Section: Neurology

Original Research Article

AUTONOMIC DYSFUNCTION IN PATIENTS WITH GUILLAIN- BARRÉ SYNDROME (GBS)

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Abstract

Background: Guillain-Barré syndrome is currently the most frequent cause of acute flaccid paralysis worldwide and constitutes one of the serious emergencies in neurology. Autonomic dysfunction (AD) is a common and important complication in GBS and may be the cause of significant morbidity or death. This study was to evaluate autonomic function studies in GBS patients and see if they carried any clinical significance. **Material & Methods:** 40 consecutive patients aged above 12 years with clinical diagnosis of GBS admitted in the department of Neurology, SMC Vijayawada, fulfilling the clinical criteria of GBS (Asburys diagnostic criteria) were included. They were assessed with nerve conduction studies and autonomic function testing. **Results:** In this study, AIDP accounted for 32% of cases, 65% were axonal variants, 3% MFS variant. Autonomic dysfunction is seen in 26 (65%) patients. 22 (55%) had sympathetic dysfunction and 9 (22%) patients had parasympathetic involvement. 7 patients had involvement of both sympathetic and parasympathetic. Sympathetic skin response(SSR) is not recordable in 10 (25%) patients. There is not much difference in sympathetic dysfunction in axonal and demyelinating GBS (42% vs 50 %). Both sympathetic and parasympathetic dysfunction is present in 20 % of axonal GBS compared to 16 % of demyelinating GBS. **Conclusion:** The patterns of autonomic involvement are qualitatively different between AIDP and AMAN. Our results suggest that SSR and other autonomic tests may be used for early detection of any autonomic involvement in patients with GBS but they didn't show any correlation with outcome.

INTRODUCTION

Guillain–Barré syndrome, which is characterized by acute areflexic paralysis with albuminocytologic dissociation (i.e., high levels of protein in the cerebrospinal fluid and normal cell counts), was described in France in1916.[1] Since poliomyelitis has nearly been eliminated, the GBS is currently the most frequent cause of acute flaccid paralysis worldwide and constitutes one of the serious emergencies in neurology. A common misconception is that the GBS has a good prognosis — but up to 20% of patients remain severely disabled and approximately 5% die, despite immunotherapy.[2]

The classic form of GBS is a nonseasonal illness that affects persons of all ages, but males are more often affected than females (1.5:1). The mean annual incidence is 1.8 per 100,000 population and has remained stable over the past 3 decades.[3] Incidence rates increase with age from 0.8 in those younger than 18 years to 3.2 for those 60 years and older.

Autonomic dysfunction is a common and important complication in GBS and occurs in approximately two-thirds of patients.[4] This rate rises to 75% in patients with quadriplegia.[5] Autonomic dysfunction of various degrees has been reported. Most of the clinically significant autonomic dysfunction occurs within the first 2 to 4 weeks of the illness, the peak period of paralysis. Its varied and complex manifestations may be related to either increased or decreased sympathetic-parasympathetic activity, resulting in orthostatic hypotension, urinary retention, gastrointestinal atony, iridoplegia, episodic or sustained hypertension, sinus tachycardia, tachyarrhythmias, anhidrosis or episodic diaphoresis, and acral vasoconstriction.

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Excessive vagal activity accounts for sudden episodes of bradycardia, heart block, and asystole. These "vagal spells" may occur spontaneously or may be triggered by tracheal suctioning or similar stimuli. Serious cardiac arrhythmias with hemodynamic instability tend to be more frequent in patients with severe quadriparesis and respiratory failure. Autonomic dysfunction can result in electrocardiographic (ECG) changes including T-wave abnormalities, ST-segment depression, QRS widening, QT prolongation, and various forms of heart block.

Autonomic function tests applied in GBS patients have shown the necessity of monitoring autonomic disturbances in every patient with GBS, with or without autonomic dysfunction signs and symptoms.[6,7] Sympathetic skin response (SSR) is a noninvasive method that can be used easily to evaluate autonomic dysfunction. It involves a recordable skin potential change following the application of an internal or external stimulus.[8]

MATERIALS AND METHODS

This is a prospective observational study. We studied 40 consecutive patients aged above 12 years with clinical diagnosis of GBS admitted in the department of Neurology, SMC, Vijayawada who fulfilled the clinical criteria of GBS (Asburys diagnostic criteria)9. The demographic data recorded included age, sex, duration of illness and preceding antecedent illness. Detailed clinical history and neurological examination were performed. Patients aged above 12 years were included. Patients with Arrhythmia, Ischemic or other heart diseases, Chronic obstructive airway disease, Diabetes mellitus, Hypothyroidism, drugs affecting autonomic nervous system were excluded from the study.

