Prognostic Indicators of Response to Plasmapheresis in Patients of Guillain Barre Syndrome

HB Prasad¹, RT Borse², AN Avate³, Neelesh Palasdeokar⁴

Abstract

Introduction: Plasmapheresis is an important modality for the treatment of GBS. Moreover the response to this treatment modality is not same in all cases. We therefore studied the various prognostic indicators of response to plasmapheresis in patients of Guillain Barre Syndrome.

Materials and Methods: 40 patients were included in the study. Thorough clinical examination was done. Nerve conduction was done to find out the type of neuropathy. All were then given plasmapheresis. Prognostic indicators with reference to Age, sex, presenting severity, time between onset of illness and arrival to hospital, time taken to start plasmapheresis, number of plasmapheresis cycles, respiratory involvement, and type of neuropathy were studied.

Results: There were 57.5% females and 47.5% males. Majority (82%) patients were in the age group of 20 to 60 years. All the patients had power grade 1 or 2 on admission but on discharge the power was grade 3 to 5 in 29 (80.55%) patients. The number of patients who received 5 cycles was 34(85%) and those who received 4 cycles of plasmapheresis was 6(15%). AIDP (acute inflammatory demyelinating polyneuropathy) was seen in 36 (90%) pts and AMAN (Acute Motor axonal Neuropathy) was seen in 4 (10%) patients. The severity at presentation and improvement was similar for all ages. Those who received plasmapheresis late showed power improvement of 2 to 3 grade in (50%) whereas those who received early showed improvement of 2 or 3 grade power in 82.14% patients indicating better improvement with early plasmapheresis. No difference was seen in grade of power improvement in 4 or 5 cycles of plasmapheresis. The number of patients on mechanical ventilation were 13 (40.62%) AIDP cases and 4 (100%) AMAN cases indicating more respiratory involvement in AMAN patients. All four patients of AMAN put on mechanical ventilation died of Ventilator associated pneumonia.

Conclusion: Early treatment with plasmapheresis has better outcome in patients of GBS. Four and five cycles of plasmapheresis are equally beneficial.

Editorial Viewpoint

- Response to plasmapheresis in GBS is variable.
- This study founds early treatment withy plasmapheresis has better outcome.
- Four and five cycles of plasmapheresis are equally beneficial.

Introduction

Guillain - Barre Syndrome - is an acute and frequently severe type of polyradiculoneuropathy of autoimmune nature. It is also known as Landry’s Paralysis. Guillain - Barre (Ghee-yan-Bharry) Syndrome is also known as acute inflammatory demyelinating polyneuropathy (AIDP) and it is an inflammatory disorder of the peripheral nerves. GBS manifests as rapidly evolving are flexic motor paralysis with or without sensory disturbance. The usual pattern is an ascending flaccid paralysis. Weakness typically evolves over hours to a few days and is frequently accompanied by tingling dysesthesias in the extremities. The treatment of GBS is either plasmapheresis or IV immunoglobulin (IVIG). IVIG is expensive though easy to administer. Plasmapheresis is the second modality which is cheaper and effective. Moreover the response of plasmapheresis is not the same in all patients.

¹Professor of Medicine Dr. V.M. Government Medical College, Solapur, Maharashtra; ²Professor of Medicine, RCSM Govt Medical College, Kolhapur, Maharashtra; ³Assistant Professor in Medicine, ⁴Assistant Professor in Neurology, B.J. Government Medical College, Pune, Maharashtra

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We therefore took up this study to assess prognostic indicators of response to plasmapheresis in patients with GBS.

Aims and Objectives

To study the various prognostic indicators of response to plasmapheresis in patients of Guillain Barre Syndrome with reference to age, sex, presenting severity, time between onset and arrival to hospital, time taken to start plasmapheresis, number of plasmapheresis cycles, respiratory involvement and type of neuropathy.

Material and Methods

40 adult patients admitted to wards and MICU of Sassoon general hospitals a tertiary care centre in Maharashtra, India for flaccid paraplegia or quadriplegia were included. Thorough neurological clinical examination was done to assess degree of weakness on admission and associated features like autonomic dysfunction, respiratory muscle weakness, cranial nerve involvement and reflexes. A detailed history of duration of illness and time from onset of illness to arrival to hospital was noted. The diagnosis of GBS was done by nerve conduction studies to see if patient had AIDP (Acute inflammatory demyelinating polyneuropathy) or AMAN (Acute motor Axonal neuropathy). Patients were then put on plasmapheresis. Plasma exchange was done with 8 fresh frozen plasma (50 ml/kg).

