

BRAINSTEM AUDITORY EVOKED POTENTIAL AS AN INDEX OF CNS DEMYELINATION IN GUILLAIN -BARRÉ SYNDROME (GBS)

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ABSTRACT

Background: Guillain-Barré Syndrome (GBS) is an acute, frequently severe and fulminant polyradicular neuropathy that is autoimmune in nature. GBS manifest as rapidly evolving areflexic motor paralysis with or without sensory disturbances. It mainly involves peripheral nervous system and autonomic nervous system. There are rare evidences about the involvement of central nervous system (CNS) in GBS. **Aims:** The main objective of the study was to assess the CNS involvement in GBS using the Brainstem Auditory Evoked Potential (BAEP). **Methods & Material:** The study was conducted in the clinical neurophysiology lab in the department of physiology, CSMMU Lucknow. Study group involved 26 subjects (n=26) having GBS and control group involved 30 normal subjects (n=30). BAEPs were recorded by Neuroperfect- EMG 2000 EMG/NCV/EPsystem. The data so obtained were subjected to analysis using Statistical Package for Social Sciences (SPSS) Version 13.0. **Results & Conclusions:** There was significant increase in PIII & PV peak latencies and PI-PIII & PI-PV interpeak latencies in both left and right ear in the study group, which showed the CNS involvement in GBS which can be assessed using BAEP.

INTRODUCTION

Guillain-Barré Syndrome (GBS) is an acute, frequently severe and fulminant polyradicular neuropathy that is autoimmune in nature. GBS manifest as rapidly evolving areflexic motor paralysis with or without sensory disturbances. The usual pattern is ascending paralysis i.e. weakness begins in distal limbs but rapidly advances to affect the proximal muscle functions. Lower cranial nerves are usually involved causing bulbar weakness and difficulty with handling secretions and maintaining airways. Deep Tendon Reflexes (DTR) usually disappears within in 1st few days of onset. Bladder dysfunction if present is usually transient. It occurs year-round at a rate of between 1 and 4 cases per 100,000 annually. Males are at slightly higher risk for GBS than females, and adults are more frequently affected than children^[1].

In severe cases of GBS autonomic involvement is common. Usual features are loss of vasomotor control with wide fluctuation in blood pressure, postural hypotension and cardiac dysrhythmias. Pain is another common feature of GBS most common is deep aching pain in weakened muscles. It is an autoimmune disease with approximately 70% of cases occurring 1–3 weeks after an acute infectious process, usually respiratory or gastrointestinal^[1]. GBS shows mainly two types of pathophysiology, demyelinating form and axonal degeneration. Basis of demyelinating form is conduction block, which results in flaccid paralysis and sensory disturbances. Recovery is possible as remyelination occurs. Axonal degeneration shows slow rate of recovery and results in greater degree of residual

disability. CSF shows albuminocytological dissociation that is elevated CSF protein level (100-1000gm/dl) without accompanying pleocytosis. CSF usually remains normal when duration of illness is less than 48 hours. CSF protein level increases at the end of first week of illness. Electrodiagnostic features are mild or absent in early stages and lag behind clinical evolution. Demyelinating form shows prolonged distal latencies, slow conduction velocities, conduction block and temporal dispersion of compound action potential. Axonal form shows decrease amplitude of compound action potential without conduction slowing and prolongation of latencies. There are several clinical, pathologic and electrophysiologic evidences that have established that GBS affects predominantly the peripheral nervous system. Focal demyelination of the Schwann cell derived myelin has been described. Neuropathologic and electrophysiologic evidences for involvement of central nervous system are rare. There are few studies^[2, 3, 4, 1] which have been performed to explore the involvement of CNS in GBS. However, there exists no study in the Indian environment regarding the same.

