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Original Article

Brainstem evoked response audiometry: An investigatory tool in detecting hepatic encephalopathy in decompensated chronic liver disease

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Abstract

It is estimated that globally there is a marked increase in liver disease with reports of rising morbidity and mortality, particularly in younger age groups. Brainstem auditory evoked potential (BAEP) was recorded in 60 decompensated chronic liver disease (DCLD) subjects who fulfilled the selection criteria and compared to 60 age and gender matched healthy subjects with normal liver functions. DCLD subjects were divided into two inter groups based on presence or absence of hepatic encephalopathy (HE). Group 1 comprises of 30 subjects of grade- I HE and Group 2 included 30 subjects without hepatic encephalopathy (NHE). Absolute and interpeak wave latencies were measured. Results were analysed by student independent t- test using SPSS software 11 version. Statistical significance was tested using P value. From the present study it can be concluded that the central nervous system is involved in liver cirrhosis evidenced by an abnormal BAEP latencies parameters. This shows that there may be progressive demyelination occurring along with axonal loss or dysfunction in liver cirrhosis HE. This study suggests that periodic evaluation of cirrhotic individuals to such test will help in monitoring the progress of encephalopathy. The prime goal of this study is early diagnosis and initiation of treatment before the onset of coma can reduce the fatality rate.

Introduction

Hepatic encephalopathy is a reversible neuro psychiatric state that complicates liver disease. Hepatic encephalopathy due to chronic liver disease has become one of the most important chronic health problems (1). Prevalence of hepatic encephalopathy is typically higher if ascertainment is based on electrophysiological measurements. Chu NS, Yang SS 1988 indicated that SEP may be useful in detecting sub clinical HE and in monitoring its clinical course and further stated that chronic portal- systemic shunting in liver cirrhosis may result in a minimal impairment of cerebral function and sensory conduction in the CNS (2). Chu NS 1997 found that," Evoked potentials are objective and quantitative methods capable of evaluating functions of both peripheral and central nervous systems (PNS and CNS) (3). Daniel B. Nora et al, in 2000 has quoted"

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Visual evoked potentials (VEPs) and brainstem auditory evoked potentials (BAEPs) have been proposed as tools in the diagnosis of sub clinical hepatic encephalopathy (HE) (4, 5). SU Changchun in 2008 concluded that, BAEP could supply the objective basis for early diagnosis and treatment on SHE patients (6). Clinical observation of the neuro psychiatric condition (7-10), psychometric tests (11, 12), and EEG recording (12) have been used to differentiate the degrees of hepatic encephalopathy due to liver cirrhosis, but none of them seems objective or sensitive enough to quantify the degree of coma, nor to detect, as well, the preclinical stages of hepatic encephalopathy. Halliday stated evoked potentials can reflect not only pure nerve diseases but also demyelination processes (13) and neurotransmitterchanges (14) in cortical and sub cortical neurones. By storing the EEG trace for a pre selected period after the stimulus and by averaging these tracers it is possible to cancel the random components of EEG and to average the evoked response (12, 15, 16, 17, 18). Neuro physiological tests can be used during follow up to demonstrate change in a patient's condition (19, 20, 21, 22).

The measurement of somatosensory, visual and auditory evoked potentials is standard technique for assessment of neurotoxicity including subclinical state as a result of exposure to various chemicals and toxins. These potentials reflect functional integrity of sensory tract in the brain and help in identifying the sites impaired due to neurotoxic factors. The aim of this study is to evaluate the involvement of central nervous system in chronic liver disease induced hepatic encephalopathy and to test for recognition of the preclinical stage of HE. The objective is to use Brainstem Evoked Response Audiometry as a tool to assess conduction in auditory pathway in decompensated chronic liver disease subjects and compare with the controls.

Materials and Methods

Sample size 60

Study Design : Cross-sectional study. The present study has been conducted in the Neurophysiology laboratory of Research Wing, Department of Physiology, Stanley Medical College, Chennai - 1 from 2010 to 2011 using Neuro Perfect Plus-Medicaid Polyrite. Ethical approval from the Institutional Ethical Committee, Stanley Medical College, Chennai - 1 was obtained for the study. Study group: 60 decompensated chronic liver disease subjects were selected from liver clinic and Department of Medical Gastroenterology, control group: 60 age and gender matched healthy subjects with normal liver functions from the Master Health Check Up of our hospital. The ultrasound of healthy subjects performed under MHC package was taken to assess the well being of their liver and portal venous system, no evidence of psychiatric or neurological disorders, and no alcohol intake within last 6 weeks. Inclusion Criteria: age group - 30 to 50 years, both genders diagnosed decompensated liver disease subjects irrespective of aetiology. Child Pugh Criteria- A, B. Exclusion Criteria: Child Pugh Criteria C, smokers, alcohol intake within last 6 weeks, subjects with any hearing impairment of clinical causes and drug induced, systemic diseases like diabetes mellitus, hypertension, drugs acting on central nervous system, chronic associated disorders as cardiac decompensation, renal disease, subjects with cochlear implant/cardiac pacemaker, history of head injury or cerebrovascular accidents. The participants were made to relax and be comfortable prior to the test. The written and informed consent was obtained before subjects entered the study. The complete examination of external ear was done for both ears, wax was removed and audiometry was done. The laboratory temperature was maintained uniformly using air conditioner. The basic parameters of subjects like height, weight, pulse including body temperature were recorded.

