Genetic factors explain 30 to 40% of total susceptibility: at least 10 loci are involved, with the HLA class II locus IDDM having by far the greatest effect.Environmental factors that have been implicated include viral infection (particularly Coxsackie B), bovine serum albumin from cow's milk (by immunological cross-reactivity) and other toxins.

Although type 1 DM most commonly develops before the age of 30, an autoimmune beta cell destructive process can develop at any age. Several years of progressive autoimmune damage usually precede the clinical onset of diabetes. Type 1 diabetes mellitus (T1DM) is one of the most common pediatric endocrine illnesses. Of these, over half are living in developing nations, with India being home to an estimated 97,700 children with T1DM [(1)]. The incidence of T1DM continues to increase, and it has serious short-term and long term implications.

Peripheral neuropathy is a frequent complication of diabetes mellitus. But the incidence of cranial neuropathies has not been studied in detail. The exact pathophysiology of the central nervous dysfunction is not clear, but it seems to be multifactorial, involving vascular and metabolic factors, similar to the pathogenesis of diabetic peripheral neuropathy. Optic nerve affection manifested as optic atrophy, as a result of diabetes alone is estimated to occur in about 0.6% cases [(2)]. Evaluation of the Visual Evoked potentials (VEP) furnishes a diagnostic tool for the assessment of functional anomalies of the optic pathway, even at an early stage of the pathogenetic process.

Visual evoked potentials are electrical potential differences recorded from the scalp in response to visual stimuli. Normal cortical responses are obtained if the entire visual system is intact and disturbances anywhere in the visual system can produce abnormal VEPs. Therefore the localizing value of VEP is limited. VEP is an objective and reliable method for detecting abnormalities in the optic pathways especially anterior to optic chiasma.

AIM OF THE STUDY : To detect subclinical optic neuropathy in type 1 diabetes mellitus patients, using Visual Evoked Potentials (VEP) as an investigative tool.

MATERIALS AND METHODS

The study was conducted in the Neurophysiology Lab of the Department of Physiology, Stanley Medical College, Chennai.

CASES:

INCLUSION CRITERIA

- Type 1 Diabetes mellitus patients (based on WHO criteria) [(3)] attending Diabetology out-patient department
- Age: 10 to 30 years, both gender
- Type 1 diabetic patients on Insulin treatment and with fairly good glycemic control
- Type 1 DM patients with duration of disease > 2 years
- Patients with normal visual acuity

EXCLUSION CRITERIA

- Smokers
- Alcoholics
- Hypertension, Coronary artery disease, Renal disorders, Thyroid disorders
- Patients with corneal opacity, squint, colour blindness or any ocular pathology.

CONTROLS

30 age and gender matched healthy subjects attending the Master health check up programme, Stanley Medical College.

Study Design : Cross-sectional study.

The study protocol was approved by the Ethical committee of Stanley Medical College.

The detailed procedure and purpose of the study was explained in the regional language, and then an informed and written consent was obtained from the subjects if they were 16 years of age or over and from their parents if they were younger than 16 years.

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METHODOLOGY OF V.E.P.

By using the standard RMS EMG EP MARK II machine, VEP recordings were done by using standard procedures.

PRE –REQUISITES:

1. Avoid hair spray or oil after hair wash.
2. If subject has refractory error, the usual glasses are put on during the test.
3. Any miotic or mydriatic drug is avoided 12 hours before the test.

EQUIPMENT SET UP FOR VEP STUDY:

MONTAGE:

Channel 1 - FPz – Reference electrode.

Vertex - Cz – Ground electrode.

C - Oz - Active electrode.

RECORDING CONDITIONS:

1. Filter: high filter cut: 100 – 300 Hz.
2. Amplification between 20,000 – 1,00,000
3. Sweep Duration: 300 msecs.
4. Number of epochs: 100 are averaged.
5. Electrode impedance kept below 5 Kilo ohms.

STIMULATION:

Black and white Checkerboard was used. Distance between subject and screen was 100 cm.