The present study is an effort to explore the CNS involvement in GBS by measuring auditory evoked potentials. This test evaluates the integrity of auditory (Brainstem Auditory Evoked Potential) pathway by measuring evoked potentials. Evoked potentials are recorded as electronic impulses by surface electrodes attached to the scalp. A computer extracts these low

amplitude impulses from background brain wave activity and averages the signals from repeated stimuli. Brainstem auditory evoked potentials, produced by delivering clicks to the ear, and help to locate auditory lesions and evaluate brainstem integrity.

MATERIAL & METHODS

Clearance from the institutional ethical committee was obtained written informed consent had been taken from the entire subjects study and control group. The study was conducted on clinically diagnosed cases of GBS of both sexes. For selecting the normal healthy controls a thorough clinical examination was conducted. It was ensured that the subjects included as controls do not have any apparent clinical illness that may affect the evoked potentials. The subjects were diagnosed on the basis of history, clinical examination, and typical CSF profile (albuminocytological dissociation) and electrophysiological evidences of demyelination. Subjects having prior neurological illness, apparent hearing and visual impairment, AFP due to another cause were excluded from the study group. A total of 30 subjects were included in the study and 26 subjects were included in the control group. All the subjects of study and control group were tested under similar laboratory conditions. Subjects were given sufficient time to relax rapport had been established so that they feel comfortable and cooperate during investigation

Recordings of BAEPS:

BAEPS were recorded by Neuroperfect- EMG 2000 EMG/NCV/EP sytem. The EPs were recorded with disc electrode from standard scalp location.

Electrode were placed at vertex (Cz,reference electrode), ipsilateral and contralateral mastoid process (Ai and Ac active electrode) and forehead (Fz, ground electrode) after proper cleaning the scalp or skin site with alcohol followed by EEG conducting paste.

For recording 2000 click stimuli at the rate of 11Hz/sec with duration of 0.1 ms were delivered at 70 dB. The other ear was masked by pure white noise at 40 dB. This click generated by passing 0.1 ms square pulses trough shielded headphone. Electrical impedance was kept less than 5 kilo ohm. Peak latencies of all the waves I., II, III,IV and V and interpeak latencies of I-III,II-V and I-V were determined for both right and left ears separately.

STATISTICAL ANALYSIS: The data so obtained were subjected to analysis using Statistical Package for Social Sciences (SPSS) Version 13.0. The data has been shown as mean±SD, to compare the difference between the normal and healthy controls; “t” test for independent samples has been carried out. The confidence limit of the study was kept at 95%, hence a “p” value less than 0.05 denoted statistically significant difference.

RESULTS:

Table 1: Peak Brainstem Auditory Evoked Potentials for Left& Right Ears

Peak Order	Left Ear		Right Ear	
	Control Group (n=30)	Study Group (n=26)	Control Group (n=30)	Study Group (n=26)
PI	1.59±0.11	1.56±0.23	1.59± 0.10	1.67±0.33
PIII	3.25±0.15	3.51±0.18***	3.25±0.13	3.59±0.24***
PV	5.67±0.22	6.00±0.53**	5.42±0.23	5.74±0.57**

** p<0.01, *** p<0.001

Table 2: Inter-peak latencies for BAEP for Left& Right Ears

Inter-Peak Difference	Left Ear		Right Ear	
	Control Group (n=30)	Study Group (n=26)	Control Group (n=30)	Study Group (n=26)
PI-PV	4.08±0.19	4.41±0.55**	3.84±0.21	4.07±0.46*
PI-PIII	1.65±0.12	1.96±0.21***	1.66±0.12	1.92±0.21***
PIII-PV	2.43±0.19	2.48±0.48	2.18±0.17	2.15±0.52

