Neurology Asia 2024; 29(2) : 381 – 384

Effectiveness of limited plasma exchange in Guillain-Barré syndrome

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Abstract

Objective: The aim of this study is to compare the efficacy of limited plasma exchange against supportive and standard treatments in treatment of Guillain-Barré syndrome (GBS). *Method:* A total of 90 GBS patients admitted to Yangon General Hospital, Yangon, Myanmar were recruited over 1.5-year-period from January 2017 to June 2018 and they were divided into 3 groups according to the treatment they received (convenience sampling method): supportive (n=36), limited plasma exchange (LPE) (n=35) and standard (therapeutic plasma exchange - TPE or IVIg) (n=19)). Their clinical features, electrophysiological subtypes and severity were compared at baseline, and outcome (change in GBS disability score (GDS) at 30 days after entry) was assessed and compared. *Results:* Baseline characteristics such as gender, GBS subtypes and respiratory involvement were comparable, but standard treatment group had older patients, and LPE group had shorter latency to nadir and more cases with antecedent diarrhea, which are poor outcome predictors. At 30 days from entry, mean GDS improvement was 0.9 ± 0.6 in supportive, 1.4 ± 0.6 in LPE and 1.2 ± 0.8 in standard treatment groups respectively. The difference between LPE and supportive treatment was statistically significant (p 0.002) but there was no difference between LPE and standard treatment (p = 0.512). Regarding untoward effects, apart from one transient hypotension and 2 anemic cases, no other serious adverse effects were noted from LPE therapy.
Conclusion: LPE may be superior to supportive treatment and may not be inferior to standard treatment. Therefore, LPE may be an alternative effective treatment for GBS patients who are not accessible to standard treatments especially in low income countries with limited resources.

Keywords: Limited plasma exchange, small volume, Myanmar

INTRODUCTION

Guillain-Barré syndrome (GBS) is an acute post-infectious immune related inflammatory polyneuropathy with resultant weakness and diminished reflexes. Standard treatments for GBS are immunotherapies such as therapeutic plasma exchange (TPE) and intravenous immunoglobulin (IVIg), both of which are costly. Availability, accessibility and affordability of standard treatments is limited in developing countries including Myanmar. Limited plasma exchange (LPE) is a modified, small-volume, manual form of plasma exchange. LPE was first used in management of Myasthenia Gravis crisis in intensive care unit (ICU) of Yangon General Hospital since 1995 and it has been used since 2010 in Neuro-medical ward of YGH for those who are unaffordable or inaccessible to standard TPE or IVIg with the same indications and contraindications as standard TPE.[1] The same method of modified plasma exchange was found to be used and studied in Sri Lanka in 1987 on six patients with GBS and the study participants were concluded to have rapid recovery although there was no comparison group.[2] The basic principle of LPE is similar to standard therapeutic plasma exchange (TPE). Estimated blood volume (EBV) = weight (kg) x average blood volume (mL/kg) = 50kg x 65 mL/kg = 3.25 litres. The safe allowable blood loss (ABL) per day for an average person with body weight 50 kg, average blood volume 65 ml/kg and hematocrit (Hct) 45% is EBV x (Hi - Hf)/ Hi = 3.25 x (45-30)/45 = 1 liter (L) or 2 units of whole blood (Initial Hct (H_i) = 45%,

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Date of Submission: 13 November 2023; Date of Acceptance: 16 January 2024
https://doi.org/10.54029/2024ejd

Final acceptable Hct (H_f) = 30%). In LPE, two units of whole blood are withdrawn per day for 10 days. Since one unit of whole blood contains about 300 mL of plasma, total exchange amount in LPE will be 6 L. This is equivalent to about 60% of plasma volume exchanged in TPE because the total amount of plasma exchanged in TPE (200 ml/kg) for an average size adult of 50 kg is 10 L.

Materials needed for LPE are 18 G Cannula, double disposable blood bags, transfusion sets, centrifuge and cell separator; 2 units of matched fresh frozen plasma (FFP) or old plasma a day for 10 days or alternatively 20% albumin 100 ml plus 0.9% normal saline (NS) as replacement fluid. Advantages of LPE are simplicity (can be done in general ward), lower cost, reliance on basic blood banking equipment (centrifuge, cell separator) that are widely available even in small district hospitals of Myanmar. Possible disadvantages are lesser amount of exchange (60%), discomfort to patients due to multiple punctures, tiresomeness to health care providers, sepsis, venous thrombosis, blood loss, hypotension, blood-borne infections, allergic reaction to blood products which are mainly due to replacement plasma. Since LPE is simpler and cheaper without the need of expensive equipment, it is feasible in resource-limited countries. Although it has been used in Myanmar for more than a decade, it was not properly studied and published. So the current study aimed to study GBS patients treated with LPE in comparison with supportive and standard treatments.

