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Small check size pattern reversal visual evoked potentials (VEPs) in patients with chronic idiopathic intracranial hypertension

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Abstract--Background: The condition known as idiopathic intracranial hypertension is characterized by elevated intracranial pressure. The most feared complication of IIH is visual loss due to papilledema and optic nerve atrophy. Visual evoked potentials are sensitive and non-invasive method. They are considered an important objective test in investigating suspected optic nerve disease. This study aims to clarify the effect of chronic increased ICP on the optic nerve. Methods: This case-control study was performed at Beni-Suef University Hospital on 60 female patients divided into two equal groups; Group (I): thirty female patients with chronic idiopathic hypertension and Group (II): thirty age and sex-matched healthy controls. All subjects were subjected to full neuro-ophthalmological assessment by PVEP, a lumbar puncture to measure CSF pressure, and radiological assessment using MRI. SPSS version 20 was used for the statistical analysis. Results: Right Pattern reversed VEP; for the check size 15min, the mean value of P100 latencies of chronic IIH was 109.88 ± 10.46 and for controls was 97.35 ± 4.23 . The mean value of P100 amplitudes of chronic IIH was 11.73 ± 5 and for controls was

11.95±3.3. Left pattern reversed VEP; for the check size 15min, the mean value of P100 latencies of chronic IIH was 111.42±11.5 and for controls was 97.13±4.32. The mean value of P100 amplitudes of chronic IIH was 10.82±4 and for controls was 12.67±4.54. Conclusions: A significantly increased ICP in IIH patients was associated with delayed P100 latency in check size 15 minute of PVEPs with positive correlation between P100 latency and increased ICP and papilledema's degree.

Keywords---PVEP, optic nerve, idiopathic, intracranial hypertension.

Introduction

The increased intracranial pressure (ICP) could be known as sustained elevated pressure > 20 mmHg and is usually associated with poor clinical outcomes in patients with neurological insult.⁽¹⁾ The optic nerve and the space surrounding it are a continuation of the subarachnoid space of the brain. With an increase in the ICP, the CSF is directly redistributed to the space around the optic nerve.⁽²⁾ Assessment of the optic nerve functions and evaluation of the transmission time between the retina and the occipital cortex could be performed by the pattern visual evoked potential (PVEP). Any change in the peak time or the amplitude of PVEP could reflect injury to the optic nerve.⁽³⁾ This study aimed to clarify the effect of chronic increased ICP on the optic nerve by studying the findings of small check size (15 min) of pattern visual evoked potential (PVEPs) in patients with chronic idiopathic intracranial hypertension.

Patients and Methods

This is a case-control study performed at Beni-Suef University Hospital between the start of January 2019 to the end of December 2020 after approval from the local research ethics committee and obtaining informed written consent from literate candidates. Included patients were classified into two equal groups;

- **Group (I):** thirty female patients with chronic idiopathic hypertension
- **Group (II):** thirty age and sex-matched healthy controls.

The studied subjects were diagnosed as having chronic idiopathic intracranial hypertension according to modified Dandy criteria,⁽⁴⁾ patients with disease duration exceeding 6 months and age more than 18 years. Patients with ocular diseases (e.g., cataract, uveitis or glaucoma), which could impact the visual functions or tests, patients with MRI brain showing structural lesion, subjects with concurrent medical or metabolic illness could affect vision, patients with exposure history to drugs as cyclosporine, minocycline, hydroxychloroquine, ethambutol, topiramate and anticholinergics, toxic substances as lead and ethylene glycol, alcohol, industrial agents, heavy metals, or any substance known to affect vision and pregnant patients were all excluded from the study. The patients and controls were subjected to the following assessments:

Neuro-ophthalmological assessment

History taking regarding the presence of manifestations of increased intracranial hypertension: headache, blurred vision, vomiting, tinnitus, transient visual obscurations, visual acuity testing with Snellen chart, ophthalmoscopic examination for determining the grade of papilledema and cranial nerves examination 2nd, 6th and 7th.