30 ml /Kg body weight of plasma was removed using plasmapheresis filter. They were monitored for neurological improvement and need for ventilation and when indicated patients were put on ventilator. Thorough systemic examination for other systems was done. Patients were assessed daily for improvement in power till the completion of cycles of Plasmapheresis and then till discharge.

Statistical Analysis

Statistical analysis was done using SPSS software version 17 for windows. t test was done for age, duration of illness and early or late PP. Chi square and Fisher Exact was used to find association between sex, power on admission, type of neuropathy (AIDP, AMAN), neurodeficit on admission and early or late PP. Proportion test was used to find the significance difference of number of plasmapheresis cycles, Mechanical ventilation, survival, power on discharge, preceding illness between early and late PP. A P Value l<0.05 was considered as significant.

Observation Tables

33(82.5%) patients showed at least 2 grade improvement in power

All 5 i.e. 100% showed power improvement of grade 2

Grade 2 improvement was seen in 34 i.e. 97.14% cases

23 out of 27 i.e. 85.18% patients showed improvement in power by 2 grades whereas 5 patients i.e 18.51% showed improvement of power of 1 grade

9 out of 13 pts i.e. 69.23% showed improvement in power by 2 grades, 3 out of 13 i.e. 23.07% showed improvement in power of 1 grade.1 out of 13 i.e. 7.69% showed improvement by grade 3 power

Results

Most patients were in the age group of 21 to 60yrs (90%). There were 19(47.22%) males and 21 (52.77%) females. 28(77.5%) patients had weakness of 3 to 6 days. 36 patients ie (90%) came with quadriplegia and 4 (10%) with paraplegia. All the patients had power grade 1 or 2 on admission but on discharge the power was grade 3 to 5 in 33 (82.55%) patients. Thirty-four (85%) patients received 5 cycles and 6 (15%) received 4 cycles of plasmapheresis. AIDP (acute inflammatory demyelinating polyneuropathy) was seen in 36 (90%) pts and AMAN (Acute Motor Axonal Neuropathy) was seen in 4 (10%) patients. The overall grade power improvement after plasmapheresis was 1 to 2 grade in 7 (17.5%) patients and 1 to 3 in 17 (42.5%) pts. 1 to 4 in 1 (2.5%) patients, 2 to 3 in 1 (2.5%) patient and 2 to 4 in 14 (35%) patients. Twenty-seven (67.5%) patients received early plasmapheresis within 4 days and 13 (32.5%) received late plasmapheresis after 4 days. Diarrhoea was preceding illness in 2 (5%) pts, respiratory infection was seen in 1 (2.5%) patient and 37 (92.5%) had none. The prognostic factors - Those who received plasmapheresis late showed power improvement.
of 2 grade in (69.23%) whereas those who received early showed improvement of power by grade 2 or 3 in (85.18%). The P value was <0.05 significant. All 5 patients ie 100% who received 4 cycles showed grade 2 improvement in power whereas 34 (97.14%) patients who received 5 cycles showed grade 2 improvement in power. The p value was <0.05 ie significant. The severity at presentation and improvement was similar for all ages.13 (40.62%) AIDP cases and 4 (100%) AMAN cases were on mechanical ventilation indicating more respiratory involvement in AMAN patients. 4 out of 17 (23.52%) patients put on mechanical ventilation died of ventilator associated pneumonia. Thus Age, sex, preceding illness, duration of weakness, type of neuropathy and power on admission did not significantly affect the response to plasmapheresis. The p value was >0.05.

**Discussion**

**Age**

In this study the commonest age group was 21 to 60 yrs (90%). In a study by Dhadke et al the age group commonly affected was 13-40 yrs. whereas in study by Netto et al mean age was 33.5 ± 21 years)

**Sex**

There were 19(47.22%) males and 21 (52.77%) females indicating slight female preponderance. In the study by Dhadke et al18 the male:female ratio was 1.5:1 and the study by Netto et al out of 173 there were 118 men and 55 women indicating male preponderance in both these studies moreover sex did not affect recovery in all these studies including our study.

