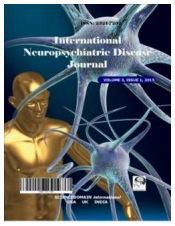

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Relevance of Brain Stem and Visual Evoked Potentials in Diagnosis of Central Demyelination in Guillain Barre Syndrome

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

Aims: Guillain Barre Syndrome (GBS) is an auto-immune mediated demyelination polyradiculo-neuropathy. Clinical features include progressive symmetrical ascending muscle weakness of more than two limbs, areflexia with or without sensory, autonomic and brainstem abnormalities. The purpose of this study was to determine subclinical neurological changes of CNS with GBS & to establish the presence of central demyelination in GBS.
Study Design: A prospective study to find out early Central demyelination in clinically diagnosed patients of GBS.
Place and Duration of Study: Department of Physiology, Pt. B.D. Sharma Post-Graduate Institute of Medical Sciences, University of Health Sciences, Rohtak, Haryana, India, between January 2014 and June 2015.
Methodology: The patients were referred from the Department of Medicine to our Department for electro-diagnostic evaluation. The study group comprised of 40 subjects (20 clinically diagnosed GBS patients and 20 healthy individuals) aged between 6-65years. Brain stem and visual evoked potentials were done in both groups using RMS EMG EP Mark II machine. BAEP parameters included the latencies of waves I to IV, inter-peak latencies I-III, III_IV & I-V while VEP included latencies of P100 waves.

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Results: Statistically significant increase in absolute peak and inter-peak latency in the GBS group as compared to the control group was noted. Prolongation of latency of P100 wave latency in both the right and left eyes was also recorded in the GBS group.
Conclusion: Results of evoked potentials reflect impairment of auditory and visual pathways probably due to focal demyelination in Schwann cell derived myelin sheaths that cover the extra-medullary portion of the auditory nerves and also due to demyelination of optic pathways. Prolonged central conduction time in BAEPS & VEPS suggest the subclinical auditory and optical involvement in GBS. Early detection of the sub-clinical abnormalities is also important as timely intervention reduces morbidity and mortality.

Keywords: Demyelination; Guillain Barre Syndrome; evoked potentials; brainstem; visual.

1. INTRODUCTION

GBS is an autoimmune mediated de-myelinating polyradiculoneuropathy. Males and females are equally at risk. Clinical features include progressive, symmetrical ascending muscle weakness of more than two limbs, areflexia with or without sensory, autonomic and brainstem abnormalities. Weakness is predominant in leg muscles as compared to arms. Cranial nerve involvement may affect airway and facial muscles, eye movements and swallowing [1]. It usually presents with numbness and tingling in feet. [2]. In 1949, Haymaker & Kernuhan reported the histo-pathological features of 50 fatal cases of GBS. The earliest features were edema of proximal nerves followed by degeneration of myelin sheath within the 1st week of illness [3]. Electrodiagnosis plays an important role in early detection & characterization of inflammatory de-myelinating polyradiculopathies [4,5]. The reported incidence rates for GBS are 1to 2/10,000 population [6,7]. Nerve conduction abnormalities become more prominent during the initial weeks of the disease even if patients clinical status is improving [8,9]. Early nerve conduction findings include abnormal or absent F waves with low CNAP's, an abnormal upper extremity sensory nerve action potential combined with normal sural response [4,5]. Although the cranial nerves are often involved in GBS, the optic nerves are usually spared; presumably, they are part of central nervous system [10]. A few studies have revealed optic nerve involvement and evoked potential abnormalities in GBS [11-14].

2. MATERIALS AND METHODS

2.1 Aims

The primary purpose of the study was to determine the change in auditory and visual evoked potential & to establish the presence of the central demyelination in GBS in 1st week of illness.

The present study was carried out on clinically diagnosed cases of GBS in the 1st week of illness that were sent for electrophysiological studies to the Dept of Physiology from the Dept of Medicine (University of Health Sciences, Rohtak) which is a tertiary referral facility for a large part of North West India.