METHODS

This study is a hospital-based prospective study on GBS patients admitted to Neuro-medical ward of Yangon General Hospital from January 2017 to June 2018. Part of this study originally was doctorate thesis of Dr Yan Lynn Aung where only supportive and LPE groups were analyzed.[3] We included standard treatment group admitted during the same period to study and analyze. Total 90 patients with GBS (> 12 years of age) admitted to Yangon General Hospital with GBS disability score (GDS) < 5 were included and divided into 3 groups according to the treatment they received (convenience sampling method): supportive (n=36), LPE (n=35) and standard treatment (TPE or IVIg) (n=19)). This depends upon their affordability and choice. Their clinical characteristics, electrophysiological subtypes and severity were studied at baseline. Change in GDS at 30 days after entry was used as the primary outcome measure. As secondary outcome measures, days of hospitalization and possible adverse effects related to treatment such as hemodynamic instability, thrombophlebitis, venous thrombosis, significant hemoglobin drop, blood-borne infection and allergic reactions were recorded. It was done under approval of Academic Board of Study and Research and Ethics Committee of the University of Medicine (1), Yangon.

The protocol for LPE were: Informed consent; Venesect blood from antecubital vein and send it to blood bank to be centrifuged; Discard the plasma fraction; Re-infuse patient's packed cell; Infuse donor's fresh frozen plasma (FFP) or intravenous albumin 25 g and normal saline (NS) 500 mL in place of patient's plasma; Two units of exchange a day for 10 days; Monitor vital signs (temperature, blood pressure, pulse rate, respiration) before and after every procedure and check full blood cunt (FBC) at baseline and day 8.

RESULTS

A total 90 patients with GBS were recruited, 40% (36/90) were on supportive treatment only, 38.89% received LPE and 21.1% (19/90) were treated with standard treatments (standard TPE or IVIg). Out of total 19 patients who received standard treatments, 7 had TPE and 12 had IVIg. The baseline characteristics, electrophysiological subtypes and GDS score of the three groups are shown in Table 1. There was no difference with regard to gender, GBS subtypes, and respiratory involvement among the groups. However, standard group had older patients and LPE group had shorter latency to nadir and more cases with antecedent diarrhea, which are factors predictive of poor outcome. Baseline GDS was lower in supportive group but comparable between LPE and standard treatment groups.

As shown in Table 2, at 4 weeks from entry, mean GDS improvement was 0.9 ± 0.6 in supportive, 1.4 ± 0.6 in LPE and 1.2 ± 0.8 in standard treatment groups respectively. The difference in GDS reduction between LPE and supportive treatment was statistically significant ($p = 0.002$). There was no difference between LPE and standard treatment ($p = 0.512$). LPE is less costly than standard treatment group. Duration of hospitalization was shorter in supportive and standard- IVIg group and comparable between LPE and standard-TPE group.

Table 1: Baseline characteristics of different treatment groups

Baseline characteristics, mean (SD)	Treatment groups			P
	Supportive (n=36)	LPE (n=35)	Standard (n=19)	
Age (years)	30.0 (15.8)	32.2 (19.6)	48.2 (14.2)	0.001
Gender : Male Female	22 (61.1) 14 (38.9)	23 (65.7) 12 (34.3)	12 (63.2) 7 (36.8)	0.922
Latency to nadir (days)	9.1 (7.2)	5.4 (3.7)	7.2 (4.6)	0.036
Antecedent diarrhoea	0 (0)	5 (14.3)	2 (10.5)	0.037
Ventilatory requirement	1 (2.8)	3 (8.6)	2 (10.5)	0.498
GBS subtypes : axonal	18 (50.0)	18 (51.4)	9 (47.4)	0.481
GDS at entry	3.3 (0.8)	3.7 (0.6)	3.8 (0.4)	0.017

SD: Standard deviation, LPE: Limited plasma exchange, GBS: Guillain-Barré syndrome, GDS: GBS disability score

