

## Original Research Article

# Visual evoked potentials in children with type 1 diabetes mellitus

Meenal Batta<sup>1</sup>, Rajeev Sharma<sup>1</sup>, Naveenta Gupta<sup>1</sup>, Sonia Garg<sup>1</sup>, Gurmeet Kaur<sup>2</sup>,  
Shashi Kant Dhir<sup>2\*</sup>, Amarpreet Kaur<sup>2</sup>

<sup>1</sup>Department of Physiology, <sup>2</sup>Department of Pediatrics, Guru Gobind Singh Medical College, Faridkot, Punjab, India

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### \*Correspondence:

Dr. Shashi Kant Dhir,

E-mail: [drshashikantdhir@gmail.com](mailto:drshashikantdhir@gmail.com)

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### ABSTRACT

**Background:** Insulin-dependent (type 1) diabetes mellitus is associated with different degrees of neuropathies affecting peripheral as well as central neural pathways. The subclinical neurological involvement in diabetic children can be assessed by changes appearing in the electrophysiological parameters like Visual Evoked Potentials (VEPs). The objective of the study was to assess the effect of type I diabetes mellitus on the visual evoked potentials in children.

**Methods:** This cross-sectional case-control study was done on 30 children with type 1 diabetes mellitus of minimum two years duration as cases and 30 age and gender matched euglycemic children with normal HbA1c taken as controls. Visual Evoked Potentials (VEPs) were done on both the groups of children and the latencies (ms) of waves - N<sub>75</sub>, P<sub>100</sub>, N<sub>145</sub> and amplitude (μV) of wave P<sub>100</sub> were recorded. The data was compiled in the pre-designed proforma and statistically analysed using student t-test.

**Results:** The increase in the mean latencies of waveforms of VEPs N<sub>75</sub>, P<sub>100</sub> and amplitude P<sub>100</sub> were found to be highly significant statistically ( $p < 0.001$ ) in both the eyes among the children with type 1 diabetes mellitus. The mean latency of waveform N<sub>145</sub> was found to be statistically insignificant in the two groups ( $p > 0.05$ ).

**Conclusions:** The type 1 diabetes does affect the visual pathways in children. Visual Evoked Potentials are helpful in the detection of early changes in the conduction across the neural pathways in the sub-clinical diseases.

**Keywords:** Children, Type 1 diabetes mellitus, Visual evoked potentials

### INTRODUCTION

Diabetes mellitus is associated with different neuropathic syndromes, ranging from a mild sensory disturbance to severe neuropathy leading to disability.<sup>1</sup> Diabetic neuropathies are one of the major complications of insulin dependent diabetes mellitus.<sup>2</sup> There is a tendency of increased frequency of neuropathy with the duration of disease and poor glycemic control.<sup>3</sup> Subclinical disease usually precedes the overt form of the neuropathy. During this period an abnormality in the electrophysiological parameters like Visual Evoked

Potentials (VEPs) and Brainstem auditory evoked response (BAER) is usually the first sign of such involvement.<sup>4,5</sup>

Visual evoked potentials are electrophysiological parameters used to evaluate disturbances in the central visual pathways which may give insight to the visual neuropathies associated with the diabetes mellitus in children.<sup>6</sup> The electrical activity of the visual cortex produces VEPs in response to light or pattern stimulation of the eye. The functional loss from the retina to the visual cortex in the visual pathways can be detected by

VEPs.<sup>7</sup> In diabetes mellitus, both vascular disease and metabolic abnormalities, affecting the retina, optic nerve and visual pathways can result in visual deficits. These severe complications can only be averted when signs of the disease are detected early when timely intervention can be planned to decrease long term disabilities.

The follow up of patients having the altered potentials will give us more insight about the pathophysiology of the diabetic neuropathies and at the same time will give us a better chance to cope up with the sub clinical cases. This study was planned with the objective of providing the correlation of the visual evoked potentials in the children having type 1 diabetes mellitus.

## METHODS

This study was an observational study done in Pediatrics and Physiology departments of Guru Gobind Singh Medical College, Faridkot over a period of one year. The study was approved by the Institutional ethics committee of the institute. Informed consent was taken from one of the parents of enrolled patients. Confidentiality and privacy of the subjects was maintained.