The study was conducted on 40 subjects (20 diagnosed with GBS and 20 as control group) between the age group of 6-65 yrs using RMS EMG EP Mark-II, Chandigarh. There was no issue of ethical committee approval during this study as the patient were referred from dept. of medicine of our institute for electrical evaluation.

The criteria for clinical diagnosis of GBS was according to Dutch Guillain Barre group criteria [15].

2.2 Exclusion Criteria

Prior neurological illness, apparent hearing and visual impairment, botulism, myasthenia gravis, poliomyelitis, toxic neuropathy.

For selecting the normal healthy controls, a thorough clinical examination was conducted.

2.3 Measurement Protocol Includes

The recording was done by using RMS EMG EP MK2 machine, Chandigarh.

2.4 Brainstem Auditory Evoked Potential

BAEP are potentials recorded from the ear & vertex in response to brief auditory stimulations to assess the conduction through auditory pathways upto midbrain. When sound reaches the cochlea it is converted into electrical impulse and passes from cochlea to auditory cortex through the following pathway as: Spiral ganglion in coclea ventral & dorsal cochlear nuclei in brain stem superior olivary nucleus in pons lateral

lemniscus in midbrain inferior colliculus in midbrain medial geniculate body in thalamus auditory area in cerebral cortex.

The normal BAEP consists of 5 or more vertex positive and vertex negative waves arising within 10ms of auditory stimulus which are labeled using Roman nomenclature.

Waveforms	Generators
I	VIII nerve
II	Cochlear nucleus
III	Superior Olivary nucleus
IV	Lateral Lemniscus
V	Inferior Colliculus

2.5 Interpeak Latencies (IPLs)

The commonly used IPLs in clinical slide are

I-III – It is the latency difference between waves III & I & it is used as a measure of acoustic nerve across subarachnoid space into the core of the lower pons (peripheral conduction time).

III-V – It is the latency difference between wave III-V & is a measure of conduction from lower pons to midbrain (central conduction time).

I-V – It is the latency difference between waves V & I & is a measure of conduction from proximal auditory nerve through pons to midbrain (total conduction time).

2.6 Equipment setup for BAEP

Stimulus parameters: Auditory click stimuli having intensity 90dB above normal hearing threshold will be presented to both the ears monoauraly. During stimulation in one ear, the passing 1ms square pulses through shielded headphones to both ears. Rate of stimulation was 11.1 per sec.

Filters – Low – 100 Hz
High – 3 KHz

Recording electrodes for BAEPs – The volume conducted evoked responses are picked up from the scalp by using disc type of Ag/AgCl electrodes placed as per 10-20 international system of placement. Two reference electrodes will be attached to left & right mastoid designated as A1 & A2 respectively, one active electrode is placed over the vertex labeled as Cz and one as ground electrode to the forehead labeled as Fz. All the electrodes will be plugged into function box. Skin to electrode impedance will be monitored and kept below 5 KΩ.

2.7 Recommended Montage for BAEPs

Channel 1 – Cz-A1
Channel2 – Cz-A2
Ground – Fz

The signals will be picked up by the electrodes and will be filtered, amplified, averaged, displayed on screen of evoked potential recorder (RMS EMG EP MK2) & recorded. [16].

Absolute peak wave latency of wave I,III,V & interpeak latencies I-III, III-V, I-V were recorded for each ear separately.

2.8 Measurement of Visual Evoked Potential (VEP)

VEP s are electrical potential difference recorded from the scalp in response to visual stimuli. It is primarily reflection of activity originating in the central 3º to 6º of visual field which is related to the surface of occipital lobe.

2.9 Statistical Analysis

Excel p value<0.05 denotes statistically significant values.

3. RESULTS AND DISCUSSION

The mean of absolute peak latency were statistically significant higher in the case groups as compared to the controls in both the ears ($p<0.001$) whereas the mean of interpeak latency were statistically significant higher for iii-v ($p<0.05$) in right ear & for iii-v, i-v in left ear ($p<0.05$), though the mean value was higher for i-v, i-iii in right ear and also for i-v in left ear. The mean latency of visible evoked potentials was statistically significantly higher in case groups as compared to control in both the eyes ($p<0.001$).

