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Plasma-exchange therapy in acute immune-mediated neuropathy: Effects on muscle strength and functional outcomes

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ABSTRACT

Background and objectives. This study explores the impact of plasma exchange therapy (TPE) on muscle strength and functional outcomes in patients with acute immune-mediated neuropathy.

Materials and methods. We retrospectively analyzed clinical data from patients diagnosed with acute immune-mediated neuropathy at the Department of Neurology, Bolan University of Medical Sciences, Baluchistan, from January 2016 to December 2021.

Results. The study, comprising 141 patients with various neurological disorders, underscores the efficacy of plasma exchange therapy in improving muscle strength and functional outcomes, particularly in Guillain-Barré Syndrome (GBS). Notably, after four weeks of treatment, a significant proportion of patients demonstrated improved mobility, with 51.8% able to walk without assistance. However, despite the positive response to therapy, a small percentage (2.8%) experienced unfavorable outcomes marked by expiration. Additionally, the study identifies significant associations between treatment outcomes and patient characteristics, such as the number of plasma exchange cycles and diagnosis ($p < 0.05$), emphasizing the importance of personalized treatment approaches in managing neurological disorders.

Conclusions. Our findings underscore the effectiveness of plasma exchange in enhancing muscle strength and functional outcomes in acute immune-mediated neuropathy, particularly GBS.

Keywords: plasma-exchange therapy, neurological disorders, Guillain-Barré syndrome, muscle strength, functional outcomes

Abbreviations (in alphabetical order):

ACD-A	– Anticoagulant Citrate Dextrose Solution A
AChR	– Acetylcholine Receptors
ANOVA	– Analysis of Variance
ASFA	– American Society of Apheresis Rating Scale
FFP	– Fresh Frozen Plasma
GBS	– Guillain-Barré Syndrome
MFS	– Miller-Fisher Syndrome
MG	– Myasthenia Gravis
MRC	– Medical Research Council
NIH	– National Institutes of Health
PGMIQ	– Postgraduate Medical Institute Quetta
SD	– Standard Deviation
TPE	– Therapeutic Plasma Exchange
TRFs	– Treatment-related Fluctuations
TTP	– Thrombotic Thrombocytopenic Purpura

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INTRODUCTION

Therapeutic plasma exchange (TPE) has emerged as a crucial component in managing a spectrum of neurological disorders, offering a pivotal extracorporeal therapy avenue for patients grappling with conditions such as Guillain-Barré syndrome (GBS) and myasthenia gravis (MG) [1]. Stemming from its Greek origin meaning "to remove" or "take away". TPE encompasses a procedure wherein a patient's plasma is extracted and substituted with an appropriate fluid [2]. Its historical evolution traces back to its initial application in 1952 for addressing hyper viscosity in multiple myeloma, gradually solidifying its position as a cornerstone treatment modality for neurological ailments by the 1970s [3].

The overarching objective of TPE lies in eliminating a wide array of pathogenic entities, including alloantibodies, autoantibodies, immune complexes, toxins, and pathological proteins. Its efficacy is contingent upon various factors, such as the volume of plasma removed relative to the patient's total plasma volume and the distribution of the targeted substance between intravascular and extravascular compartments [4,5]. The American Society of Apheresis (ASFA) guidelines of 2016 underscore the extensive applicability and efficacy of TPE, delineating it as primary or secondary adjunctive Therapy for numerous diseases and syndromes, covering 87 diseases with 179 indications [6-8].

GBS and MG emerge as significant focal points among the plethora of neurological disorders where TPE demonstrates efficacy. GBS manifests as an acute and typically ascending paralyzing disorder characterized by peripheral nerve inflammation, while MG presents with weakness and fatigability of skeletal muscles. GBS, with an estimated annual incidence rate of 0.5 to 2 cases per 100,000 persons, often follows infections. In contrast, MG presents approximately 30 new cases per million annually, with a subset experiencing myasthenia gravis crisis (MGC) [9].

Despite their distinct pathophysiological mechanisms, both GBS and MG share autoimmune origins. GBS involves antibodies targeting peripheral nerve myelin or axon components, whereas MG results from an autoimmune attack targeting acetylcholine receptors (AChR) at the neuromuscular junction. While GBS predominantly affects the myelin sheath in acute inflammatory demyelinating polyradiculoneuropathy [2], MG predominantly involves antibodies targeting AChR, muscle-specific tyrosine-kinase receptor, or low-density lipoprotein receptor-related protein 4 [10-13].

Therapeutic interventions such as TPE play a pivotal role in managing acute or severe cases of both GBS and MG, aiming to stabilize the disease and prevent complications, such as respiratory failure. Emphasizing the early initiation of TPE holds particular significance, as it has been associated with improved outcomes in both conditions. Therefore, this study aims to explore the impact of plasma exchange therapy on muscle strength and functional outcomes in patients with acute immune-mediated neuropathies.