The patients who came to either outpatient department or got admitted in the Pediatrics department of Guru Gobind Singh Medical College, Faridkot and had type 1 diabetes mellitus of minimum two years duration were the subjects. The definition of diabetes mellitus was taken as per WHO classification.<sup>8</sup> A thorough history regarding the diabetes mellitus was taken and the baseline variables including height, weight and body mass index were noted. Complete treatment details including the type of insulin used and the duration of diabetes and glycemic status was noted. Each subject did undergo detailed physical and neurological examination to rule out any primary neurological illness. All the patients were included irrespective of their glycemic status and mode of insulin therapy. The children having, established neurological or metabolic disease other than diabetes, taking drugs known to influence peripheral and central nerve function were excluded. The patients having established diabetic retinopathy, glaucoma or opacification, cataract, migraine, thyroid dysfunction, refractive errors were also excluded as they might alter the VEPs per se. The parents who refuse to participate in the study were not enrolled. Age and gender matched hospitalised children for illness other than diabetes mellitus and who were euglycemic and having normal HbA1c were taken as controls. All the participants were provided with detailed written and verbal information about the test.

All patients underwent fundoscopic examination of each eye before the VEPs testing. The subjects were asked to come with their hair washed and without any oil applied to improve the accuracy of the results. Any miotic or mydriatic drugs taken by subjects were discontinued 12 hours before the test. Subjects were also instructed to not

to sleep during the procedure and to fix the gaze at the red flash of light in the goggles.

The visual evoked potentials were recorded in the research laboratory of Physiology department of GGS Medical College, Faridkot using Data Acquisition and Analysis System, Neurostim, (NS4) Medicaid Systems, Chandigarh, India<sup>TM</sup>. Equipment was set up for VEPs study as recommended by International Federation of Clinical Neurophysiology (IFCN) committee.<sup>8</sup> Montage consisting of single channel (Channel 1 Oz- Fpz.) was used for recording VEPs.

The subjects were asked to relax and sit in a comfortable position. Each eye was tested at a time. The area of the scalp at the point of placement of the electrodes was cleaned with the help of a cleaning gel. The recording electrode was placed at occiput (Oz), the reference electrode slightly above the nasion (Fpz) and the ground electrode at the vertex (Cz), using electrode paste. Light Emitting Diode (LED) goggles were placed in front of eyes with adjustable elastic band. The visual stimulus in the form of red flashes of light was delivered by LED goggles. The low-cut filter was set at 2Hz and high cut filter at 200Hz for recording flash visual evoked potentials. Adjustments for sweep speed at 50ms/div and sensitivity at 2 $\mu$ V/div. were done. Averaging of about 200 epochs was done. The impedance of electrodes was kept less than 5kilo ohms. The response of the visual stimulus was recorded in the form of waveforms consisting of first negative peak (N<sub>75</sub>) at about 75msec, followed by a positive peak (P<sub>100</sub>) at about 100msec and then again, a negative peak (N<sub>145</sub>) at about 145msec from both the eyes separately. The data was filled in a validated pre-designed proforma.

## Statistical analysis

The data was collected by the investigators and compiled in a pre-designed proforma and was statistically analysed by applying student t-test using Microsoft Excel<sup>TM</sup>. The p value less than 0.05 was considered to be statistically significant.

## RESULTS

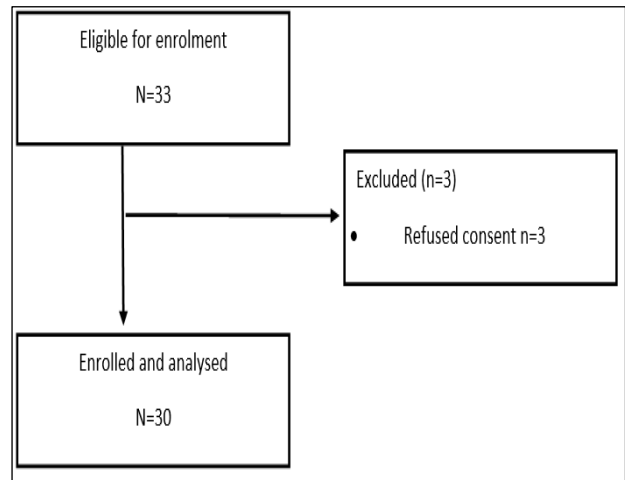
A total of 33 cases were enrolled during this study. Out of these three patients were excluded because of non willingness for taking part in the study. The study flow and reasons of exclusions are mentioned in Figure 1. Equal number of controls were taken. The mean age of the children in years was 5.6 $\pm$ 0.7 and 5.7 $\pm$ 0.7 in cases and controls respectively and was similar in both groups. The baseline variables like age, gender, weight, height and body mass index (BMI) were not statistically significant in the two groups and are given in Table 1. The comparison of the latencies of different waveforms (ms) of VEP (N<sub>75</sub>, P<sub>100</sub>, N<sub>145</sub>) and amplitude P<sub>100</sub> ( $\mu$ V) of both the eyes between the case and controls has been shown in Table 2.