Lumbar puncture

Using an 18- or 20-gauge spinal needle and a manometer positioned at a 90° angle to the spine, patients had their CSF pressure measured by a lumbar puncture. Subjects in lateral decubitus posture with legs extended, head and spine perfectly horizontal and as relaxed as possible were put in a position where the opening pressure was measured. The pressure was allowed to stabilise for a sufficient amount of time. The same skilled physician conducted each and every lumbar puncture.

Radiological assessment

Every patient participating in the research had an MRI of the brain with MRV (Magnetic Resonance Venography). T1- weighted images (axial, sagittal), T2-weighted images (axial, coronal) and fluid-attenuated inversion recovery (FLAIR) sequence was used.

Neurophysiological assessment

Neurophysiological tests were carried out in the Neuro-diagnostic and Research Center (NDRC), Beni Suef University Hospital, including pattern Visual evoked potential (PVEP) using Roland consult electrophysiological diagnostic systems. VEPs record was done using the Reti-Scan 21 (Roland Consult, Brandenburg a.d. Havel, Germany) Roland RETI system (Roland, Germany) according to the International Society for Clinical Electrophysiology of Vision (ISCEV) standards 2011.

Pattern Visual evoked potential (PVEP).

Using Roland consult electrophysiological diagnostic systems.

Equipment

VEPs record was done using the Reti-Scan 21 (Roland Consult, Brandenburg a.d. Havel, Germany) Roland RETI system (Roland, Germany) Figure 1

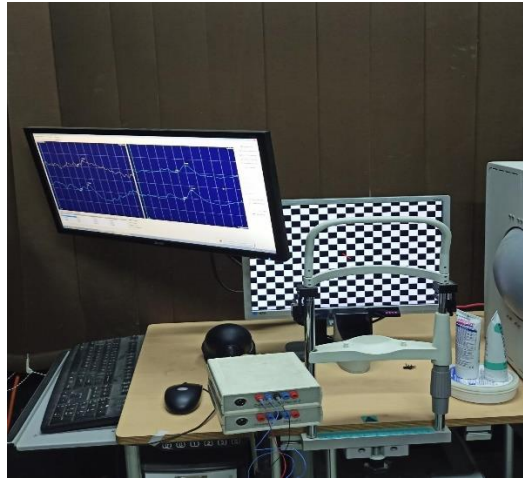


Figure 1. Reti-Scan 21 (Roland Consult, Brandenburg a.d. Havel, Germany)
Roland RETI system (Roland, Germany)

Procedures

Subject preparation

The test was explained to the subject, who was seated on a comfortable chair, before the test proper sterilization of the scalp skin with alcohol and gel was done, subjects were asked to look at the red cross fixation at the center of checkerboard stimuli at a distance of 1 meter.

Protocol used

According to International Society for Clinical Electrophysiology of Vision (ISCEV) standards 2011, The protocol used include the following:

Recording electrodes

The EEG silver cup electrodes were used for the recording, the active, reference and ground electrodes were placed respectively on the occipital area (Oz), the mid frontal (Fz) and the vertex (Cz). According to anatomical landmarks using a standardized "International 10/20system" measurement method to keep the impedance below 5 K Ohm. Computerized signal averaging is used to extract the time-locked VEPs from the spontaneous brain activity (EEG).

The stimulus type and size

reversing checkerboard of black and white checks in sizes of 15 minute of arc at contrast was used to record the VEP. The VEPs were recorded monocularly (right and left eyes) in a quiet, room with a constant temperature (27-30°C).

Measurements

The components of VEP are termed as N75, P100, and N145 to indicate their polarity and approximate latency (in msec.).

P100 latency

It is the time from the stimulus to the prominent positive component (upward), latency are usually measured in milliseconds (msec).

Amplitude of N75-P100

It is measured from the peak N75 to the trough of P100. It measured in millivolts (mv).

Statistical analysis

Statistical analysis was performed using SPSS software version 20. Quantitative variables in both patients and control subjects were expressed as mean and standard deviation (SD). Categorical variables in both patients and control subjects were expressed as numbers and percentages. Independent samples T-test was used to compare between patients and control subjects in quantitative variables, while the chi-square test was used to compare between patients and control subjects in categorical variables. Pearson's correlation was used for the association between quantitative variables. P-values ≤ 0.05 (2-sided) were considered statistically significant.

