Current Neurobiology 2012; 3 (2): 117-122 ISSN 0975-9042

Central Demyelination in Guillain-Barre syndrome.

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Abstract

Guillain- Barre syndrome (GBS) is an acute inflammatory demyelination polyrediculoneuropathy which may lead to tetraparasis. GBS mainly affects the peripheral nervous system (PNS) .The present study is an effort to explore the CNS involvement in GBS. A case control study was conducted in North Indian population. 26 subjects with GBS and 30 normal subjects (control) were selected from Department of Medicine, Neurology and Paediatrics, CSMMU, Lucknow. We used Neuro-perfect 2000 EMG/NCV/EP system to collect, analyse, print and store evoked potential data. Result indicates that the mean interpeak latency difference was significantly higher in study group in both Ears. Statistically a significant difference was seen between two groups for both eyes with mean value for latencies in study group being higher as compared to control group. Prolonged central conduction time in Brainstem auditory evoked potentials (BAEPs) and Visual evoked potentials(VEPs) suggest the subclinical auditory and optical pathway involvement in GBS.

Key words: Guillian –Barre Syndrome (GBS), Demyelination, evoked potential.

Accepted November 20 2012

Introduction

Gullian –Barre Syndrome (GBS) is an acute onset immune mediated disorder of the peripheral nervous system. The term GBS is often considered to be synonymous with acute inflammatory demyelinating polyradicular neuropathy (AIDP), but with the increasing recognition over the past few decades of variants, the number of diseases that fall under the rubric GBS have grown to include axonal variants and more restricted variants such as Miller Fisher syndrome. (MFS) [1,2]. GBS affects both genders, involves people of all ages, and in the post-polio era, it is the most common cause of an acute generalized paralysis. The clinical features are distinct and on examination generally lead to a high suspicion of the diagnosis that can be confirmed by supportive laboratory tests and electrodiagnostic studies [3].The clinical features of GBS were described by Landaryin 1859[4]. In 1949, Haymaker and Kernohan described the clinical and histopathological features, including the inflammatory changes of the peripheral nerves in 50 fatal cases of GBS [5].

The reported incidence rates for GBS are 1 to 2 per 100,000 populations [6-8]. The lifetime likelihood of any individual acquiring GBS is 1:1000 [9]. Any other unremarkable infection, such as an upper respiratory infection often predates the onset of GBS by 10 to 14 days [6, 9]. Neurological examination will demonstrate distal and often proximal relative symmetrical weakness. Sensory examination is often normal in the early phase of the disease [10]. Widespread areflexia or hyporeflexia is the rule [11,12]. Approximately one third of hospitalized GBS patients require mechanical ventilation because of respiratory muscle or oropharyngeal weakness [2, 3, 5, 6, 10, 13-19]. Autonomic disturbances are seen in more than 50% cases [20-26]. In early GBS, prolonged distal compound muscle action potential (CMAP) latencies and temporal dispersion are more commonly demonstrated than slow motor conduction velocities and conduction block [27-29]. On the other hand, temporal dispersion was seen in at least in nerve in more than 50% cases and significantly prolonged distal CMAP latencies were seen in at least one nerve of approximately two third of the patients studied within the first week [29].

The primary purpose of the study was to determine the change in auditory and visual evoked potential and establish the presence of the central demyelination in Guillian-Barre syndrome (GBS).

Material and Methods

This is a case control study conducted in the North Indian population. Subjects were divided into study and control groups. Study group comprised of 26 people with Guillian-Barre syndromes (GBS) and control group comprised of 30 age-matched healthy people without GBS. For this purpose cases and controls were selected from Depart-

ment of Medicine, Neurology and Paediatrics, King George's Medical University, Lucknow.

A structured Performa was filled to collect the information regarding their medical, personal, family and dietary history. The study was approved by the ethical committee of KGMU, Lucknow. Written consent was obtained from all the participants.

Subject selection

Inclusion Criteria: Progressive weakness of two or more limbs due to neuropathy, Areflexia, course of disease less than four weeks, relative symmetric weakness, mild sensory involvement, absence of fever, Typical cerebro- spinal fluid profile (albumin-cytological dissociation), electrophysiological evidence of demyelination.