Table 1: Diagnostic Criteria for Gullian Barre Syndrome

FEATURES REQUIRED FOR DIAGNOSIS • Progressive weakness of both legs and arms • Areflexia
CLINICAL FEATURES SUPPORTIVE OF DIAGNOSIS • Progression over days to 4 weeks • Relative symmetry of symptoms and signs • Mild sensory symptoms or signs • Bifacial palsies • Autonomic dysfunction • Absence of fever at onset • Recovery beginning 2–4 weeks after progression ceases
LABORATORY FEATURES SUPPORTIVE OF DIAGNOSIS • Elevated cerebrospinal fluid protein with <10 cells/μL • Electrodiagnostic features of nerve conduction slowing or block.

Functional disability: Patient disability at the peak of the deficit was assessed using Modified Hughes functional grading scale.[10]

- Grade 0: Normal
- Grade 1: Able to run with minor signs and symptoms
- Grade 2: Able to walk 5 m independently
- Grade 3: Able to walk 5 m with aid
- Grade 4: Bed or chair bound
- Grade 5: Requires assisted ventilation
- Grade 6: Death

Electrodiagnostic studies: Nerve conduction studies were performed within 4 weeks of onset of neurological symptoms and were repeated if the initial conduction studies were normal.

Patients were classified as having AMAN or AIDP on the basis of the electrodiagnostic criteria proposed by Ho et al.[11]

When patients had one of the following findings in two (or more) nerves during the first 2 weeks of illness, they were classified as having AIDP

- CV< 90% of the lower limit of the normal if the amplitude is >50% of the lower limit of normal and <85% if the amplitude is <50% of normal.
- Distal latency >110% of the upper limit of normal if the amplitude is normal;
- 120% of the upper limit of normal if the amplitude is less than the lower limit of normal.
- Evidence of unequivocal temporal dispersion.
- F response latency >120% of the normal.

When patients had no evidence of demyelination as defined and had a decrease in CMAP amplitude to <80% of the lower limit of normal in two (or more) nerves, they were classified as having AMAN. None of the features of AIDP, dCMAP<80% LLN in at least 2 nerves and SNAP <50% LLN in at least 2 nerves was classified as AMSAN.

A diagnosis of acute sensory axonal neuropathy (ASAN) was made when motor conduction studies were normal but sensory nerve conduction studies showed decreased or absence of sensory nerve action potentials of sural nerves.

Clinical testing of autonomic function

Sympathetic functions are assessed by postural hypotension, sustained handgrip.

Parasympathetic functions assessed by resting heart rate, heart rate response to deep breathing, valsava ratio, heart rate response to standing by CANS machine in all patients.

Normal reference values used for interpretation

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Table 2: Parasympathetic functions

TEST	NORMAL	BORDERLINE	ABNORMAL
Resting	<100 BPM		>100 BPM
Deep breathing (E-I Difference)	<14 BPM	11-14 BPM	<11 BPM
Standing (30:15 ratio)	>1.03	1.01-1.03	<1.01
Valsalva ratio	>1.2	1.10-1.20	<1.10

Table 3: Sympathetic functions

TEST	NORMAL	BORDERLINE	ABNORMAL
Standing	<11mmHg	11-29mmHg	>29mmHg
Handgrip	>15mmHg	11-15mmHg	<11mmHg

Sympathetic skin response: For the palmar SSR, surface electrodes were used with the active recording electrode placed on the palm of the hand and the reference electrode located at the wrist on the dorsum of the hand. SSR parameter included the latency to the onset of depolarization which was indicated by the first continuous deflection from the baseline. The amplitude was measured from peak to peak.

Statistical Analysis

The data was presented as mean ± standard deviation or percentage of cohort affected. The significance between means of two parameters was compared using unpaired 't' test. The p value of less than 0.05 was considered statistically significant. For the statistical analysis SPSS software was used.

RESULTS

The study included 40 consecutive cases with clinical diagnosis of GBS admitted in the Department of Neurology, SMC Vijayawada. The basic characteristics of the cases is given in the Table 4.

In this study, AIDP accounted for 32% of GBS cases, 65% were constituted by axonal variants (AMAN, AMSAN, ASAN), 3% by MFS variant. Both AIDP and axonal variants had male preponderance.

Autonomic dysfunction is seen in 26(65%). Sympathetic dysfunction is seen in 22(55%) patients. Parasympathetic involvement is seen in 9(22%). In 7 patients both sympathetic and parasympathetic involvement is seen. Sympathetic skin response(SSR) is not recordable in 10(25%) patients. There is not much difference in sympathetic dysfunction in axonal and demyelinating GBS (45% VS 52%). Both sympathetic and parasympathetic dysfunction is present in 20% of axonal GBS compared to 16% of demyelinating GBS [Table 4].