Brainstem auditory evoked potentials were first recorded in 60 normal subjects. In order to establish reliability of the method, several repetitions of brainstem auditory evoked potential recording were performed. 60 age and gender matched chronic liver disease subjects of mixed aetiology were studied. 30 DCLD subjects were categorised as grade I hepatic encephalopathy and 30 DCLD without HE. The gold plated disc copper disc electrodes filled with conducting paste were placed on scalp because they are painless, have better stability and less

chances of infection. The electrodes recorded from ipsilateral and contralateral mastoid processes were referred to as Oz and Cz respectively and ground, as Fz. Vertex is the suitable location since waves II–V has good amplitude with little muscle artefact. Montage Chosen: Active electrode- Ipsilateral mastoid: Oz. Reference electrode- vertex: Cz. Ground electrode-contra lateral mastoid: Fz. The electrode impedance was kept below 5 kΩ. The low filter is set at 100 Hz and high filter at 3000 Hz. The pulse moves the earphone diaphragm away from the subject's ear, which is a rarefaction phase stimulus. Wave I amplitude is greater with rarefaction compared to condensation stimulus. Since recognition of wave I is very important, rarefaction click polarity was chosen. A 10 ms epoch after the click stimulus is averaged, amplified and displayed on the computer monitor. The click acoustic stimuli at a rate of 11 pulse per second at an intensity of 90 dB hearing level to the ear stimulated and masking sound (white noise) of 40 dB in non stimulated ear was given through head phone supplied by Medicaid (23, 24, 25). All the techniques of measurement, duration, instruments including research laboratory temperature were maintained uniformly throughout the study Parameters studied: The wave latency I, II, III, IV and V, inter peak latency I-III, I-V, III-V and amplitudes of waves were measured.

Results

In this study, BAEP was recorded in 60 decompensated chronic liver disease (DCLD) subjects diagnosed by Medical Gastroenterology unit, who fulfilled the selection criteria and compared to 60 age and gender matched healthy subjects with normal liver functions. Brainstem auditory evoked potential of both the ears was tested. Absolute and interpeak wave latencies were measured. DCLD subjects were divided into two inter groups based on presence or absence of hepatic encephalopathy (HE). Group 1 comprises of 30 subjects of grade-I HE and Group 2 included 30 subjects without hepatic encephalopathy (NHE). Results were analysed by student independent t- test using SPSS software 11 versions. Statistical significance was tested using P value. The baseline characteristics of this study and control group showed the mean age of study group is 45.18±3.76 and controls are 44.17±4.76. The mean BMI of study group is 27.55±1.22 and controls are 27.15±1.96. The gender ratio of study group to control is 1:1. There is statistically significant prolongation of absolute latencies of waves III and V and interpeak latencies I-III, I-V and III-V between DCLD and control groups. There was also significant prolongation of

TABLE I: Left ear absolute and interpeak latencies of decompensated chronic liver disease (DCLD) subjects and control group.

Variables wave latency (ms)	*DCLD subjects n=60 Mean±SD*	*Controls n=60 Mean±SD*	*P value*
I	1.44±0.05	1.44±0.05	0.62
II	2.72±0.12	2.721±0.12	0.76
III	3.70±0.16	3.53±0.07	<0.001
IV	4.92±0.09	4.89±0.07	0.06
V	5.91±0.34	5.66±0.07	<0.001
I–III	2.22±0.19	2.06±0.07	<0.001
I–V	4.47±0.37	4.19±0.09	<0.001
III–V	2.16±0.22	2.06±0.09	0.001

P≤0.05 Significant.

TABLE II: Right ear absolute and interpeak latencies of decompensated chronic liver disease (DCLD) subjects and control group.

