PLASMAPHERESIS IN THE TREATMENT OF GUILLAIN-BARRE SYNDROME; OUTCOMES AND COMPLICATIONS

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ABSTRACT

Objective: To assess the outcome of plasmapheresis in treatment of Guillain-Barre syndrome and factors related to poor outcome at hematology unit of a tertiary care teaching hospital of Pakistan.

Methodology: This cross-sectional study was conducted on 44 patients of Guillain-Barre syndrome managed with plasmapheresis at Neurology department Pak Emirates Military Hospital Rawalpindi from January 20, 2018 to January 20, 2019. Demographic profile included age, gender, variant of Guillain-Barre syndrome and duration of illness. All the complications of the procedure were recorded. Outcomes included recovery, shifting to intensive care unit and death. Pearson chi-square test was applied to relate the factors with presence of complications or poor outcome.

Results: Out of 44 patients, 27 were male and 17 were female. Allergic reaction occurred in 4 (9.1%) patients while abdominal pain during or after the plasmapheresis was observed in 3 (6.8%) patients. Out of 44 patients, 35 (79.5%) recovered, 10 (22.7%) had minor complications, 03 (6.8%) were shifted to the intensive care unit and 03 (6.8%) died. Delay in getting the definitive treatment and variant of Guillain-Barre syndrome had a significant relationship with presence of complications or poor outcome (p-value <0.05).

Conclusion: Plasmapheresis is effective treatment for Guillain-Barre syndrome with very limited side effects.

Key Words: Guillain-Barre syndrome; outcome; plasmapheresis

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INTRODUCTION

Guillain-Barre syndrome (GBS) is a common diagnosis at neurology clinics all over the world[1]. It was in early 1900 that first case was reported and the disease was labeled after the scientist who discovered the first case[2]. There are various types but flaccid paralysis of lower limbs is the most common presentation of this immune mediated neurological disorder. Different patterns seen in this disease and number of systems involved has made it more of a clinical syndrome than just a demyelinating condition[3].

Neurological illnesses have been on the rise in their frequency. Lack of availability of trained staff in underdeveloped countries makes treatment more difficult for the patients[4,5]. Exact diagnosis and a specially tailored management plan is required to save the patients from death or other untoward complications[6]. Steroid therapy, plasmapheresis and intra venous immunoglobulins have been the treatment modalities which have been used to manage the disorders with immunological basis either autoimmune or secondary to some other process[7-9].

Plasmapheresis has been in practice for neurological and other immune based disorders for quite a long time now. Even under developed countries have been using it effectively despite limited resources and expertise. A recent study revealed that neurological disorders were the second common group of disorders for which this modality was used as treatment. Only 4.3 percent of the patients had adverse effects and serious adverse effects were even less common[10]. Another large study done on plasmapheresis for both neurological and non-neuro-

logical patients revealed that adverse reaction occurred only in 9 percent of the patients and they too were not very severe or alarming[11]. A trial performed in Bangladesh on the patients of GBS revealed that out of 33 patients studied, only 3 needed mechanical ventilation and one developed sepsis. It was concluded that this was a safe and effective procedure for GBS with very limited mortality and morbidity[12].

Pakistan is a country with developing health system. Many people cannot afford the expensive treatment options and either rely on long waiting time in government set up or have to live with the disease and follow the natural course. Very limited local data is available on the treatment and outcome of GBS and that too comprise of few case reports and reviews[13,14]. No proper study has been conducted so far at a tertiary care military hospital receiving patients from all over Pakistan including the public sector hospitals. This study was aimed to assess the outcome and complications of plasmapheresis in treatment of Guillain-Barre syndrome (GBS) and factors linked to poor outcome.

