Low-volume Plasma Exchange In Immune-mediated Neurological Diseases : A tertiary care center study

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ABSTRACT

BACKGROUND

The optimal cost benefit of standard plasma exchange (SPE) has not been met where most of the patients do not afford the treatment. As an alternative, low volume plasma exchange (LVPE) is cost-effective than SPE where albumin replacement is eliminated. The aim of this study was to analyse the efficacy and safety of LVPE in various Immune mediated neurological diseases (IMND).

METHODS

A hospital-based retrospective study was conducted in patients with IMND who were admitted in TUTH between October 15, 2020, and October 14, 2022. Hemodynamically stable patients over the age of 18 who met the plasma exchange criteria were eligible. Outcomes and treatment-related complications were studied separately for the different diseases.

RESULTS

Of the 29 patients enrolled, 3 had Myasthenia gravis (MG), 6 had Neuromyelitis optica spectrum disorder (NMOSD), 11 had Gullian Barre syndrome (GBS), 6 had Chronic inflammatory demyelinating polyneuropathy (CIDP), and 3 had Autoimmune encephalitis (AE). Patients with MG, GBS, and CIDP all showed statistically significant improvement in mRS scores from 2.3±0.6 to 0 (p value = 0.0198), 3.03±1.8 to 2.2±1.4 (p value=0.0046) and 2.5±1.4 to 1.8±1(p value=0.025) respectively by the time they were discharged following treatment. Two patients developed Deep vein thrombosis (DVT), and two developed anaphylaxis during the course of their treatment, although none deteriorated further while in the hospital.

CONCLUSION

LVPE was effective in MG, GBS and CIDP. Myasthenia crisis patients who re-quired mechanical ventilation demonstrated complete resolution with LVPE making it a potential life-saving alternative for those who cannot afford standard therapy.

Keywords: Low-volume plasma exchange; immune-mediated neurological diseases

INTRODUCTION

Immune-mediated neurological diseases (IMND)(1), therapeutic plasma exchange is employed to prevent long-term impairment and produce good outcomes (2). Standard plasma exchange (SPE) due to albumin, or intravenous immunoglobulin (IVIG) is costly. The expense of albumin can be greatly decreased with a small volume exchange with plasmalyte (Crystalloid) with daily plasma volume exchanges.

A study of low volume plasma exchange(LVPE) for GBS found it to be a safe and practical alternative treatment to (SPE) or Intravenous immunoglobulin (IVIG) (3). However, there is a scarcity of data on LVPE in IMND and more clinical efficacy randomized controlled trials in low- and middle-income countries are needed. Indications of plasma exchange differ widely depending upon the disease severity and long-term disability.

To evaluate efficacy outcomes and study the safety and complications of LVPE, we retrospectively examined the data of patients with different IMND spectrums treated with LVPE.

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METHODS

STUDY POPULATION:

SELECTION AND DESCRIPTION OF PARTICIPANTS

Patients admitted to Tribhuvan University Teaching Hospital (TUTH) with IMND requiring plasma exchange from October 15, 2020, to October 14, 2022, comprised the study population. Patients were eligible for the study if they were over the age of 18, hemodynamically stable and diagnosed with an IMND (MG, GBS, CIDP, AE, or NMOSD), and could not afford SPE. LVPE was performed in acute attacks presenting with severe encephalopathy, uncontrolled seizures or refractory epilepsy in AE, complete paraplegia, bilateral severe optic neuritis, brain stem symptoms in NMOSD, severe relapse with significant neurological disability in MS, Myasthenic crisis or impending bulbar failure in MG and severe muscle weakness in CIDP. All the hemodynamically unstable patients or patients affording conventional treatment were excluded.

STUDY OUTCOMES

Disability as per Modified Rankin Scale(mRS)(5) and Treatment-related complications commonly encountered as Deep vein thrombosis, Anaphylaxis, Hemodynamic instability, Sepsis, Catheter related infection assessed(6). The mRS was routinely calculated at the time of admission and discharge. The mRS discharge score of zero was categorized as a complete improvement, while any decrement in the mRS score without complete improvement was classified as a partial improvement. No change in mRS and increase in mRS scores were categorized as static and deteriorating, respectively.

STUDY PROCEDURE

Patients were identified by reviewing TUTH Hemodialysis department logs for IMND patients who received LVPE therapy. The identified participants' charts were obtained from TUTH central record section and reviewed for the purpose of the study. Data on demographics, mRS, and treatment problems were collected in a study proforma and then uploaded to SPSS for analysis.

LVPE PROCEDURE

This is a routinely done procedure in TUTH, where a femoral line is made access initially to allow adequate blood flow for LVPE. About 600 ml of plasma volume is removed through plasmaflux filter in a hemodialyzer machine at the flow rate 150 ml/hr on daily basis targeting about 6 liters of plasma removal over a period of 8 to 10 days. Replacement of plasma volume and clotting factors is done by 600 ml of plasmalyte (Crystalloid)(7) and II pint FFP in daily basis. Prophylactic antibiotics with one gram Cefazolin and Ceftriaxone is given after each plasma exchange.