**Plasmapheresis**

There are two modalities of treatment for GBS are Immunoglobins and plasmapheresis. Immunoglobulins are expensive and most of our patients cannot afford the same hence plasmapheresis was given to all our 40 patients. All the patients who received plasmapheresisimproved. Early initiation of plasmapheresis resulted in better power improvement in most of the patients 85% of our pts received 5 cycles of plasmapheresis and 15% received 4 cycles but all showed response confirming the fact that any treatment is effective

A number of studies have shown that PP is associated with faster and better recovery in patients with GBS AK Meenaetal in their guidelines for treatment of GBS emphasized the importance of early and adequate PP. In a meta-analysis of 6 class II trials comparing plasma exchange (PE) to supportive care alone for adults with GBS, it was found that PE reduced the risk of developing respiratory failure.4,5

In our study the patients were observed for 10 days minimum and for longer duration according to hospital stay. All of them recovered by 1 to 2 grade power in 10 days

**Number of Cycles**

Most of our patients received 5 cycles ie 85.5% and about 15% received 4 cycles of plasmapheresis. The improvement in grade of power by 2 grades was seen in all 5 ie 100% cases who received 4 cycles and in 97.14% cases who received 5 cycles indicating that any number of plasmapheresis started was beneficial (Tables 1, 2, 3). This was also shown by Yuki et al that in mild GBS, two sessions of PE are superior to none. In moderate GBS, 4 sessions are superior to 2. In severe GBS, 6 sessions are no better than 4. In line with these findings they reported that at least 2 PE are needed to significantly reduce the circulating immunoglobulin complexes.6 In developing countries where cost is the limiting factor, small volume PE may be used. In India small volume PE was used by Tharakan et al7 withcomparable results. They used 15 mL/kg body weight/day to be continued till the progression of the disease got arrested or recovery started. This protocol is still performed in various centers in developing countries with good results

In the study by Dhadke et al out of 40 patients, 14 patients received Intravenous immunoglobulin and 4 patients received plasmapheresis. Patients who received IVIg early in the course of disease had faster recovery as compared to patients who received only supportive line of treatment

In a study by The French Cooperative Group on Plasma Exchange in Guillain-Barré Syndrome. They randomized 556 GBS patients according to severity and number of exchanges as follows: Zero versus 2 PEs for patients who could walk-with or without aid-but not run, or who could stand up unaided (mild group); 2 versus 4 PEs for patients who could not stand up unaided (moderate group); and 4 versus 6 PEs for mechanically ventilated patients (severe group). In the mild group, 2 PEs were more effective than none for time to onset of motor recovery (median, 4 vs 8 days, respectively). In the moderate group, 4 PEs were more beneficial than 2 for time to walk with assistance (median, 20 vs 24 days) and for 1-year full muscle-strength recovery rate (64% vs 46%). Six PEs were no more beneficial than 4 in the severe cases. Patients with mild GBS on admission should receive 2 PEs. Patients with moderate and severe forms should benefit from 2 further exchanges

The GBS study group compared plasmapheresis with conventional therapy in 245 patients with the Guillain-Barré syndrome of recent onset. Statistically significant differences, favoring the plasmapheresis group, were found in terms of improvement at 4 weeks, time to improve one clinical grade, time to independent walking, and outcome at 6 months. Plasmapheresis was not effective for all patients, but was particularly effective for patients who received
this treatment within 7 days of onset and for patients who required mechanical ventilation after entry into the study. They concluded that Plasmapheresis appears to be of benefit in patients with Guillain-Barré syndrome of recent onset.4,5

Another study in a Randomised trial of plasma exchange, intravenous immunoglobulin, and combined treatments in Guillain-Barré syndrome showed that in treatment of severe Guillain-Barré syndrome during the first 2 weeks after onset of neuropathic symptoms, PE and IVIg had equivalent efficacy. The combination of PE with IVIg did not confer a significant advantage.

Since all our patients received only plasmapheresis we could not compare it with immunoglobulin.

**Plasmapheresis and Respiratory Failure**

In our study 17 patients were on mechanical ventilation indicating respiratory muscle involvement but only 4 died of VAP and 13 recovered well in response to Plasmapheresis. In a meta-analysis of 6 class II trials comparing plasma exchange (PE) to supportive care alone for adults with GBS, it was found that PE reduced the risk of developing respiratory failure.4,5

In the study by Dhadkeetal One third (32.5%) patients developed respiratory paralysis and needed ventilatory support.

A study by Sunder et al:10 Comparing the clinical data in the ventilated and non-ventilated groups concluded that early progression to peak disability, bulbar dysfunction and autonomic instability predicted the development of neuromuscular respiratory paralysis in GBS. Early electrodiagnostic studies in this series suggest axonopathic GBS as a predictor of respiratory paralysis, a finding that needs to be evaluated with sufficient data to permit statistical analysis. In our study all 4 cases with AMAN had respiratory paralysis.