METHODOLOGY

This cross-sectional study was conducted at neurology department Pak Emirates Military Hospital Rawalpindi from January 2018 to January 2019 on 44 patients. Ethical approval was taken from the ethics review board of the hospital before the start of this study. Sample size was calculated by using WHO sample size calculator taking prevalence of GBS as 2.9%[10], confidence interval 95% and margin of error as 5%. Sample was collected with non-probability consecutive sampling technique. All patients between the age of 12 and 65 years admitted in the neurology department, diagnosed as GBS and managed with plasmapheresis in liaison with hematology department, were included in the study. Patients who were referred from other military, public sector and private hospitals with the same diagnosis were also included in the analysis in addition to the referrals from the other wards of own hospital. Diagnosis of GBS was made with diagnostic criteria from the national institute of neurological disorders and stroke[15] which includes; acute progressive symmetric weakness of the extremities with areflexia or hyporeflexia, albuminocytological dissociation in cerebrospinal fluid (raised protein and total cell count of $\leq 10/mm^3$) and demyelinating axonal neuropathy on electrophysiological studies.

All suspected cases of GBS underwent electrophysiological studies within 48 hours of admission. Needle electromyogram was also performed. At least one motor and one sensory nerve was tested on the upper and lower limbs. F response was recorded in all the extremities. (F wave is a late response that follows the motor response (M) and is elicited by supramaximal electrical stimulation of a mixed or a motor nerve). Additionally, routine motor conduction studies were performed on the median, ulnar and tibial nerves using conventional procedures. Sensory nerve studies were performed on the median and sural nerves. The amplitude of the negative phase was measured for compound muscle action potentials and sensory nerve action potentials.

The patients were classified into acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN), Miller-Fisher syndrome (MFS) group or cranial nerve variant (CNV) based on the electro diagnostic criteria[15,16]. Exclusion criteria were the patients with less than 12 years of age or those with unclear medical diagnosis. Pregnant patients or those with cerebrospinal fluid India ink stain positive for fungal growth or those with suspected tuberculous meningitis or encephalitis were also excluded from the study. Patients with post traumatic meningitis or those with post injection syndrome or poliomyelitis were also part of the exclusion criteria. Patients with diabetes, neoplasia, hypothyroidism, renal failure, vasculitis, or history of intoxication were also excluded from the study.

Clinical and laboratory investigations like ECG, chest X-ray, cardiorespiratory status and serology were carried out before this procedure. Anti coagulation with citrate was systematically used. Replacement of plasma removed during the session was performed with isotonic sterile saline, to make up one-half of the volume and with 5% purified human albumin and fresh frozen plasma to complete it. Careful monitoring of hemodynamic parameters was done, and complications during or following therapeutic plasma exchange were recognized and reverted by rational interventions of the medical staff that assisted the procedure. Calcium replacement with 10 ml of 10% calcium gluconate was infused over 15 min approximately halfway through the procedure to avoid citrate toxicity. Patients were observed for the adverse effects during the procedure and till 48 hours after the procedure[16-18]. Outcome was classed as patients returning to ward without any major event due to this procedure or shifting to ICU or death during or soon after the procedure due to any lethal complication of the procedure but not due to underlying illness or any other cause.

Statistical analysis was performed using the Statistical Package for Social Sciences version 23.0 (SPSS-23.0). Mean and standard deviation for the age of study participants was calculated. Frequency and percentages for gender, variants of GBS, complications of plasmapheresis and outcome was calculated. Pearson chi-square was used to see relationship between sociodemographic factors and presence of poor outcome or complications among the study participants.

RESULTS

Out of 44 patients, 27 were male and 17 were female. Male to female ratio was 1.6:1. Mean age of patients was 31.23 (± 2.341). Other characteristics of study population are summarized in Table 1. Allergic reaction occurred in 4 (9.1%) patients while abdominal pain during or after the plasmapheresis was noted in 3 (6.8%) patients (Table 1). Out of 44 patients, 35 (79.5%) recovered, 10 (22.7%) had minor complications, 03 (6.8%) were shifted to intensive care unit and 03 (6.8%) died (Tale 2). Pearson chi-square result showed that delay in start of definitive treatment and type of GBS had significant relationship with presence of complications or poor outcome (p-value < 0.05) (Table 3).