Exclusion Criteria

Prior neurological illness, apparent hearing and visual impairment, Botulinism, Myasthenia, Poliomyelitis, toxic neuropathy, abnormal porphyrin metabolism and purely sensory syndrome without weakness.

For selecting the normal healthy controls, a thorough clinical examination was conducted. It was ensured that the subjects included as controls didn't have any apparent clinical illness that may affect the evoked potentials.

Measurement Protocol includes Neuroperfect-EMG 2000 EMG/NCV/EP system to collect, analyze, print and store evoked potentials data. Evoked potentials are voltage change monitored from the electrically excitable tissue of the cerebral cortex, brainstem and spinal cord in response to various applied sensory stimuli. The functions of three different CNS sensory areas (Somato- sensory cortex, the visual cortex and the auditory region of the brainstem) can be evaluated using electrophysiological tests.

To test these areas, appropriate sensory modality was examined under the normal circumstances. The sensory stimuli activated the respective sensory receptor and action potentials were initiated and propagated and peripheral and/or central nervous system pathways and subsequently altered the electrical activity of the cerebral cortex cell that was associated with the processing of the incoming sensory information. The change in the electrical activity of the cortical area was monitored by the use of surface recording electrode placed over the appropriate regions of the cortex or brainstem.

Measurement of BAEP (Brainstem auditory evoked potentials)

The subjects were asked to lie down supine on the coach in relaxed position. Brainstem auditory evoked potentials (BAEPs) were recorded from the ear and vertex in response to brief auditory stimulation to assess the conduction through auditory pathway up to mid brain.

There were five or more distinct waveforms recorded within 10ms of the auditory stimulus. In 1990 Chiappa KH emphasized:*wave I* originates from peripheral portion of VIII cranial nerve adjacent to cochlea; *wave II* originates from cochlear nucleus; *wave III* from superior olivary nucleus; *wave IV* from lateral lemniscus and *wave V* from inferior colliculi.

I-V inter peak latency(IPL)- the latency difference between wave V and wave I is a measure of conduction from proximal VIII nerve through Pons to mid brain. The typical upper limit of normal I-V IPL is 4.5ms. Normal right to left asymmetry should not be more than 0.5ms. I-V IPL prolongation is usually seen in focal damage produced by demyelination.

I-III inter peak latency - the latency difference between wave III and I is a measure of conduction from VIII nerve across subarachnoid space into the core of the lower pons. The upper limit of normal for I-III IPL is about 2.5ms and right and left asymmetry should not be less than 0.5ms. Prolongation of I-III IPL indicates involvement of proximal portion of VIII nerve, pontomedullary junction or lower pons around superior olive or trapezoid body.

III-V interpeak latency - It is a measure of conduction from lower pons to mid brain .Upper limit of III-V IPL is 2.4ms and right and left asymmetry should be less than 0.5ms. Prolongation of III-V IPL is considered abnormal when associated with prolongation of I-V IPL also.

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

Measurement of VISUAL EVOKED POTENTIAL (VEP)

Visual evoked potential (VEP) is primarily reflection of activity originating in the central 3^0 to 6^0 of visual field, which is related to the surface of occipital lobe. Visual evoked potentials are electrical potential differences recorded from the scalp in response to visual stimuli. The VEPs represent a mass response of cortical activity possibly the subcortical areas. It consists of a series of waveform of opposite polarity. Negative waveform is denoted as "N" & positive deflection as "P", which is followed approximate latency in ms. The commonly used waveforms are N_{75}, P_{100}, $N_{145.}$

P_{100} of VEP is generated in the striate and peristriate occipital cortex not only due to activation of primary cortex but also due to thalamocortical volleys. The exact generator sources and temporal sequence of these are not well defined. On giving pattern of flash stimulation, not only is

there increased metabolism in 'primary visual area' but also in the 'visual association areas' (area 18 &19) (Phelps et al; 1981).

Normal cortical responses are obtained if the entire visual system is intact and disturbances anywhere in visual system produce abnormal VEPs, therefore the localizing value of VEP is limited. Each experiment was repeated twice with a comfortable time gap in order to avoid bias owing to repetition.