STUDY VARIABLES

The study variables collected for demographic characteristics are age, gender, socioeconomic status(8), and geographical location. Admission status of patient for respiratory failure, need for mechanical ventilation, hospital stay days and disease related complications were assessed. Serum auto-antibodies, Cerebrospinal fluid (CSF) analysis, radiological findings and treatment related complications during hospital were also accessed. Any additional requirement of prior methylprednisolone and maintenance immune-modulators were looked for.

ETHICAL APPROVAL

Ethical approval was obtained from the research ethics committee of the Institutional Review Committee (IRC) of the Institute of Medicine (IOM) [Reference no. 229(6-11) E2]. Confidentiality of the information was maintained thoroughly.

STATISTICS

Over a two-year period, all patients admitted to TUTH with IMND who were eligible for the therapy were enrolled in the study. The mean age, gender proportion, socioeconomic status scores, and whether or not the patient required mechanical ventilation were all described. Age groups were defined as <20, >=20 to <=40, >40 years old. Continuous variables were presented in the form of mean and standard deviation. The paired T-test was used to compare the Modified Rankin Scale for all patients at admission and the following therapy at the time of discharge. Deep Vein Thrombosis, Anaphylactic reaction, Anaphylactic shock, Sepsis, Catheter-related infection, and Hemodynamic instability were also classified as treatment-related problems. Fisher exact test was used to examine the relationship between patient variables (age groups, gender, socioeconomic level, and the need for mechanical breathing) and treatment-related problems.

RESULT

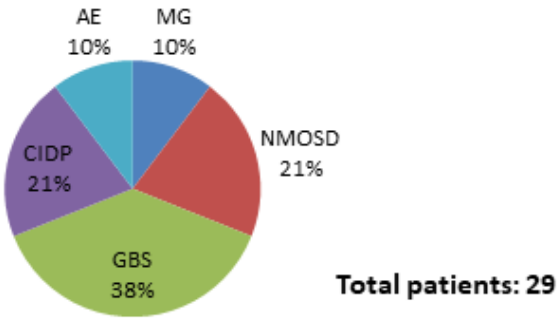
PATIENT CHARACTERISTICS

A total of 29 participants included 3 patients with MG, 6 with NMOSD, 11 with GBS, 6 with CIDP, and 3 with AE. Overall, the mean age of 3 MG patients was 47±14.5 years with 2 male patients and 2 from middle-class, and 1 form lower class family; and all of the patients needed mechanical ventilation. Six patients were diagnosed with NMOSD; the mean age was 35±12.4 years with all patients as female, 67% were middle class, 33% were low class, and 33% required mechanical

ventilation. The mean age of 3 with AE was 47.7±24.2 years; 2 were male; 2 were in the middle class while 1 was in the lower class; and 1 needed mechanical ventilation.

Among 11 patients diagnosed with GBS, the mean age was 36±11.8 years, 45% were female, and 55% were male, 82 % belonged to the middle class, 18% belonged to lower class socioeco-nomic status and 27% of patients required mechanical ventilation. Six patients were diagnosed with CIDP where the mean age was 58.3±11.6 years, 33% were female, 67% were male, 50% belonged to the middle class, 50% belong to higher class socioeconomic status, and none of the patients required mechanical ventilation.

Figure 1: Spectrum of Immune mediated neurological diseases



Study outcomes

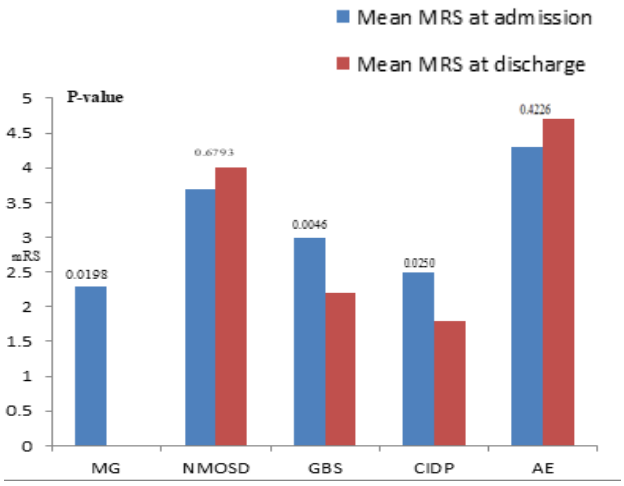
We found improvement in mRS at discharge after treatment in patients of MG, GBS and CIDP (i.e. p-value of 0.0198, 0.0046 and 0.0250 respectively). 66% of patients had partial or complete improvement in terms of mRS score.

Table 1: Different outcomes of the patients undergoing Low volume plasma exchange

Diseases[n]	MG[3]	NMOSD [6]	GBS [11]	CIDP [6]	AE [3]	Total [29]
Outcomes						
Partially improved	0	2	8	4	0	14
Completely improved	3	0	2	0	0	5
Static	0	3	1	2	2	8
Deteriorating	0	1	0	0	1	2
Death	0	0	0	0	0	0

As shown in Fig.2, patients with MG, GBS, and CIDP all showed statistically significant im-provement in mean mRS scores from 2.3±0.6 to 0 (p value = 0.0198), 3.03±1.8 to 2.2±1.4 (p val-ue=0.0046) and 2.5±1.4 to 1.8±1 (p value=0.025) respectively by the time they were discharged following treatment. Whereas, patients with NMOSD and AE showed increase in mean mRS scores from 3.7±1.8 to 4.0±1.6 (p value = 0.6793), 4.3±0.6 to 4.7±0.6 (p value=0.4226) respectively which was statistically insignificant.