In a review study by Archana B Netto et al which studied Prognostic factors in patients with Guillain-Barré syndrome requiring mechanical ventilation concluded that that modifiable risk factors, such as pulmonary involvement, autonomic dysfunction, hypokalemia, sepsis, bleeding, and nutritional complications, had prognostic significance and their modification may reduce the mortality and morbidity associated with GBS. We did not study these aspects.

**Timing of Plasmapheresis**

67.5% of our patients received plasmapheresis early ie within 4 days and 32.5% received late ie after 4 days. The grade power improvement by 1-2 grades in early plasmapheresis was better in 85.18% patients as compared to 69.23% patients in late Plasmapheresis (Tables 4, 5).

A better outcome was demonstrated with plasma exchange in French Study Group when compared with North American Study Group.4 This is due to the fact that treatment was initiated within 2 weeks in the former study group and within 4 weeks in the latter. Hence PE is more beneficial when started within 7 days after disease onset rather than later, but was still beneficial in patients treated up to 30 days after disease onset.

**Severity on Admission and Plasmapheresis**

All our patients received plasmapheresis irrespective of initial power on presentation. American academy of Neurology in 2003 concluded that PE hastens recovery in nonambulant patients who get treatment within 4 weeks of onset, and PE hastens recovery of ambulant patients with GBS who are examined within 2 weeks. PE is usually administered as one plasma volume, 50 mL/kg, on 5 separate occasions over 1-2 weeks.4 All patients with mild, moderate, and severe GBS benefit from treatment. Patients who need even minimum assistance for walking, who are steadily progressing and those who are bed- and ventilator-bound should be advised PP. In our study all the patients had power grade 1 or 2 on admission but on discharge the power was grade 3 to 5 in 33 (82.55%) patients. The overall grade power improvement after plasmapheresis was 1 to 2 grade in 7 (17.5%) patients and 1 to 3 in 17 (42.5%) pts. 1 to 4 in 1 (2.5%) patients, 2 to 3 in 1 (2.5%) patient and 2 to 4 in 14 (35%) patients. Though these observations were seen clinically the same were not statistically significant.

**Treatment of AMAN and AIDP**

Four patients in our study had AMAN and 36 had AIDP. All the four cases of AMAN were on mechanical ventilation indicating respiratory involvement but the degree of recovery in both groups was same. AIDP is the most common GBS variant in North America and European nations; the axonal variant AMAN is most often seen in Asian nations, including Japan and China. Although there are many clinical trials including patients with the demyelinating AIDP variant from European and North American centers, data outlining the use of immunomodulatory therapies in AMAN are limited. One small retrospective study found that patients who received IVIG recovered more rapidly than those who received PE. Similar results were reported elsewhere.12,13 However, another retrospective review reported better outcomes with PE in severe axonal GBS patients, some of whom had failed prior IVIG therapy.14 Another analysis of 44 AMAN patients reported no difference in the rate of recovery between those who received IVIG or PE.15 Because AMAN generally follows a similar clinical course as AIDP, IVIG and PE are assumed to be appropriate treatment interventions, especially in patients with severe presentations.

Plasmapheresis effectively
hastens recovery from AIDP, not all patients will tolerate it.\(^5\) Additionally, some will demonstrate an inadequate response and others may subsequently relapse following initial benefit.\(^5\)

**Preceding Illness and GBS**

In our study two patients had diarrhoea, one had respiratory infection and 37 had none. Since antecedent infection was absent in most of our cases it could not be correlated.

In the study by Dhadke et al\(^1\) antecedent infection was seen in 55% patients. A history of antecedent events was present in 83 (48%) patients in the study by Netto\(^2\) all and all these patients were on mechanical ventilation indicating its correlation to the severity of initial presentation.

Van Koningveld et al\(^1\) studied 388 patients with GBS and developed a simple clinical scoring system to predict outcome at 6 months i.e. inability to walk independently at 6 months. They included 3 variables that were predictive of poor outcome at 6 months i.e. age, preceding diarrhoea, and GBS disability score at 2 weeks after entry. Scores ranged from 1 to 7, with three categories for age, two for diarrhoea, and five for GBS disability score at 2 weeks. Predictions corresponding to these prognostic scores ranged from 1% to 83% for the inability to walk independently at 6 months. Predictions agreed well with observed outcome frequencies (adequate calibration) and showed a very good discriminative ability (AUC 0.85) in both data sets.

**Conclusion**

Patients with GBS benefit from plasmapheresis irrespective of initial severity and any number of PP are beneficial. PP should be started early as the benefit is more in terms of recovery. AMAN type of GBS is uncommon and has more respiratory involvement.

**References**