MATERIALS AND METHODS

Study design

This prospective cohort study aimed to investigate the efficacy of plasma exchange therapy in acute immune-mediated neuropathy patients.

Setting

The study was conducted at the Department of Neurology within Bolan Medical Complex Hospital, Quetta, Baluchistan, from January 2016 to December 2021.

Participants

The study prospectively enrolled 141 patients meeting specific inclusion criteria. These criteria included individuals diagnosed with acute immune-mediated neuropathy, encompassing sensorimotor, pure motor, or pure sensory GBS, along with localized variants and Miller-Fisher syndrome. Patients exhibiting classical GBS/MFS overlap were categorized as GBS.

Variables

Clinical severity was evaluated using both the Medical Research Council (MRC) sum score and the GBS disability scale [14,15], wherein higher scores indicated more severe disease. Mild GBS was characterized by a GBS disability scale of 0–2, while severe GBS was defined by a GBS disability scale of 3–6. Treatment-related fluctuations (TRFs) referred to clinical deterioration following initial stabilization or improvement [16]. Nerve conduction studies were assessed according to Rajab Ally's criteria [17]. Patient records were reviewed to ascertain the number and sequence of treatments, as well as the time from clinical onset to treatment administration.

Plasma exchange therapy (TPE)

Plasma exchange therapy (TPE) was promptly initiated upon hospital admission, utilizing the Spectra Optia Apheresis system manufactured by Terumo BCT. This therapy involved the administration of a specialized exchange fluid comprising a combination of fresh frozen plasma (FFP) and 5% albumin solution, supplemented with Anticoagulant Citrate Dextrose Solution A (ACD-A) at a ratio of 10:1 whole blood to citrate. The flow inlet rate during TPE ranged from 30 to 70 ml/min, adjusted based on factors such as the replacement fluid type and peripheral venous access

functionality. Peripheral venous access was established using two 16-gauge catheters placed in the antecubital veins on both sides to facilitate the inlet and outlet circuits. Additionally, patients received prophylactic calcium supplementation via 10% calcium gluconate infusion during TPE to prevent symptomatic plasma-ionized calcium reduction due to citrate anticoagulation.

Data sources/measurement

Patient charts were reviewed to extract relevant clinical data, including baseline characteristics, clinical assessments, and procedural details. Data pertaining to the number and order of treatments, time to treatments from clinical onset, and procedural specifics of plasma exchange therapy were meticulously recorded.

Bias

Efforts were made to minimize bias through the use of standardized assessment tools and criteria for diagnosis and evaluation.

Study size

The sample size of 141 patients was selected based on the expected number of acute immune-mediated neuropathy cases at our hospital throughout the study period and the feasibility of enrollment. We carried out internal pilot research to evaluate the feasibility of recruiting because there were no prior studies that guided sample size estimation for plasma exchange therapy in this cohort. Achieving sufficient statistical power to identify clinically meaningful variations in efficacy outcomes was our goal, and we balanced rigor and feasibility to accomplish the study's goals in the allotted time.

Statistical methods

Data analysis was performed using the SPSS version 21.0 software package. Descriptive statistics were used to summarize the study variables. Measures such as mean, median, standard deviation, and range are calculated for continuous variables like age, while frequencies and percentages are determined for categorical variables such as gender, diagnosis, and outcomes. Comparative tests, including chi-square tests or Fisher's exact tests, were used to assess the association between categorical variables. Additionally, analysis of variance (ANOVA) was conducted to compare means of continuous variables; p-value <0.05 was considered statistically significant.

Ethical consideration

Ethical approval was obtained from the Ethics Committee of the Postgraduate Medical Institute Quetta (PGMIQ) before the commencement of the study (Reference # PGMI/ERC/926).

RESULTS

Table 1 provides a comprehensive overview of the baseline characteristics of the study participants. The gender distribution reveals a higher representation of males at 73.8%, and the mean age of the hundred forty-one patients cohort is 34.08 years with a standard deviation of 8.19. The primary diagnoses include Guillain-Barré Syndrome (GBS) in the majority at 91.5%, followed by Myasthenia Gravis (7.1%), and rare cases of Transplant Rejection and Thrombotic Thrombocytopenic Purpura (TTP) each at 0.7%. Notably, outcomes after the study period show 45.4% of participants requiring assistance while walking, 51.8% managing without assistance, and a 2.8% incidence of expiration. The distribution of Plex cycles reveals variability, with the highest frequency observed in the five-cycle category at 48.2%.