Figure 2: Bar graph of mRS score at admission and discharge



Treatment related complications

Among total number of 29 patients, 4 patients developed treatment related complications related to LVPE. Two patients in NMOSD group developed DVT and 2 patients in GBS group developed anaphylactic reaction and none of the patients deteriorated or had poor outcome. We didn't find any association of treatment related complications with age, gender, socioeconomic status and need for mechanical ventilation.

Table 2: Complications related to Low volume plasma exchange

Diseases[n]	MG[3]	NMOSD [6]	GBS [11]	CIDP [6]	AE [3]
Complications					
Deep vein thrombosis	0	2	0	0	0
Anaphylactic reaction	0	0	2	0	0
Hemodynamic instability	0	0	0	0	0
Sepsis	0	0	0	0	0
Catheter related infection	0	0	0	0	0

Table 3: Association of Patient's characteristics with treatment related complications

	No complica-tions	DVT	Anaphylactic reaction	Other complications	Total	p-value
Variables						
Gender						
Male	12	0	2	0	14	
Female	13	2	0	0	15	0.234
Total	25	2	2	0	29	
Age group						
<20	2	0	0	0	2	
20-40	9	1	2	0	12	0.576
>40	14	1	0	0	15	
Total	25	2	2	0	29	
Socioeconomic status						
Low	3	1	0	0	4	
Middle	17	1	2	0	20	0.556
High	5	0	0	0	5	
Total	25	2	2	0	29	
Mechanical ventilation						
Yes						
No	9	0	0	0	9	
Total	16	2	2	0	20	0.568
	25	2	2	0	29	

DISCUSSIONS

In our study, we have evaluated the effectiveness and safety of LVPE. After LVPE, we observed a significant improvement in the mRS score at discharge for immune-mediated neurological disorders affecting the neuromuscular junction and peripheral nerves (MG, GBS and CIDP). Patients with myasthenia crisis were discharged without any disability. We found DVT and ana-phylaxis as common complications. Patient variables (age, gender, socioeconomic level, and res-piratory failure status) were not observed to be associated with LVPE complications.

There are limited studies that have been conducted in LVPE. In a Phase two trial, LVPE as safe and alternative method of treatment to SPE was unable to establish LVPE efficacy. In this study, plasma volume was replaced by an equal volume of the crystalloid solution alone and no treatment-related complications were seen. In contrast to the above study where no treatment-related complications were seen, our study encountered DVT and anaphylactic reaction. And these complications might be attributed to FFP transfusion causing anaphylaxis and hypercoagulable state. The association of Venous thromboembolism (VTE) with FFP is unknown but one of the study showed increased VTE risk by 25% with each unit of FFP (9). Another retrospective study of LVPE among Acute on chronic liver failure (ACLF) patients showed improved survival without treatment related complications where 1.5 L plasma volume of FFP replaced at each session for three consecutive days(10). Compared to oue study where 4L of FFP being transfused over 10 days, the study done among ACLF patients had 4.5 L of FFP transfused over 3 days which was relatively shorter duration of time. Howeover, ACLF patients had no complications of VTE which might be due to suppressed coagulation factors (11). Moreover, in our study 2 cases of NMOSD presenting with paraplegia developed DVT which might as well be disease related complication.

In countries like Nepal and other low-income countries, where the costs of IVIG or SPE is relatively high, early and effective treatment remains a challenge for many patients diagnosed with immune mediated neurological diseases. The LVPE exchanges slightly lower volume of plasma at 0.6L /day compared to SPE (four sessions at a rate of 50 mL/kg plasma removal per session with approximate 12 L of total plasma volume removal over 10 to 14 days)(12). The potential advantages of LVPE are its low cost (approximately NRS 100,000) and shorter time over 8 to 10 days compared to SPE(13). In developing countries, there is as well an

increasing prevalence of immune-mediated neurological diseases recently, perhaps related to increasing awareness and advancing diagnostic investigations(14). Therefore, for acute treatment, LVPE would be a less costly alternative in IMND, especially MG. Limitations of this study are there as this is a single-centered study with a small sample size, and all data has been retrospectively analyzed, so patients were not followed up after discharge to access any further improvement at maximum after LVPE. The mRS might not well represent the disability score for symptoms of a seizure, visual impairment and cognitive decline, which are common in cases of NMOSD and AE(15, 16).

CONCLUSION

In the study low volume plasma exchange showed treatment effectiveness in MG, GBS and CIDP and showed complete improvement in all cases of Myasthenia crisis requiring mechanical ventilation. So, LVPE could be a lifesaving alternative for the patients of Myasthenia crisis and further randomized controlled trial are needed regarding LVPE.

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