Evaluation of Visual Evoked Potentials in The Patients with Chronic Viral Hepatitis

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Abstract

Background: The visual evoked potential (VEP) is a wave generated in the occipital cortex in response to a visual stimulation. It measures the conduction time of neuronal activity from the retina to the occipital cortex.
Infection with viral hepatitis leads to a wide spectrum of clinical presentations ranging from an asymptomatic carrier state to self-limited acute or fulminate hepatitis to chronic hepatitis with progression to cirrhosis and hepatocellular carcinoma. The neurological complication is one of the extrahepatic manifestations of chronic viral hepatitis, where the involvement of the central nervous system (CNS) impairment has been reported.
Objectives: To assess the visual evoked potential changes in patient with chronic viral hepatitis.
Methods: Evaluation of visual evoked potentials in (27) normal subjects (18 male and 9 female) and (51) patients with documental chronic viral hepatitis disease (34 male and 17 female), divided according to type of virus to two group (30) CVHB patients, and (21) CVHC patients.
Results: The VEP abnormalities in both eyes were recorded in (23.33%) of CVHB patients and (42.89%) of CVHC patients, and the VEP abnormality in one eye was recorded in (10%) of CVHB patients. The bifid W waveform of abnormal VEP was recorded on both eyes in (10%) of CVHB patients and in (19%) of CVHC patients, the bifid W waveform recorded on (10%) of CVHB patients and (4.8%) of CVHC patients.
Conclusions: The abnormal VEPs and the bifid W shape are can be reported in chronic viral hepatitis patients as the early central sign of chronic viral hepatitis.
Keywords: visual evoked potential, chronic viral hepatitis

الخلاصة

التحفيز الكامن للعصب البصري هي الموجة المسجلة والمولودة في القشرة الخلفية للدماغ تجاوبا للتحفيز البصري والتي تبين فعالية العصب في سرعة التوصيل العصبي من شبكية العين إلى الدماغ.
و الإصابة بالتهاب الكبد الفيروسي قد يودي الى أعراض واسعة للمصابين تبدء من حامل المرض وبدون اعراض الى المرض المفاجيء والى اصحاب التهاب الكبد الفيروسي المزمن. والتطورات العصبية واحدة من العراض الخارج الكبد التي تصيب هولاء المرضى. وقد يكون مصحوبا بإصابة الجهاز العصبي المركزي.
الغاية: تقييم التغيرات التي تطرى على مرض التهاب الكبد الفيروسي المزمن في التحفيز الكامن للعصب البصري.
الطريقة: تخطيط التحفيز الكامن للعصب البصري لسبعة وعشرون شخصا سويا مقارنة مع واحد وخمسون شخصا مريضا بالتهاب الكبد الفيروسي المزمن ومنقسم الى مجموعتين احداهما

مكونه من ثلاثون مريضا بالتهاب الكبد الفيروسي نوع بي والثانية مكونة من واحد وعشرون مريضا بالنوع سي.
النتائج: التحفيز الكامن للعصب البصري الغير طبيعي سجل في كلا العينين لدى 23.33% مريضا بالتهاب الكبد الفيروسي بي و42.8% مريضا بالتهاب الكبد الفيروسي نوع سي. اما التغير الذي سجل في عين واحدة سجل في (10%) مرضا بالتهاب الكبد الفيروسي بي.
وسجلت الموجة الثنائية في التحفيز الكامن للعصب البصري في كلأ العينين بنسبة (10%) لدى مريضا بالتهاب الكبد الفيروسي بي و 19% مريضا بالتهاب الكبد الفيروسي نوع سي بينما سجلت الموجة الثنائية في التحفيز الكامن للعصب البصري لعين واحده بنسبة (10%) لدى مريضا بالتهاب الكبد الفيروسي بي.
الخاتمة: التغيرات التحفيز الكامن للعصب البصري الغير طبيعي مع الموجة الثنائية سجلت لدى مرضى التهاب الكبد الفيروسي كعلامة عصبية مركزية لالتهاب الكبد الفيروسي المزمن.