TABLE 1. Baseline characteristics of the study participants

Variable		N(%)
Gender	Male	104(73.8)
	Female	37(26.2)
Age (years); Mean ± SD		34.08±8.19
Diagnosis	GBS	129(91.5)
	Myasthenia Gravis	10(7.1)
	Transplant Rejection	1(0.7)
	TTP	1(0.7)
Outcomes	Walk with Assistance	64(45.4)
	Walk without assistance	73(51.8)
	Expired	4(2.8)
Plex Cycles	One Cycle	13(9.2)
	Two Cycles	19(13.5)
	Three cycles	25(17.7)
	Four Cycles	16(11.3)
	Five Cycles	68(48.2)

Table 2 presents the evolution of patient muscle strength, assessed using the Medical Research Council (MRC) scoring system, over four weeks. At Week 0, most participants started with MRC scores of 0 and 1, constituting 33.3% and 49.6%, respectively. As the weeks progressed, there was a notable shift in scores, with a decreasing trend in MRC 0 and 1 and an increase in higher scores. By Week 4, the distribution significantly changed, showcasing improvements in muscle strength. MRC 4 and 5 scores exhibited substantial increments, reaching 45.4% and 51.8%, respectively, suggesting a positive response to the intervention. Moreover, the table highlights that 2.8% of

TABLE 2. Patient presentation of different MRC Scoring at 4 weeks

	Week 0	Week 1	Week 2	Week 3	Week 4
MRC 0	47(33.3)	29(20.6)	13(9.2)	2(1.4)	-
MRC 1	70(49.6)	51(36.2)	12(8.5)	2(1.4)	-
MRC 2	12(8.5)	22(15.6)	21(14.9)	-	-
MRC 3	9(6.4)	16(11.3)	51(36.2)	38(27.0)	-
MRC 4	3(2.1)	18(12.8)	30(21.3)	41(29.1)	64(45.4)
MRC 5	-	5(3.5)	14(9.9)	58(41.1)	73(51.8)
Expired	-	-	-	-	4(2.8)

participants experienced an unfortunate outcome marked by expiration.

A notable proportion of individuals, constituting 45.4%, were observed to walk with assistance after four weeks of plasma exchange therapy (Figure 1). In contrast, 51.8% demonstrated the ability to walk without assistance, indicating a relatively higher degree of functional independence. Unfortunately, a small portion, accounting for 2.8%, experienced an unfavorable outcome marked by expiration.

DISCUSSION

In our retrospective analysis of treatment practices among patients diagnosed with acute immune-mediated neuropathy over five years at the Bolan Medical Complex Hospital in Quetta, we aimed to elucidate the treatment trends and outcomes associated with therapeutic interventions in this patient cohort. Our findings underscored a remarkable adherence to treatment protocols, with nearly all patients receiving some form of immunomodulatory Therapy.

We observed a consistent pattern of high treatment initiation rates throughout the five-year observation period. Regardless of the severity of the GBS subtype, patients were consistently treated at a high rate over the entire five-year period. This consistency suggests a standardized approach to clinical decision-making regarding treatment initiation. This remained unchanged despite the limited data on patients with milder forms of GBS and Miller-Fisher syndrome (MFS). While emerging evidence, including findings from trials advocating for two plasma exchanges over none in patients with mild GBS [19], suggests potential benefits in customized treatment approaches, the predominant focus of existing studies on severe GBS cases underscores the need for further exploration of treatment strategies across the spectrum of disease severity [9,14,20]. The higher treatment initiation rates observed in our study setting may be attributed to the tertiary care status of our hospital, despite the challenges posed by limited economic resources and the demographic characteristics of the patient population.

Regarding outcomes associated with plasma exchange therapy, our study demonstrated notable improvements in muscle strength, as evidenced by the evolution of Medical Research Council (MRC) scores over four weeks. These findings are consistent with observations from similar studies [21], where significant neurological improvements were noted following plasma exchange therapy, including regression of motor deficit and functional status enhancement.

Specifically examining outcomes linked to plasma exchange therapy, a substantial proportion of patients exhibited varying degrees of functional improvement. Notably, approximately 45.4% of patients demonstrated the ability to walk with assistance after four weeks of plasma exchange therapy, while 51.8% achieved ambulation without assistance. These outcomes underscore the potential benefits of plasma exchange in enhancing functional independence among GBS patients. However, it is important to