Table 1: Characteristics of patients admitted with GBS

Age (years)	
Mean ± SD	31.23 (± 2.341)
Range (min-max)	12 - 59 years
Gender	
Male	27 (61.3%)
Female	17 (38.7%)
Complications	
Allergic reaction	04 (9.1%)
Abdominal pain	03 (6.8%)
Chest discomfort	02 (4.5%)
Dysesthesia	01 (2.3%)
Convulsions	01 (2.3%)
Fever	01 (2.3%)
Hypotension	02 (4.5%)
Others	01 (2.3%)
Variants of GBS	
AIDP	23 (52.2%)
AMAN	09 (20.4%)
AMSAN	07 (15.9%)
MFS	04 (9.1%)
CNV	01 (2.3%)

Table 2: Outcome of patients diagnosed as GBS and treated with plasmapheresis

Total	Recovery	Minor complications	Shifted to ICU	Death
44	35 (79.5%)	10 (22.7%)	03 (6.8%)	03 (6.8%)

Table 3: Pearson Chi-square for relationship of variables

Socio-demographicfactors Total N=44	No complication or good outcome N (%) 30 (68.2)		Presence of complication or poor outcome N (%) 14 (31.8)		p-value
Age					
18-30 year	14	46.7	04	28.6	0.249
>30	16	53.3	10	71.4	
Gender	17	56.7	10	71.4	0.343
Male Female	13	43.3	04	28.6	

Duration of untreated illness					
<2 weeks	25	83.3	07	50	0.024
>2 weeks	05	16.7	07	50	
Smoking					
Non Smoker	27	90	10	71.4	0.129
Smoker	03	10	04	28.6	
Variant of GBS					
AIDP	16	53.3	07	50	0.002
AMAN	09	30	00	00	
AMSAN	01	3.3	06	42.8	
MFS	03	10	01	7.1	
CNV	01	3.3	00	00	

DISCUSSION

Intra venous immunoglobulin is quite expensive so we mostly use plasmapheresis in our setup. Plasmapheresis emerged as fairly safe and effective procedure in our study. Most of the patients recovered without any complications or with minor complications. Studies done by Schmidt et al. in 2018 and Bobati et al. in 2017 have similar results in this regard stating plasmapheresis as the treatment of choice for GBS[10,11]. Allergic reactions and mild abdominal pain were commonest complications reported by the patients which were also not surprising as existing literature has already reported these untoward effects among such patients. Patients studied by Bobati et al. in a study published in 2017 faced similar profile of adverse effects.[11]

Most of our patients (80%) had a good recovery and were discharged from the neurology ward after treatment. Three patients needed mechanical ventilation and shifting to critical care unit which highlights the importance of managing such case at a tertiary care hospital with life saving facilities. Three patients died within 48 hours of the procedure. This outcome spectrum is also in accordance with the outcome of such patients undergoing plasmapheresis in other centers of the world. Studies of Bobati et al. and Islam et al. published in 2017 and 2018 respectively are very important in this regard showing excellent results and recovery rates among patients of GBS undergoing plasmapheresis[11,12]. It is also difficult to distinguish that mortality and morbidity was due to disease itself or the treatment.

Long duration of untreated disease and variants other than AIDP were associated with poor outcome and complications in our analysis. Previous studies have also highlighted this fact. Zhang et al.[19] generated interesting results in this regard and concluded that long duration of untreated illness has been significantly related to poor outcome (p-value (<0.05) whereas ADP variant of GBS has a significant relationship with good outcome and response to the treatment with plasmapheresis. This again can be contributed more to the pathogenesis of disease than due to the plasmapheresis treatment. More studies with proper study design can explain this association in a better way.

The study design we opted for this study pose a major limitation and results cannot be generalized. Sample was from a single military hospital, and results could not be regarded as representative of the whole population. Enrolling the patients from public and private settings and comparing various treatment modalities may guide the clinicians to formulate some local guidelines in this regard.

CONCLUSION

Plasmapheresis is fairly effective treatment for GBS with limited side effects.

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CONTRIBUTORS

MA conceived the idea, made plan for the project, collected data, prepared and finalized initial draft. HMR and AM helped execution of the plan, data collection and interpretation and bibliography. NA and MAA helped data acquisition and interpretation, refining the manuscript, statistical analysis and corrections of the final draft. All authors contributed significantly to the submitted manuscript.