Introduction

The visual evoked potential (VEP) is primarily a relatively large, positive polarity wave generated in the occipital cortex in response to visual stimulation. It measures the conduction time of neuronal activity from the retina to the occipital cortex and is used clinically as a measure of the integrity and function of that pathway [(1)]. The responses produced in this way by rapidly repeating the pattern reversal were easier to detect and measure than flash responses and more consistent in waveform from one individual to another. The expected latency for the positive polarity, pattern-shift visual evoked responses is near 100 ms (thus the term "P 100"); an absolute latency over approximately 118 ms or a difference in latencies of greater than 9 ms between the two eyes signifies involvement of one optic nerve. Bilateral prolongation of latencies, demonstrated by separate stimulation of each eye, could be due to lesions in both optic nerves, in the optic chiasm, or in the visual pathways posterior to the chiasm[(2)]. Pattern shift visual evoked potentials detect conduction delays caused by subtle and often asymptomatic lesions at various points in the visual pathways [(3)] and Study of optic nerve, optic chiasm and optic tract and used mainly to diagnose prechiasmatic lesion [(4)]. A compressive lesion of an optic nerve will have the same effect as a demyelinative one. Many other diseases of the optic nerves, including toxic and nutritional amblyopias, ischemic optic neuropathy, and the Leber type of hereditary optic neuropathy show abnormalities of the pattern-shift visual evoked responses. VEPs are usually very precise for an individual over repeated trials, even months and years apart. An excessive difference in the latencies on the two sides (usually 6–10 ms) is also considered abnormal. If the two peaks have normal latencies but an excessive difference between them, this raises concern for an abnormality in conduction in the visual pathway with the longer latency. This is not as reliable clinically as a prolonged latency itself [(1)]. VEP peak latency, amplitude, and waveform are age-dependent. The description of standard responses below reflects the typical response of an adult aged 18–60 years of age. VEP peak latency refers to the time from stimulus onset to the maximum positive or negative deflection or excursion; thus, the term VEP peak latency corresponds to the term implicit time used to describe the time from the stimulus to the maximum deflection of electrore-tinograms. VEP peak latency may also be referred to as 'time to peak' or peak time. [(6)] The current standard presents basic respon-

ses elicited by three commonly used stimulus conditions using a single, midline recording channel with an occipital, active electrode [6]

The VEP or visually evoked cortical potential is typically read by an expert who identifies the stimulus-elicited signal within the waveform, scores its latency or amplitude, and then decides whether the patient is normal based on the magnitude of the patient's score relative to those from normal subjects [7]. The VEP is an evoked electro-physiological potential that can be extracted, using signal averaging, from the electroencephalographic activity recorded at the scalp. The VEP can provide important diagnostic information regarding the functional integrity of the visual system [6].

Zamir (2002) reported the early detection of hepatic encephalopathy by recording visual evoked potential (VEP) [8]. The visual evoked potential (VEP) record in response to a pattern stimulus is a non invasive and reliable method of detecting central and peripheral nerve system abnormalities, and have been proposed as diagnostic tools in the evaluation of hepatic encephalopathy [8,9,10].

Viral hepatitis is a term commonly used for several clinically similar yet etiologically and epidemiologically distinct diseases [11]. Chronic liver disease is defined as liver injury occurring over more than 6 months, in contrast to acute liver injury [12]. There are two mechanisms of liver injury in viral hepatitis: direct cellular injury and immune responses against viral antigens in infected hepatocytes. The immune-mediated mechanisms of injury have been most closely studied in viral hepatitis. It is thought that the extent of inflammation and necrosis depends on the person's immune response [13].

Chronic viral hepatitis, both type B and type C, has been associated with a spectrum of autoimmune phenomena [14]. McMurray and Elbourne (1997) summarized many of the reported autoimmune complications of Chronic Viral hepatitis [15].

Chronic hepatitis C and chronic hepatitis B are generally asymptomatic and therefore frequently hidden to both the patient and the clinician. Since a history of risk behaviour is often not disclosed to doctors, a reason to offer testing and diagnosis may not present itself. When symptoms do occur, they are largely non-specific and common symptoms that may be the result of a myriad of diseases. Consequently, the diagnosis of HCV or HBV infection can be easily missed. Being alert to the possibility of chronic viral hepatitis as a cause of many clinical presentations will allow early diagnosis and the offer of treatment [16]. Clinical manifestations of chronic VH infection range from no signs or symptoms of disease (most patients) to the warning signs of end-stage liver disease [17]. The pathogenesis of these extrahepatic disorders has likely involves an aberrant immunologic response to extrahepatic viral proteins [18]. Hepatic encephalopathy also may be present in advanced liver disease and may be subclinical in early stages. A history of reversal of diurnal sleep patterns, forgetfulness or inappropriate behavior may signal the onset of early hepatic encephalopathy. Presence of either hepatic encephalopathy or oesophageal varices indicates a poor prognosis [16].

Subjects & Method

This study was conducted at the neurophysiology unit, Gazy AL-Harriry Surgical Specialties Teaching Hospital, Medical City from January 2009 to November 2009, Fifty one patients (34 male and 17 female)

included in these study, age ranged between 12-65years with a mean age of 37.12 ±14.03 years, divided according to type of virus to two group (30) CVHB patients, and (21) CVHC patients. All patients included in this were study chosen according to these criteria:

1. History of chronic viral hepatitis disease for more than 6 months.
2. Had records in Iraqi hepatic center.
3. Have not received treatment for this disease.
4. Patients with diabetes, kidney disease as uremia, any blood disease as thallasemia, amyloidosis, alcoholic abuse, and nutrition or lipid metabolism disorders or with a family history of peripheral or central nerve disorders were excluded.
5. They had no known history of peripheral or central nerves involvement.
6. All patients were diagnosed and referred by a consultant physician and were examined by a consultant Neurologist.