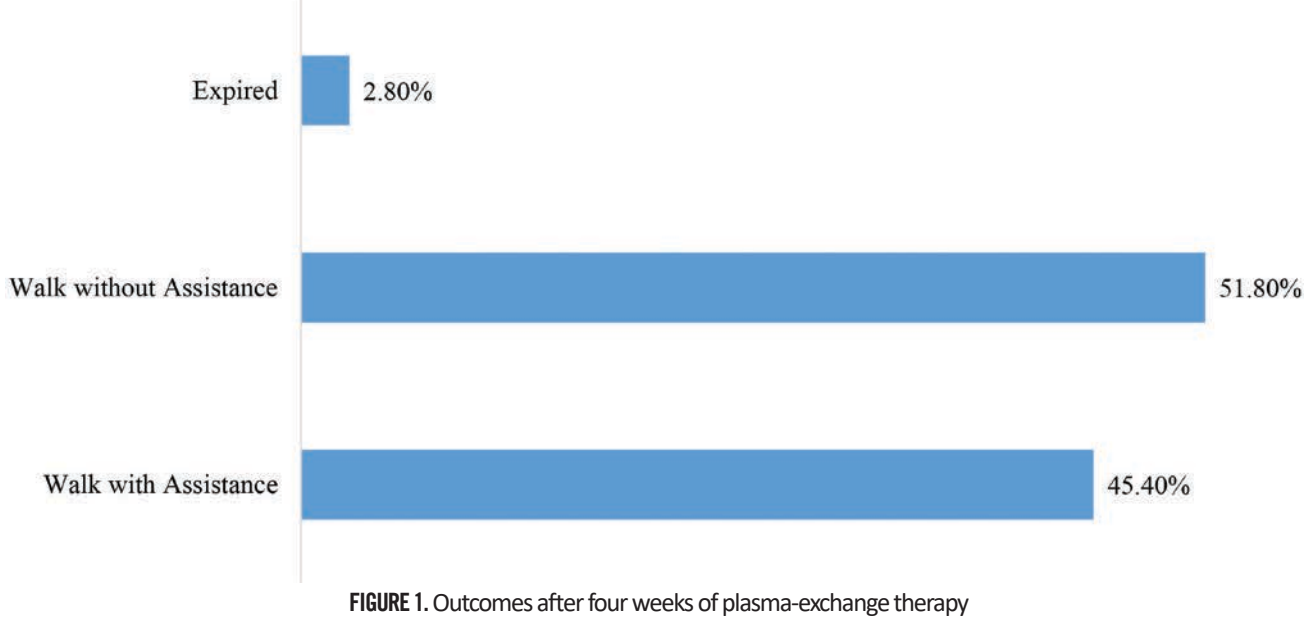

FIGURE 1. Outcomes after four weeks of plasma-exchange therapy

TABLE 3. Effect of patient characteristics on outcomes

Variables		Outcomes			p-value
		Walk with Assistance N(%)	Walk without Assistance N(%)	Expired N(%)	
Age (years) Mean±SD		33.35±8.40	34.38±7.60	40.25±14.08	0.241
Gender	Male	44(68.8)	56(76.7)	4(100.0)	0.275
	Female	20(31.3)	17(23.3)	-	
Plex Cycles	One Cycle	6(9.4)	4(5.5)	3(75.0)	0.002*
	Two Cycles	10(15.6)	9(12.3)	-	
	Three cycles	12(18.8)	13(17.8)	-	
	Four Cycles	5(7.8)	11(15.1)	-	
	Five Cycles	31(48.4)	36(49.3)	1(25.0)	
Diagnosis	GBS	62(96.9)	65(89.0)	2(50.0)	0.022*
	Myasthenia Gravis	2(3.1)	6(8.2)	2(50.0)	
	Transplant Rejection	-	1(1.4)	-	
	TTP	-	1(1.4)	-	

**p <0.05 is considered statistically significant*

note that a small yet notable percentage of patients experienced unfavorable outcomes, underscoring the necessity for meticulous monitoring and complication management during treatment.

Building upon our study findings, it is imperative to contextualize them within the broader landscape of evidence derived from large-scale randomized controlled trials investigating the efficacy of plasma exchange in GBS management [22,23]. These trials consistently highlight benefits such as shortened recovery times and reduced reliance on assisted mechanical ventilation among patients undergoing plasma exchange therapy. Furthermore, studies have explored the optimal number of plasma exchange sessions based on disability severity, providing valuable insights into treatment optimization strategies.

CONCLUSION

This study revealed that moderate-quality data shows that plasma exchange significantly improves symptoms in individuals with acute immune-mediated neuropathy. There was a slight but substantial increase in the risk of relapsing in those treated with plasma exchange compared to those who were not treated. Despite this, plasma exchange increased the chances of complete strength and power recovery after a year and decreased the chances of significant residual weakness and ventilatory support.

Author's contributions:

Noor Ahmed Khosa: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data Curation, Project administration.

Syed Muhammad Essa: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data Curation, Writing - Original Draft, Supervision.

Muhammad Samsoor Zarak: Conceptualization, Methodology, Software, Validation, Formal analysis, Data Curation, Review & Editing.

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Ismail A. Ibrahim: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data Curation, Writing - Review & Editing.

Tamor Mumtaz: Methodology, Validation, Formal analysis, Investigation, Resources, Data Curation, Writing - Review & Editing, Project administration.

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