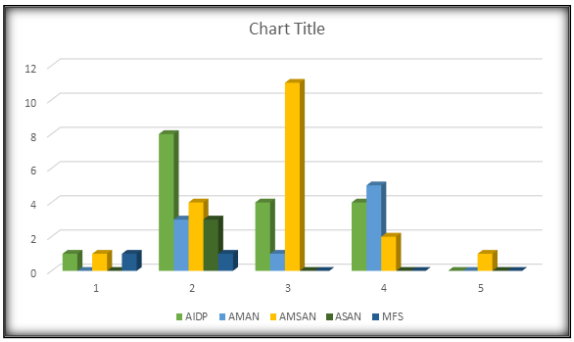

Figure 1: Hughes functional grading in GBS subtypes

Most of the patients with AIDP presented with Hughes functional disability grade of 2 or 3 whereas axonal forms presented with Hughes functional disability grade of 3 or 4.

33 patients recovered completely with Hughes functional disability grade of 1 at the end of 3 months. Of the remaining 7 cases, 5cases of AMAN and 2 cases of AMSAN had incomplete recovery with Hughes grade of 2 or 3.

No significant relationship was found between autonomic dysfunction and severity of motor disability status according to Hughes functional grading.

Autonomic dysfunction in Guillain-Barre syndrome did not appear to have any prognostic significance, as there was no significant difference in the outcome in both the groups [Table 5].

The mean score of Hughes grade at 3 months in axonal GBS (1.39±0.803) was found to be significant when compared to demyelinating GBS (1.0) (p value=0.05) [Table 6].

Table 4: Demographic and clinical features of GBS patients

	Number(n)	Percentage
Male	27	68
Female	13	32
Mean age ± SD	35±12	
Motor weakness	36	90
Sensory symptoms	26	65
Cranial nerve Involvement	12	30
Respiratory muscle weakness	8	20
Autonomic symptoms	12	30
Antecedent illness	12	30
CSF albumin cytologicaldissociation	22	55

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Table 5: Outcome vs Autonomic Dysfunction (AD)

	AD – Present (n=26)	AD – Absent (n=14)	P value
Hughes at nadir (Mean ± SD)	2.85 ± 1.019	2.56 ± 0.727	.312
Hughes at 3 months (Mean ± SD)	1.29 ± 0.719	1.13 ± 0.500	.401

Table 6: Outcome vs GBS subtype

	Axonal variant (n=26)	Demyelinating variant (n=13)	P value
Hughes at nadir (Mean ± SD)	2.90 ± 0.908	2.65 ± 0.931	0.359
Hughes at 3 months (Mean ± SD)	1.39 ± 0.803	1.00 ± 0.000	0.050

DISCUSSION

GBS affects all ages, but is more frequent in adults over 40 years of age. Mean age in our study was 35 years, similar to the previous studies. In present study, there was male gender predominance (M:F =2.12:1). Axonal GBS constituted 65% in the present study and is similar to the previous studies in asian countries. This is similar to a study conducted in Bangladesh by Islam Z, Jacobs BC et al in 2010 where 67% of patients had an axonal variant of GBS12. A study done on variants of GBS, by S. Gopi et al in our population concluded that axonal variant is common than AIDP and constituted 55% of total 110 cases. In contrast, the most frequent form (90%–95%) in North America and Europe is the acute inflammatory demyelinating polyradiculoneuropathy (AIDP) (Hughes and Cornblath,2005). Axonal GBS accounts for 30%–60% of GBS cases in countries such as China, Japan, South America, and Bangladesh (Ramos-Alvarez et al., 1969; Ho et al., 1999; Islamet al., 2010).[13,14,15]

The involvement of autonomic system i.e., both sympathetic and parasympathetic, was comparable to the results found in the studies done by Singh N K et al,[16], Bansal et al,[17] Tuck and Mc Leod et al,[18] in patients with GBS.

Although Flacheneckeret al,[19] reported that autonomic dysfunction was highly correlated to motor disability in GBS, many clinical studies disagree on the relationship between autonomic dysfunction and motor disturbance in GBS.[20] Tuck and McLeod and Bansal et al. found that the severity of autonomic involvement did not relate to the degree of motor and sensory disturbance and electrophysiological abnormalities. In accordance with the above studies, in our study also no significant relationship was found between autonomic dysfunction and severity of motor disability status according to Hughes functional grading. Thus, autonomic dysfunction is present not only in GBS patients with severe functional disability but also in patients with mild GBS.

The mean score of Hughes grade at 3 months in axonal GBS (1.39±0.803) was found to be significant when compared to demyelinating GBS (1.0) (p value=0.05) showing that axonal GBS had a poor outcome when compared to demyelinating GBS at the end of 3 months. Autonomic dysfunction in Guillain-Barre syndrome did not appear to have any prognostic significance, as there was no significant difference in the outcome in both the groups. This is in accordance with the study done by Singh N K et. al., and is in contrast to the study done by Anna Lisette Bazan-Rodriguez et al.[21]

CONCLUSION

Axonal variant of GBS is common in our subset of population. The patterns of autonomic involvement are qualitatively different between AIDP and AMAN. Our results suggest that SSR and other autonomic tests may be used for early detection of any autonomic involvement in patients with GBS but they didn't show any correlation with outcome.

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