StatisticalAnalysis

The data so obtained were subjected to analysis using statistical package for social science (SPSS) version 13.0. Data has been shown as mean ±SD to compare the difference between the subjects of study group and healthy control group. "t" test for independent samples was carried out. The confidence limit of the study was kept at 95%, hence a "P" value less than 0.05 denotes statistically significant difference.

The mean interpeak latency difference were significantly higher in study group in both Ear for I-V (P= 0.003) & (P= 0.015) and I-III (P< 0.001) & (P< 0.001), However there was no statistically significant difference between the two groups for interpeak latency difference III-V, though the mean value was higher for study group as compared to control group.

The mean visible evoked potentials in control group 98.67± 1.65, 99.25 2.30 and 98.99±2.55 respectively for both eyes left eye and right eye respectively where as in study group these were 105.42±7.64, 107.46± 7.27 and 108.58± 6.51 respectively, statistically a significant difference was seen between two groups for both eyes, left eye and right eye with mean value for latencies in study group being higher as compared to control group.

Observations and Results

Table 1. *Peak Brainstem Auditory Evoked Potentials for Left Ear in Two groups*

S.No	Absolute Peak Latency	Control Group (n=30) (ms)	Study Group (n=26) (ms)	Statistical Significance	
				"t"	"p"
1.	I	1.59±0.11	1.56±0.23	0.712	0.480
2.	III	3.25±0.15	3.51±0.18	6.017	<0.001
3.	V	5.67±0.22	6.00±0.53	2.996	0.004

❖ *On comparing the study and control group: Statistically no significant difference was seen for P1.Whereas statistically significant difference was seen for P111 and PV.*

Table 2. *Inter peak latencies for Brain Stem Auditory Evoked Potentials for Left ear in two groups*

S. No	Interpeak Latency (IPL)	Control Group(n=30)(ms)	Study Group (n=26)(ms)	Statistical Significance	
				"t"	**"p"**
1.	I-V	4.08±0.19	4.41±0.55	3.080	0.003
2.	I-III	1.65±0.12	1.96±0.21	6.823	<0.001
3.	III-V	2.43±0.19	2.48±0.48	0.566	0.574

Mean interpeak latency differences were significantly higher in study group for I-V(p=0.003) and 1-III(p<0.001),however there was no statistically significant difference between the two groups for interpeak latency difference for III-V,though the mean value was higher for study group as compared to control group.

Table 3. *Peak Brainstem Auditory Evoked Potentials for Right Ear in Two groups*

S.No	Absolute Peak Latency	Control Group (n=30)(mv)	Study Group (n=26)(mv)	Statistical Significance	
				"t"	"p"
1.	I	1.59±0.10	1.67±0.33	1.300	0.199
2.	III	3.25±0.13	3.59±0.24	6.728	<0.001
3.	PV	5.42±0.23	5.74±0.57	2.752	0.008

Table 4. *Interpeak latency for Brain Stem Auditory Evoked potentials for Right ear in two groups*

S.No	Absolute Peak Latency	Control Group (n=30)(mv)	Study Group (n=26)(mv)	Statistical Significance	
				"t"	"p"
1.	I-V	3.84±0.21	4.07±0.46	2.515	0.015
2.	I-III	1.66±0.12	1.92±0.21	5.894	<0.001
3.	III-V	2.18±0.17	2.15±0.52	0.312	0.756

Mean interpeak latency differences were significantly higher in study group for IPL I-V(p=0.015) and I-III(p=<0.001),however there was no statistically significant difference between the two groups for IPL difference III-V,though the mean value was higher for study group as compared to control group.