DISCUSSION

GBS is the commonest cause of peripheral neuropathy that needs hospital admission at our center.[4] Impact of GBS on activities of daily living, work and social activities is considerable. Its standard treatments such as IVIg and TPE are of high cost. The cost of IVIg in Myanmar is 7000 USD and TPE costs about 3000 USD. TPE machine exists in only few centers in Myanmar. Subsequently, most GBS patients in Myanmar do not have access to or cannot afford to both treatments. That is why, even in tertiary hospital like Yangon General Hospital (YGH), only 35.1% (26 of 74 GBS patients) in 2017, 32.5% (25 of 77 GBS patients) in 2018, and 13.9% of GBS patients in 2019 received these standard treatments (Yangon General Hospital, Neuro-medical ward registry).[5] The remaining patients who were not affordable or not accessible (eg. those in ICU where there was no TPE machine) were treated conservatively with supportive measures or limited plasma exchange (LPE).

According to Table 1, baseline characteristics of the three groups were not significantly different in gender, GBS subtypes, and respiratory involvement. But the standard group had older patients and LPE group had shorter latency to nadir and more cases with antecedent diarrhea, which are factors predictive of poor outcome according to previous studies. So actually more patients with poor outcome were included in LPE group. Baseline GDS was lower in supportive group but comparable between LPE and standard treatment groups. This might be because milder patients chose conservative treatment more.

As shown in Table 2, GDS score reduction at 30 days from entry was significantly higher in LPE and standard treatment groups than supportive group, and there was no significant difference between LPE and standard treatment group; p

Table 2: Outcome comparison among different treatment groups

Outcomes, mean (SD)	Treatment groups		
	Supportive (n=36)	LPE (n=35)	Standard (n=19)
GDS score reduction	0.9 (0.6)	1.4 (0.6)	1.2 (0.8)
Cost (USD)	0	0-100	3000-6000
Hospital stay (days)	11.3 (9.6)	16.9 (4.9)	17.2 (16.6) IVIg: 12.2 (4.5) TPE: 16 (3.7)
Complications	None	8.57% (1 hypotension, 2 anemia)	IVIg (n=12): None TPE (n=7): 28.57% (1 hypotension, 1 pulmonary embolism)

SD: Standard deviation, GDS: GBS disability score, LPE: Limited plasma exchange, USD: United States dollars, IVIg: Intravenous immunoglobulin, TPE: Therapeutic plasma exchange

0.002 in LPE versus supportive group, and p 0.512 in LPE versus standard treatment group. It means LPE treatment may be superior to supportive treatment and LPE may be comparable to standard treatments. Regarding the cost of treatment, LPE is far less costly than standard treatment group since the former only needs ordinary blood transfusion sets. Among the standard treatments, IVIg is far more costly than standard TPE. LPE is done everyday for 10 days and TPE is done alternate day for 5 times, so both LPE and TPE take more or less the same period. Regarding hospital stay, patients who received LPE has slightly longer hospital stay than TPE but this was not statistically different (p 0.649). IVIg treatment was given in 5 days, so its group has significantly shorter hospital stay (p 0.003) than plasma exchange groups. In terms of complications, there is no complication noted among patients who received IVIg, but 1 case of hypotension (BP 80/50 easily reversed with normal saline), and 2 cases of anemia with hemoglobin drop to 8.7 and 9 g% respectively were noted in LPE group. Both anemic cases received whole blood one unit instead of FFP on their last day. Causes of anemia could be due to blood loss in the tubing during repeated venesection followed by transfusion, and possible hemolysis during handling, transportation, and centrifugation of blood bags. One case of hypotension (BP 80/50) and 1 case of pulmonary embolism in standard TPE group. So patients undergoing LPE suffer less complications than standard TPE in our cohort: 8.57% (3 out of 35) vs 28.57% (2 out of 7) although our sample size in TPE group was small.

The major limitation of our study is the absence of randomization that could have accounted for various confounders. In addition, it was a short-term study. We need further studies on efficacy and safety of LPE with larger sample size, proper sampling method and longer follow up.

In conclusion, LPE may be superior to supportive treatment and may not be inferior to standard treatments. Therefore, LPE, which is simple and in principle can be applied at basic medical facilities, may be an alternative effective treatment for GBS patients who are not accessible to standard treatments especially in low income countries with limited resources.

DISCLOSURE

Conflicts of interest: None

Financial support: None

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