Contrast: 80%

Size of the pattern element: 14x16 minute

Rate of stimulation: 4 – 8 Hz.

PROCEDURE:

The subject was asked to sit comfortably on a chair with their footwear.

Each eye was tested separately.

The other eye was kept covered with an opaque eye shield, which prevents entry of light into that eye. The skin at the point of placement of electrodes was cleansed with spirit.

Three surface disc type electrodes were used.

Using electrode paste, the **recording electrode** was placed at Oz – 5cm above the inion (ridge between the back of neck & skull).

The **reference electrode** was placed at FPz – 12cm above the nasion (indentation between forehead and nose).

The **ground electrode** was placed at the midline in forehead.

The electrodes were connected through the pre amplifier to the Cathode ray Oscilloscope.

The subject was instructed to fix the gaze at the centre of the screen.

The lights were switched off. The visual stimulus was delivered by photo stimulator at frequency of 10 flashes/sec. The response obtained was displayed on the T V monitor and the peak latency and peak to peak amplitude of the waves were measured.

NORMAL VEP: VEP consists of series of wave forms of opposite polarity, the negative wave form (denoted as N) & a positive wave form (denoted as P), which is followed by the approximate latency in millisecond [(4)]

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TABLE 1

ANTHROPOMETRIC MEASUREMENTS OF SUBJECTS

(Age, Height, Weight & BMI expressed as Mean ± SD)

	CASES	**CONTROLS**	**'t'value**	**p value**
n	30	30	-	-
Males:Females	18:12	18:12	-	-
Age in years	23.06 ± 6.06	22.86 ± 5.92	0.12	0.89
Height in cm.	155.96 ± 9.25	156.80 ± 9.57	-0.34	0.73
Weight in kg.	53.83 ± 7.86	54.23 ± 7.88	-0.19	0.84
B.M.I. kg/m2	22.07 ± 2.31	21.98 ± 2.17	0.15	0.87

BMI – Body Mass Index

The parameters were analyzed using Student independent unpaired 't' test

$p < 0.05^{*}$ is taken as significant

TABLE 2

COMPARISON OF BLOOD SUGAR LEVEL

	GROUP (n=30)	**MEAN**	**STANDARD DEVIATION**	**Student independent 't' test**
Fasting mg%	Cases	124.06	18.20	t= 12.22
	Controls	82.33	4.29	**p< 0.01****
Post prandial mg%	Cases	158.34	31.22	t=8.77
	Controls	107.93	3.94	**p<0.01****

The parameters were analyzed using Student independent unpaired 't'test.

p < 0.05* is taken as significant ;p < 0.01** is taken as highly significant.

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TABLE 3

VISUAL EVOKED POTENTIALS RECORDED FROM LEFT EYE

VEP parameters	**Cases (n=30)**		**Controls (n=30)**		**Student independent 't'test**
	Mean	SD	Mean	SD	
N 75 ms	68.97	4.73	66.71	3.31	t= 2.14 **p<0.05***
P100 ms	96.87	5.48	89.52	2.56	t= 6.64 **p < 0.01****
N145 ms	147.05	9.78	147.18	9.21	t= - 0.052 p= 0.95
P 100 - N 75 µV	5.88	2.43	6.94	1.37	t= - 2.04 **p<0.05***

The parameters were analyzed using Student independent unpaired 't'test.

p < 0.05* is taken as significant ;p < 0.01** is taken as highly significant

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TABLE 4

VISUAL EVOKED POTENTIALS RECORDED FROM RIGHT EYE

VEP parameters	Cases (n=30)		Controls (n=30)		Student independent 't'test
	Mean	SD	Mean	SD	
N 75 ms	69.77	5.05	67.37	2.55	t= 2.32 **p<0.05***
P100 ms	96.91	6.03	89.87	2.79	t= 5.80 **p < 0.01****
N145 ms	146.27	9.25	146.65	9.41	t= - 0.15 p= 0.87
P 100 - N 75 µV	5.88	2.06	7.01	1.81	t= - 2.25 **p < 0.05***

The parameters were analyzed using Student independent unpaired 't'test.

p < 0.05* is taken as significant ;p < 0.01** is taken as highly significant

RESULTS

Statistical Package for Social Sciences (SPSS) software 11.5 version was used for statistical analysis. The Student independent unpaired 't' test was used to compare cases and controls.