Variables wave latency (ms)	*DCLD subjects n=60 Mean±SD*	*Controls n=60 Mean±SD*	*P value*
I	1.45±0.05	1.44±0.05	0.20
II	2.71±0.13	2.72±0.12	0.61
III	3.67±0.16	3.53±0.07	<0.001
IV	4.89±0.08	4.88±0.07	0.41
V	5.90±0.35	5.66±0.07	0.001
I–III	2.21±0.18	2.06±0.07	<0.001
I–V	4.44±0.35	4.19±0.08	<0.001
III–V	2.17±0.21	2.06±0.09	<0.001

P≤0.05 Significant.

TABLE III: Left ear absolute and interpeak latencies of hepatic encephalopathy (HE) subjects and non-hepatic encephalopathy (NHE) subjects.

Variables wave latency (ms)	*HE n=30 Mean±SD*	*NHE n=30 Mean±SD*	*P value*
I	1.44±0.05	1.44±0.05	0.62
I	1.45±0.05	1.44±0.05	0.49
II	2.73±0.12	2.72±0.12	0.76
III	3.81±0.16	3.60±0.07	<0.001
IV	4.94±0.10	4.89±0.07	0.01
V	6.15±0.35	5.68±0.08	<0.001
I–III	2.31±0.17	2.13±0.16	<0.001
I–V	4.64±0.40	4.30±0.25	<0.001
III–V	2.27±0.26	2.06±0.09	<0.001

P≤0.05 Significant.

TABLE IV : Right ear absolute latencies of hepatic encephalopathy (HE) subjects and non-hepatic encephalopathy (NHE) subjects.

Variables wave latency (ms)	*HE n=30 Mean±SD*	*NHE n=30 Mean±SD*	*P value*
I	1.45±0.05	1.44±0.05	0.20
I	1.46±0.60	1.44±0.05	0.08
II	2.70±0.14	2.72±0.12	0.56
III	3.79±0.14	3.56±0.08	<0.001
IV	4.91±0.09	4.88±0.07	0.28
V	6.51±0.35	5.66±0.07	<0.001
I–III	2.29±0.16	2.14±0.17	0.002
I–V	4.61±0.37	4.27±0.22	<0.001
III–V	2.29±0.23	2.06±0.09	<0.001

P≤0.05 Significant.

absolute latencies of waves III and V and interpeak latencies I-III, I-V and III-V between HE and NHE.

Discussion

Brainstem Auditory Evoked potential (BAEP) technique is a simple, non-invasive and safe method to implement as compared to the other brain structural or metabolic studies. There is prolongation of absolute wave latencies III, V and interpeak latencies I-III, I-V and III-V between study group and control group which is shown in tables 2 and 3 by the P value <0.05. There is significant prolongation of absolute wave latencies III, V and interpeak latencies I-III, I-V and III-V between interstudy group having grade I hepatic encephalopathy which is shown in tables 4 and 5 by the P value <0.05.

Our data is therefore in agreement with most other studies and indicates that BAEP can be a useful technique in the evaluation of hepatic encephalopathy. The influence of alcohol on the BAEP latencies has been referred to in some studies. In our study, the BAEP latencies were not different in alcoholic and non-alcoholic cirrhotics. From the results of the present and several other studies, a significant influence of alcohol ingestion alone and alcoholism as a cause of chronic liver disease on the latencies seems to be unlikely. In fact, studies have shown that the degree of dysfunction detected by BAEP in patients with cirrhosis appears related to the reduction in hepatic metabolic capacity. This is the study documenting the prevalence of HE using a highly validated electrophysiological test, which has been recommended for measuring this disorder, which is difficult to diagnose, but is very important for future prognosis. Till the time a gold standard is derived for detection of HE, BAEP latencies seem to be a suitable method for detection as well as follow up of patients (26). The wave I is not prolonged due to non involvement of the cochlear nerve. Prolongation of other waves, which was observed in this study, was in consonance to findings of other authors. The increase in latencies in HE is more significant for the later waves III and V than for earlier waves and interpeak latencies I- III, I-V and III-V. The increase in latencies indicates that the conduction were slower in pontine and midbrain regions of HE subjects. Moreover, all studies were only concerned about one value of BAEP variable without explaining the ear side.

Conclusion

From the present study it can be concluded that the central nervous system are involved in liver cirrhosis evidenced by an abnormal BAEP latencies parameters. There was a significant worsening of the condition as the duration of the disease increases in the central nervous system. This shows that there may be progressive demyelination occurring along with axonal loss or in liver cirrhosis HE. This study suggests that periodic evaluation of cirrhotic individuals to such test will help in monitoring the progress of encephalopathy. The prime goal of the study is early diagnosis and initiation of treatment before the onset of coma can reduce the fatality rate.

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