Results

Age of patients and control groups (Table 1)

The mean age of chronic IIH patients was 36.13 ± 10.28 years, while of controls, 36.96 ± 7.77 years with no significant difference between both groups (P-value=0.725) (Table 1). The mean value for CSF pressure of chronic IIH patients ranged from 250 to 480 mm H₂O with a mean of 317.66 ± 63.82 mm H₂O. Regarding the right eye in the present study, 3.3% of chronic IIH patients had grade I papilledema, 56.7% of patients had grade II papilledema, and 40% of patients had grade III papilledema. Regarding the left eye, about 6.7% of chronic IIH patients had grade I papilledema, 43.3% of patients had grade II papilledema, and 50% had grade III papilledema.

Neurophysiological assessment of IIH patients and control groups

The pattern reversed VEP was studied for the mean and SD of the P100 latency (ms) and amplitude (mv) on check size 15m.

- Right pattern reversed VEP:
For the check size 15min, the mean value of P100 latencies of chronic IIH was 109.88 ± 10.46 and for controls was 97.35 ± 4.23 . Patients and controls had a statistically significant difference (P-value < 0.001).

The mean value of P100 amplitudes of chronic IIH was 11.73 ± 5 and for controls was 11.95 ± 3.3 with no significant difference between the studied groups (P -value=0.845).

- Left pattern reversed VEP:

For the check size 15min, the mean value of P100 latencies of chronic IIH was 111.42 ± 11.5 and for controls was 97.13 ± 4.32 with a statistically significant difference (P -value < 0.001).

The mean value of P100 amplitudes of chronic IIH was 10.82 ± 4 that didn't differ significantly from that of controls (12.67 ± 4.54) (P -value=0.099).

Correlations between CSF Pressure and PVEP parameters in the patient group (Table 4)

- PVEP latencies of check size 15':

There was a statistically significant correlation between CSF pressure and right and left PVEP latencies (P -value < 0.001, 0.008, respectively).

- PVEP amplitudes of check size 15':

There was no statistically significant correlation between CSF pressure and right and left PVEP (p -value=0.717, 0.296).

Correlations between papilledema and PVEP parameters in the patient group (Table 4)

- PVEP latencies of check size 15':

In both eyes, papilledema grade was statistically correlated to PVEP latencies (P -value<0.001, 0.004, respectively).

- PVEP amplitudes of check size 15':

There was no statistically significant correlation between papilledema grade in both eyes and PVEP amplitudes (P -value=0.097, 0.212, respectively).

Table 1
Age of patients and control groups

	Patients (n=30)	Controls (n=30)	P-value
Age [mean (SD)]	36.13 (10.28)	36.96 (7.77)	0.725

Table 2
Clinical assessment of patients

		Patients (n=30)
Papilledema in Rt eye	Grade I [n (%)]	1 (3.3%)
	Grade II [n (%)]	17 (56.7%)
	Grade III [n (%)]	12 (40%)
Papilledema in Lt eye	Grade I [n (%)]	2 (6.7%)
	Grade II [n (%)]	13 (43.3%)
	Grade III [n (%)]	15 (50%)

* P -value ≤ 0.05 is considered significant.

RT, right; LT, left.

Table 3
PVEP values in patients and control groups

PVEP	Patients (n=30)	Controls (n=30)	P-value
RT PVEP latency 15'	109.88 (10.46)	97.35 (4.23)	< 0.001*
RT PVEP amplitude 15'	11.73 (5)	11.95 (3.3)	0.845
LT PVEP latency 15'	111.42 (11.5)	97.13 (4.32)	< 0.001*
LT PVEP amplitude 15'	10.82 (4)	12.67 (4.54)	0.099

*P-value ≤ 0.05 is considered significant.

RT, right; LT, left.

Table 4
Correlations between clinical data and PVEP in patient group

PVEP	CSF pressure		Papilledema	
	(r) coef.	P-value	(r) coef.	P-value
RT PVEP latency 15'	0.647	< 0.001*	0.738	<0.001*
RT PVEP amplitude 15'	-0.069	0.717	-0.309	0.097
LT PVEP latency 15'	0.414	0.008*	0.513	0.004*
LT PVEP amplitude 15'	-0.197	0.296	-0.235	0.212

*P-value ≤ 0.05 is considered significant.