Table 5. *Visual Evoked Potentials for both groups*

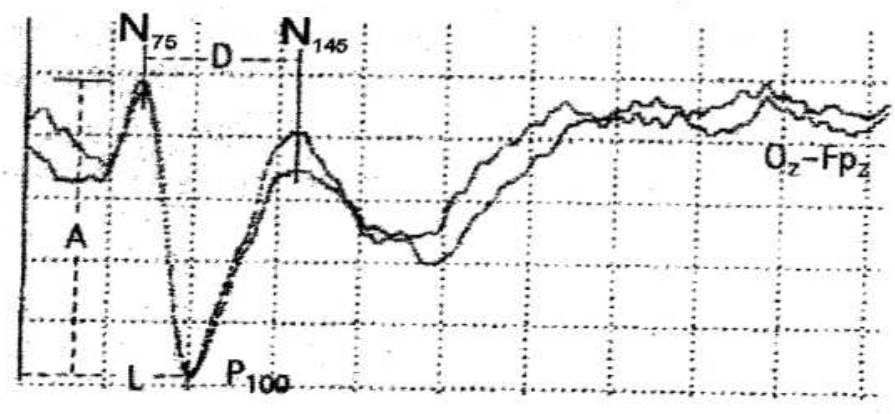
S.No	Eye	Control Group (n=30)(ms)	Study Group (n=24)(ms)	Statistical Significance	
				"t"	"p"
1.	Both Eye	98.67±1.65	105.42±7.64	4.708	<0.001
2.	Left Eye	99.25±2.30	107.46±7.27	5.841	<0.001
3.	Right Eye	98.88±2.55	108.58±6.51	7.486	<0.001

Statistically significant difference was seen between two groups for both eyes,Left eye and Right eye with mean value for latencies in study group being higher as compared to control group.

Recordings:

Pathologic BAEP of a Patient(with GBS) having higher interpeak latency.

VEP Recording:



Measurement of P_{100} L-Latency, D- Duration, A= Amplitude.
Sweep speed 50 ms/div, sensitivity 2µV/div (Mishra Kalita 2006)

On comparing the control and study group statistically, no significant difference was seen(p=0.199).However statistically significant differences were seen for wave III and V.

Discussion

The present study is 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 India. GBS is pathophysiologically characterised not only by axonal degeneration but also by reversible conduction failure at the axolemma of the Ranvier node. The lack of distinction among demyelinating conduction block, reversible conduction failure and length-dependent compound muscle action potential amplitude reduction may fallaciously classify patients with axonal GBS as having AIDP [30]. Results of evoked potentials reflected impairment of auditory and visual pathways as the brainstem auditory evoked potentials (BAEPs) show statistically significant prolongation of latencies of wave III-and V, and prolonged inter peak latency (IPL) of I-V

and I-III in right and left ears. The findings of the study of BAEPs are comparable and show similarity with the results of study done by Zgorzalewicz et al [31] except an additional finding of IPL III-V prolongation in present study. Prolong I-III IPL is indicative of lesion in the auditory nerve, Ponto- medullary junction or lower pons around superior olive or trapezoid body.

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 in Schwann cell derived myelin 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.

Here, VEPs recordings in study group showed prolongation of wave P_{100} latency in right and left eyes with the amplitude within normal limit which suggests involvement of visual pathway, most probably due to demyelination of optic pathway. These findings also showed resemblance with the study done by Zgorzalewicz (2003) in which he observed the prolongation of wave P_{100} latency along with prolongation of wave N_{145}.

It has been established that P_{100} wave form is generated due to activation of primary visual area as well as association area; Pheleps et al [32]. Though P_{100} wave abnormities cannot localize the exact anatomical site of lesion, still it gives a glance of impairment of visual pathway.

It 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[33].These results are comparable with the present study. In spite of these findings, he also observed prolongation of I-II IPL, which is not found in present study.

Nelson [34] found that the BAEPs abnormality in patients of GBS as prolongation of wave II latency and total absence of BAEPs 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 condition block was replaced as a prolongation of wave I latency. After convalescent period BAEPs became normal. In the present study there is no case present as similar complaint and BAEPs finding.

The result of present study showed prolonged central conduction time in BAEPs and VEPs observation and suggested the subclinical auditory and optic pathway involvement in GBS. These findings are compatible to demyelination.

Conclusion

Gullian Barr'e Syndrome (GBS) is regarded as a predominantly motor neuropathy with transient or absent sensory features. GBS mainly affects the peripheral Nervous system (PNS) but there are few studies which have reported involvement of Central Nervous System (CNS) , though it is not frequent.

The present study showed prolonged central conduction time in BAEPs and VEPs. Our observation suggests the subclinical auditory and optical pathway involvement in GBS because none of the patients complained of hearing and visual defects. These findings are compatible to demyelination. Early confirmation of the diagnosis has become very important and mandatory. It needs further study in large population which helps to reduce the duration,severity and complications of the disease and prevent the residual disabilities.

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