4. DISCUSSION

The present study is an effort to evaluate central nervous system involvement in patients of GBS in tertiary care hospital in Haryana. GBS is pathophysiologically characterized not only by reversible conduction failure at the axolemma of the nodes of Ranvier. The lack of distinction among demyelinating conduction block, reversible conduction failure &compound muscle action potential reduction may fallaciously classify patients with axonal GBS as having AIDP [17].

Table 1. Right side Brainstem Evoked Potential (BERA)

Right side BERA						
	I	III	V	I-III	I-V	III-V
Cases	2.14±0.42	4.11±0.34	6.23±0.36	1.92±0.4	4.03±0 .49	2.11±0.35
Control	1.45±0.17	3.4±0.26	5.46±0.26	1.95±0.3	3.96± 0.32	1.92±0.29
P value	2.13977E-07	6.32E-09	3.45E-09	0.415038	0.316804	0.033974

Unit of latency- milliseconds

Table 2. Left side Brainstem Evoked Potential (BERA)

Left side BERA						
	I	III	V	I-III	I-V	III-V
Cases	1.92±0.37	4.06±0.54	5.16±0.6	2.14±0.43	4.41±0 .57	2.28±0.36
Control	1.52±0.19	3.57±0.27	4.5±0.26	2.06±0.31	4.02 ±0.32	1.94±0.27
P value	7.55E-05	0.00057	9E-06	0.2597	0.005878	0.002889

Unit of latency- milliseconds

Table 3. Visual evoked potential latency

VEP P100		
	Right	Left
Cases	106.52±6.53	107.72±9.76
Control	98.91±3.76	99.05±3.35
P value	4.42E-05	0.000496

Unit of latency- milliseconds

Results of evoked potentials reflect impairment of auditory & visual pathways as the BAEPs show stastistically significant prolongation of latencies of waves I,III & V and prolonged interpeak latency of III-V in right ear and for III-V,I-V in left ear.

The findings of BAEPs are comparable and show similarity with the results of study done by Zgorzalewicz et al. [11] except an additional finding of IPL III-V prolongations in present study, which is similar to the study of Ghildiyal [18]. Shiff [19] also found prolonged I-III IPL in five of six patients of GBS & I-V IPL in two of six patients . He also observed prolongation of I-II IPL which is not found in the present study.

The most likely cause of these BAEP abnormalities is demyelination in Schwann cell derived myelination sheath that covers the extramedullary portion of the auditory nerves. In the present study, prolongations of I-V IPL suggest the abnormality of conduction of auditory signals from the proximal part of auditory nerve to the mesencephalon via pons & prolongation of III-V IPL suggest abnormality of conduction from lower pons to midbrain(central conduction time).

VEPs recordings in case group showed prolongations of wave P100 latency in both the eyes which suggests involvement of visual pathway, most probably due to demyelination of optic pathway. These findings also showed resemblance with the studies done by Zgorzalewicz [11], Ghildiyal [18] and Levent Gunger [20].

It has been established that P100 waveform is generated due to activation of primary visual area as well as association area [21].

The result of present study showed prolongation of central conduction in BAEPs and VEPs observation.

5. CONCLUSION

GBS is regarded as a predominantly motor neuropathy with transient or absent sensory features. GBS mainly affects the peripheral nervous system but there are few studies, which have reported involvement of central nervous system, though it is not frequent. The present study showed prolonged central conduction time in BAEPs & VEPs. Our observation suggests the subclinical auditory & optic pathway involvement in GBS because none of the patients complained of hearing and visual defects. These findings are compatible to demyelination. Electrodiagnostic techniques play important role in early detection of inflammatory demyelinating poly-radiculopathy to reduce the duration, severity & complications of the disease.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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