**Table 1: Baseline variables.**

Variable	Cases N=30	Controls N=30	P value	
Age	5.6±0.7	5.7±0.7	>0.05	
Height	103.8±5.0	104.3±4.2	>0.05	
Weight	16.3±1.8	16.2±1.5	>0.05	
BMI	15.1±1.2	14.9±1.3	>0.05	
Gender	Male	18	18	>0.05
	Female	12	12	>0.05
Religion	Hindu	14	14	>0.05
	Sikh	16	16	>0.05
Background	Rural	17	17	>0.05
	Urban	13	13	>0.05

The difference in the mean latencies (ms) of waveforms N<sub>75</sub>, P<sub>100</sub> and amplitude P<sub>100</sub> (µV) were found to be highly significant statistically (p<0.001) in the two groups. The difference in the mean latency of waveform N<sub>145</sub> was

found to be statistically insignificant in the two groups (p>0.05).



**Figure 1: Study flow for the cases.**

**Table 2: Visual evoked potential parameters of both eyes.**

Parameter	Eye	Cases	Controls	P value	Significance
Wave Latency N <sub>75</sub> (ms)	Right	85.54±3.89	78.68±1.82	<0.001	HS
	Left	85.52±3.79	78.27±2.13	<0.001	HS
Wave Latency P <sub>100</sub> (ms)	Right	118.95±3.18	108.02±1.40	<0.001	HS
	Left	118.91±3.13	107.84±1.49	<0.001	HS
Wave Latency N <sub>145</sub> (ms)	Right	147.79±2.59	147.36±1.16	>0.05	NS
	Left	147.72±2.62	147.26±1.15	>0.05	NS
Amplitude P <sub>100</sub> (µv)	Right	5.75±0.23	8.02 ±0.69	<0.001	HS
	Left	5.79±0.21	7.93±0.72	<0.001	HS

HS=Highly significant, NS=Non-significant

**DISCUSSION**

This cross-sectional case-control study was done to assess the effect of type 1 diabetes melitus on the visual evoked potentials in children. Our study has shown that there is significant increase in the latencies and decreased amplitude of the visual evoked potentials. The increase in P<sub>100</sub> latency in the present study is in agreement with the previous studies done by Kalica et al, Fierro et al, and Siedl et al, in which the latencies continued to be increased despite more than two years duration of diabetes.<sup>10-12</sup> Most of the other studies done earlier have been done on type 1 diabetic patients above pediatric age group in newly diagnosed diabetic population with variable methods, subsets as well as duration of diabetes.<sup>10,13-17</sup> The decrease in amplitude P<sub>100</sub> has also been reported in previous studies.<sup>10,16,17</sup> The finding of increase in the latency N<sub>75</sub> found in our study has been rarely reported earlier.

The increase in latency and decrease in the amplitude can be explained by the effects of the diabetes on retinal

ganglion cell damage. The neurophysiological changes in diabetes mellitus may be due to advanced glycation and hyperlipidemia induced oxidative stress and subsequent vascular dysfunction in the neural pathways.<sup>18</sup> The changes in the visual pathways as depicted by VEPs will guide for early interventions for good glycemic control and rehabilitation so that the changes could reverse to some extent.

The limitations of the study include its small sample size, study done at a single point of time, lack of correlation between the glycemic status and effect on the therapy on the VEPs. The associated malnutrition could have also lead to the decrease in conduction in the visual pathway.

Further multi-centeric studies are required with adequate sample size along with stratification of various duration of diabetes and glycemic control. The VEPs can also be done during follow up phase to ascertain the reversibility of the changes acquired during the treatment phase. More electrophysiological tests of visual pathways like oscillatory potentials, flash and pattern electroretinogram

can also be included in the analysis to get more knowledge about these pathways.

## CONCLUSION

The type 1 diabetes does affect the visual pathways in children as shown by the prolonged latencies and decreased amplitude in the VEPs. Visual Evoked Potentials are helpful in the detection of early changes in the conduction across the neural pathways in the sub-clinical diseases.

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