TABLE 1: ANTHROPOMETRIC MEASUREMENTS OF SUBJECTS

There was no statistical difference between the cases and controls with regards to age, height, weight and BMI (p > 0.05).

TABLE 2: BLOOD SUGAR:

There was a highly significant increase in fasting and post-prandial blood sugar in cases compared to controls. (p < 0.01)

TABLE 3: VISUAL EVOKED POTENTIALS RECORDED FROM LEFT EYE

N75 latency in the left eye was significantly increased in cases (p <0.05). There was a highly significant increase in P100 latency of the left eye in the cases compared to controls(p <0.01).

The amplitude of P100-N75 of the left eye was significantly reduced in cases compared to controls (p <0.05)

TABLE 4: VISUAL EVOKED POTENTIALS RECORDED FROM RIGHT EYE

The latency of N75 was significantly increased in cases (p <0.05)

There was a highly significant increase in P100 latency of the right eye in cases compared to controls (p <0.01)

The amplitude of P100-N75 of the right eye was significantly reduced in cases compared to controls (p <0.05)

DISCUSSION:

Peripheral and Autonomic nervous system involvement are frequently encountered in DM, but

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there exists few data about the incidence of central diabetic neuropathies. It is possible to reveal central nervous system involvement at an early stage by using evoked potentials.(Uzun N et al) [5] Comi G et al [6] found that Visual Evoked Potentials is a simple and reliable technique for detecting early alterations in CNS function in diabetics.

N 75

The latency of N75 in right and left eye was significantly increased in diabetics compared to controls ($p<0.05$*)

P 100

There was a highly significant increase in P100 latency ($p< 0.01$**) in diabetics compared to controls. The prolongation of P 100 latencies in diabetics is indicative of structural damage at the level of the myelinated optic nerve fibres. PG Raman et al [7] also observed a statistically significant prolongation of the mean P100 latencies in diabetic patients compared to controls.

N 145

There was no significant difference in the latency of N145 in diabetic patients compared to controls.

Alessandrini M et al [8], observed a significant delay in N75, P100 and N145 latencies. But in our study only N75 and P100 were significantly prolonged.

P100- N 75

The amplitude of P100- N 75 was significantly reduced in both eyes in cases ($p< 0.05$*)

Karlica D et al [9] found that amplitude values decrease progressively and latency values increase progressively in children with type 1 DM as the years pass.

Kamijoet et al [10] did animal experiments to demonstrate that axonal atrophy and axonal dysfunction are the two structural lesions that occur in optic neuropathy of diabetics. Our results clearly indicate that there is a significant neuronal visual loss involving the optic pathway which precedes the ophthalmoscopically detectable retinopathy in patients with type 1 DM.

LIMITATIONS: HbA1C was not estimated for Type 1 DM patients. Further studies can be done to correlate the VEP wave forms with the degree of metabolic control.

CONCLUSION

Our VEP data shows that there is a significant decrease in optic nerve conduction in Type 1 Diabetic patients. They showed a significant prolongation of the latency of P 100 and N 75 and a reduction in amplitude of the VEP wave form. Therefore electrophysiological studies should be performed in type 1 diabetics in order to detect subclinical optic neuropathy. Hence, all type 1 diabetic patients should be screened by neuro-electrophysiological tests like Visual Evoked potentials, so that the quality of life in these patients can be improved. To conclude VEP is a simple and effective method to detect early involvement of the optic pathway. Hence VEP can be considered as a useful screening test for type 1 diabetic patients.

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