Twenty-seven of the subjects were normal healthy subjects (18 male & 9 female), age ranged between 18 to 65 years with a mean age of (36.32 ± 12.37) years, symptoms free and with neither history of liver diseases, or systemic disease nor familial history of neurological illness. All of them were examined by a neurologist and physician. The subjects were medical worker, relatives, or other volunteers. All of them were instructed and informed about the aim of the study.

The activity classification according to examination of consultant physician and according to these criteria:

1. Activity of Sign and symptoms of this disease.
2. Loading of virus high or low.
3. Either investigation as ultrasonic, liver enzyme, liver aspiration.

Divided to two group (36) patients of active diseases and (15) patients of non active disease, illustrated in Table1.

Table 1: activity of CVH

VIRUS	Number	ACTIVITY		Total
		active viral	non active viral	
B virus	Number	19	11	30
	Percent	63.3%	36.7%	100.0%
C virus	Number	17	4	21
	Percent	81.0%	19.0%	100.0%

The parameters of VEP analysis in the right and left eye including duration and amplitude of NPN (N75, P100 and N145) were studied in all subjects included in this study. The percent of patients with VEP abnormalities expressed as prolongation in Latency of N75 and P100, and latency between N75 and P100 were calculated as 2SD above the mean of the normal values of control group and reductions in amplitude were calculated as 2SD below the mean of the normal values of control group. All statistical analysis was obtained using statistical package for social sciences (SPSS) version 17.0 computer soft ware. All data of each set used the Descriptive statistics expressed as mean ± 2SD (standard deviation). Data from each patient and control group were compared using ANOVA tests to calculate differences between groups.

Results

Chronic viral hepatitis patients divided according to type of virus to two group (30) chronic viral hepatitis

B patients (CVHB), and (21) chronic viral hepatitis C patient (CVHC), All the patients were examined by consultant neurologist and the results showed fife patients (9.8%) had ophthalmic manifestation, as blurring of vision.

Comparison was made between CVH patients and the control group and we found a significant difference (P<0.05) between latency of N75 and P100 and non significant between N75-P100 amplitude, these findings are illustrated in (table 3)

Table 2: VEP parameters values

Parameter	Control Mean ± 2SD	CVHB Mean ± 2SD	CVHC Mean ± 2SD	P-value CVHB	P-value CVHC
count	27	30	21		
Rt. N75 latency	68.49±8.04	83.84 ± 29.42	92.37 ± 29.67	0.024 S	0.002 S
Lt. N75 latency	67.83 ± 9.19	85.87 ± 28.36	92.33 ± 30.70	0.008 S	0.001 S
Rt. P100 latency	104.67±3.67	122.97±34.76	135.96±47.56	0.044 S	0.002 S
Lt. P100 latency	104.69±4.73	124.39±35.58	135.69±35.58	0.028 S	0.002 S
Rt. N75-P100 amplitude	5.98 ± 3.02	4.65 ± 2.23	5.51 ± 7.79	0.101 NS	0.495 NS
Lt. N75-P100 amplitude	5.37 ± 2.72	5.21 ± 2.56	5.57 ± 3.44	0.840 NS	0.899 NS
Rt. N75-P100 latency	34.95 ±10.64	39.24±14.57	44.14±24.63	0.348 NS	0.082 NS
Lt. N75-P100 latency	38.87±11.28	38.36±13.22	46.81±23.69	0.909 NS	0.158 NS

Significantly in relation to the control group The mean difference is significant at the 0.05 level (P≤ 0.05).S = Significant NS= Non significant

The electrophysiological findings showed (19) CVH patients (37.25%) had abnormal VEP, which was statistically significant difference on comparison of the CVH and control group. (P = 0.002) on comparison of the CVHB and control group. And (P =0.016) on comparison of the CVHC and control group. As illustrated in table 3.

Table3: comprise of patients with VEP abnormalities in CVH and control group.

Type of virus	Count and percentage	VEP				TOTAL
		Normal	Abnormal both eyes	Abnormal right eyes	Abnormal left eyes	
B virus	Number	20	7	1	2	30
	Percent	66.7%	23.3%	3.3%	6.7%	100%
C virus	Number	12	9	0	0	21
	Percent	57.1%	42.9%	0.00%	0.00%	100%
Control	Number	27	0	0	0	27
	Percent	100%	0.00%	0.00%	0.00%	100%
Total	Number	59	16	1	2	78
	Percent	75.6%	20.5%	1.3%	2.6%	100%

The bifid W waveform of abnormal VEP recorded on both eyes in 3 (10%) out of 30 CVHB patients and in 4 (19%) out of 21 CVHC patients, the bifid W waveform recorded on one eye in 3 (10%) out of 30 CVHB and one (4.8%) out of 21 CVHC patients, these findings are illustrated in (table 4).