* P<0.05, ** p<0.01, *** p<0.001

DISCUSSION

Guillain-Barre syndrome (GBS) is regarded as a predominantly motor neuropathy with transient or absent sensory features. Although the central nervous system is rarely involved, GBS associated with CNS, manifestations has been described in children by Okumura et. al (2002)^[6] and in adults by Maier H et. al.(1997)^[3], and Muller HD et. al.(2003)^[4]. Maier H et. al. (1997)^[3] observed histopathological changes in CNS of GBS patients. He found infiltration of macrophages microglial cells and/or lymphocyte in different areas of central nervous system. Spinal cord and brainstem shows lymphocytic infiltration and microglial activation. Histopathological feature of CNS involvement is also observed by Muller HD et. al. (2003)^[4] in form of the cellular infiltration of spinal cord though not very significant and suggested CNS involvement in GBS occur, though rare. There are few studies which had demonstrated CNS (changes) lesion in GBS on neuroimaging.

Nadkarni N et. al.(1993)^[7] observe MRI finding of CNS white matter lesion in patient of GBS who had developed symptoms of optic neuritis after plasmapheresis. These findings suggest there may be possibility of same antigenic mechanism of pathogenesis in CNS as well as peripheral nervous system.

Okumura et. al. (2002)^[6] reported the clinical course and electrophysiological and neuroimaging of a patient of GBS associated with CNS lesion. He found mild slowing of background activities without paroxysmal discharge in electroencephalogram (EEG), mildly prolonged N₂ latency with abnormal waveform in VEPs. BAEPs were unremarkable. In magnetic resonance imaging (MRI) there were multiple lesions in cortex and sub-cortex in the right occipital lobe and in the deep white matter in both frontal lobes. Despite all these lesions there was no evident CNS manifestation in the case.

This implies that an association of CNS involvement in patients with GBS could be under estimated because some lesions can be clinically silent.

The present study was an effort to evaluate central nervous system involvement in patients of GBS in Indian population because there is no study regarding the same performed in the India. In the view of known pathologic involvement of most proximal portion of peripheral nerves in GBS, the most likely cause of these BAEP abnormalities is focal demyelination of Schwann cell derived myelin sheath that covers the extra medullary portion of the auditory nerves.

Prolongation I-III IPL indicative of lesion in the auditory nerve to medullary junction or lower pons around superior olive trapezoid body. The prolongation of I-V IPL suggests the abnormality of conduction of auditory signals from the proximal auditory nerve to the mesencephalon via pons.

The findings of the study of BAEPs are comparable and show similarity with the results of study done by Zgorzalewicz M et. al. (2003)^[8], except there is an additional finding of IPL III-V prolongation in our study.

In the study done by Schiff JA et. al. (1985)^[9] had also found prolonged I-III inter peak latencies (IPL) in five of six patients of GBS and I-V IPL in two of six patients, these results are comparable with the present study. Ropper AH et. al. (1986)^[11] also find the BAEP abnormality in the form of I-III and III-V IPL prolongation

in patients of GBS, though that was not clinically significant

Whereas Nelson KR et. al. (1988)^[11], find the BAEPs abnormality in patients of GBS as prolongation of wave II latency and total absence of BAEM wave form in the early stage of disease and with the complaints of sudden onset of deafness, hearing improved with the recovery and BAEP abnormality of conduction block was replaced as a prolongation of wave I latency. After convalescent period, BAEPs become normal. In present study there was no case present as similar complaint and BAEPs finding.

Topcou M et. al. (1993)^[12] had performed evoked potential study in patients of GBS and found BAEPs and VEPs values were abnormal in some patients during early course of illness, though the values were not statistically significant.

Wong V et. al. (1997)^[13] had found BAEPs abnormality in Miller Fischer syndrome (MFS), a variant of GBS. His findings of BAEPs abnormalities suggest proximal auditory nerve and brainstem involvement.

CONCLUSION

Thus it can be concluded from our study that though often ignored, the central nervous system demyelination does occur in Guillain-Barré Syndrome (GBS) and the same can be assessed using evoked potentials like Brainstem Auditory Evoked Potentials (BAEP). But a randomized controlled study with sufficiently large number of patients and proper blinding is needed to conclusively establish the fact.

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CONFLICT OF INTEREST: None

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