RT, right; LT, left.

Discussion

IIH is described as an increase in intracranial pressure (ICP) in the absence of any brain lesion or other secondary cause, and it is most often seen in obese young women of reproductive age who are not otherwise ill.⁽⁵⁾ The visual system is particularly sensitive to chronic elevation of the intracranial pressure that may result in critical visual deterioration.⁽⁶⁾ Long-lasting visual loss due to 2nd cranial nerve atrophy is the main complication of chronic benign intracranial hypertension and can be seen in 25% of diseased patients.⁽⁷⁾ IIH can produce swelling of the optic disc (papilledema) and visual field defect, and therefore, IIH patients should be followed up with regular period to detect early evidence of optic neuropathy.⁽⁸⁾ The responses to small checks are more sensitive to disorders of the visual pathway, and smaller pattern checks are also thought to be optimal for foveal stimulation.^(9,10)

In our study, we aimed specifically to clarify the effect of chronic increased ICP on the optic nerve by studying the findings of small check size (15 min) of PVEPs in patients in chronic IIH patients. Twenty (66.6%) of our chronic IIH patients had abnormal PVEP responses while only 10 (33.3%) patients had normal PVEP responses. The abnormality of PVEP as delayed P100 latencies was reported on using check size 15 minutes, with significant P value (≤ 0.05) while P100 amplitudes were within normal ranges when compared with the controls. In IIH, Demyelination of the optic nerve may be a more likely mechanism similar to compression neuropathy that occurs in the peripheral nerves.⁽¹¹⁾ Our findings come in agreement with that reported by Sureda et al. and Kesler et al., who reported abnormally delayed VEP latencies in IIH patients with normal

amplitudes and attributed the optic nerve dysfunction in IIH to demyelination except in cases with secondary axonal loss.^(8,12)

In 1981, Kirkham and Coupland demonstrated that the most common abnormality of VEP reported in association with papilledema is p100 latency prolongation. However, Krogsaa et al. reported a higher prevalence with marked papilledema and significantly delayed pattern reversal visual evoked potential in nearly all studied patients.⁽¹³⁾ Rizzo et al. and Sorensen et al. reported abnormal responses of VEP in 28% and 31% of their IIH patients, respectively, while Bobak et al. found prolonged VEP responses in 55% of their IIH patients. and in 2016, Moss estimated the prevalence of prolonged VEP latency in IIH to be from 10 to 55%.^(14,15,16) However, Falsini et al. used more elaborated techniques to compare the effect of high and low spatial frequency stimuli on VEP amplitudes in IIH patients and controls and reported that about 55.5% of their IIH patients had decreased normalized amplitudes with high spatial frequency stimuli.⁽¹⁷⁾

A statistically linear relationship and positive correlation was found between VEP latency and opening pressure of the CSF in our results which goes with Mustafa et al., who reported the same findings.⁽¹⁸⁾ Our study showed a positive correlation between VEP and the degree of papilledema in IIH patients. In accordance with our findings, Moss (2016) reported that the most common PVEP abnormality reported in association with papilledema is prolonged P100 latency.⁽¹⁹⁾ Moreover, Kisabay et al. found that PVEP latencies of IIH patients without papilledema were closer to those in the control group, and this finding supports our results that described the positive correlation between VEP latency and papilledema.⁽²⁰⁾

Conclusions

Chronic increased ICP has a significant effect on small check size 15 minute of PVEP. A significantly increased ICP in IIH patients was associated with delayed P100 latency in check size 15 minute of PVEPs with positive correlation between P100 latency and increased ICP and papilledema's degree.

Ethics Approval and Consent to participate

Ethical approval was obtained from FM-BSU REC in 9th of Oct 2018.

Consent for publication

Not applicable as no individual data, images or videos were included in the study.

Availability of data and material

Please contact author for data requests.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable as no fund was obtained for the study.

List of Abbreviations

FLAIR: Fluid attenuated inversion recovery.

ICP: Intracranial pressure.

IIH: Idiopathic intracranial hypertension.

MRI: Magnetic Resonance Imaging.

MRV: Magnetic Resonance Venography.

PVEP: Pattern visual evoked potential.

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