Table4: Percentage of bifid W waveform with VEP abnormality.

Parameter	CVH No.	%	CVHB No.	%	CVHC No.	%
W waveform on both eye	7	13.73%	3	10%	4	19.05%
W waveform on right eye	3	5.88%	2	6.67%	1	4.76%
W waveform on left eye	1	3.92%	1	3.33%	0	0.00 %

The activity of disease had a significant effect on VEP abnormality (P=0.008). This correlation can be illustrated on table5

Table5: Percentage of patients with VEP abnormality according to activity of disease

VIRUS	VEP	Count & percent	ACTIVITY		Total
			active viral	non active viral	
B virus	normal	Number	12	8	20
		Percent	40%	26.7%	66.7%
	abnormal both eyes	Number	5	2	7
		Percent	16.66%	6.66%	23.3%
	abnormal right eye	Number	1	0	1
		Percent	3.3%	0.00%	3.3%
	abnormal left eye	Number	1	1	2
		Percent	3.3%	3.3%	6.7%
	Total	Number	19	11	30
		Percent	63.33%	36.67%	100%
C virus	Normal	Number	9	3	12
		Percent	42.9%	14.29%	57.1%
	Abnormal both eyes	Number	8	1	9
		Percent	38.1%	4.8	42.9%
	Total	Number	17	4	21
		Percent	81%	19%	100%

Each percentage is the part of total percentage of virus (B or C)

Discussion

This study showed that Comparison was made between CVH patients and the control group and we found a statistically significant difference between latency of N75 and P100 on both eyes, had high significant on comparison between CVHC patients and control group (P = 0.002) on both eyes, while is less significant on comparison between CVHB patient and control group (P = 0.024 of N75 latency and P = 0.044 of P100 latency). No significant difference between N75-P100 amplitude of CVH patients and control group. The VEP abnormality in both eyes is recorded in 7 (23.33%) out of 30 CVHB patients and 9 (42.89%) out of 21 CVHC patients, and the VEP abnormality in one eye recorded in 3 (10%) out of 30 CVHB patients these findings are either similar or near to that reported by other authors [8, 20, 21, 22, 23].

The Chronic viral hepatits as demylinating disease causes the Inflammation of the optic nerve produces the syndrome of optic neuritis [29] may result from deposition of antigen-antibody complexes formed when these particles are neutralized by anti-HBsAg antibodies, and believed to be related to vasculitis from cryoglobulin deposition in small blood vessels supplying the nerves , and Another possible mechanism for these CNS manifestations is the effect of cytokines derived from the host immune system in response to HCV [30] The visual system functions at several levels, beginning with the retina and terminating in several regions of the cerebral cortex The occipital cortex projects to the midtemporal cortex and the posterior parietal cortex. Cells in the visual cortex are most sensitive to movement and to edges [31].

Sannita (1995) described the increased latency of the cortical evoked response to contrast stimulation of pattern-reversal or pattern-onset VEPs with P100

breaking up into two positive waves (W-shaped or bifid P100s) is an established indication of impaired function in brain diseases affecting the visual pathways [27]. The bifid P100s (W waveform) of abnormal VEP recorded on both eyes in 3 (10%) out of 30 CVHB patients and in 4 (19%) out of 21 CVHC patients, the bifid W waveform recorded on one eye in 3 (10%) out of 30 CVHB and one (4.8%) out of 21 CVHC patients. Sannita. et al; (1995) and other authors described the Pattern-VEPs with P100 breaking up into two positive waves (W-shaped or bifid P100s) or with superimposed quasi-sinusoidal sequences of negative/positive waves have been described in multiple sclerosis, migraine, vascular disease, and other neurologic diseases [24, 25, 26, 27, 28]. According to my field; I could not find these changes on a study which deals with the VEP changes on chronic viral hepatitis.

Conclusion

1. The VEP is an evoked electrophysiological potential abnormallity that can be reported as the early detection of central nervous involvement in patient with chronic viral hepatitis.
2. The Bifid W shape VEP abnormality recorded on 11(21.57%) out of 51CVH patients as central neurological sign of chronic viral hepatitis.

Recommendations

1. VEP as a follow up investigation monthly to exclude the central nervous system abnormality as hepatic encephalopathy, and relation-ship with medication.
2. Additional evoked potential studies include brain stem auditory evoked potential and somatosensory evoked potential may be necessary to detect subclinical involvement.

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