Therapeutic Plasma Exchange in Various Clinical Settings at a Tertiary Hospital – A Retrospective Analysis from a Technical Point of View

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DOI: 10.56018/20250605

Abstract

Introduction: Therapeutic plasma exchange (TPE) is an extracorporeal blood purification procedure widely used in neurological and immunological diseases. While established protocols exist, patient variability necessitates individualized approaches to optimize efficacy and safety. **Methodology:** This retrospective observational study analyzed all TPE procedures performed in a tertiary hospital and blood center from January to December 2024. Clinical indications were categorized, and key parameters—including demographic characteristics, body mass index (BMI), hematocrit, calculated plasma volume (PVcalc), exchanged plasma volume (PVex), and PVex/PVcalc ratio—were recorded. Replacement fluid strategies and treatment cycles were evaluated, and statistical significance was set at $p < 0.01$. **Results:** A total of 723 TPE procedures were performed on 181 patients. Neurological disorders accounted for 83.4% of cases, mainly Guillain–Barré syndrome (62.5%), transverse myelitis (11%), and neuromyelitis optica (3.3%). Immunological diseases and vasculitis comprised 14.4%, including myasthenia gravis (11%), TTP (1.2%), and SLE (0.96%). Neurological patients had higher median hematocrit (40.2%) than the immunological group (35.7%), resulting in lower PVcalc (2376 mL vs. 2728 mL; $p < 0.01$). Despite these differences, treatment cycles remained around five across groups. Neurological patients exhibited a higher PVex/PVcalc ratio (0.92 vs. 0.77; $p < 0.01$), suggesting a more aggressive exchange approach. **Conclusion:** Significant clinical improvements occurred across all groups, even with lower-than-recommended plasma exchange volumes. These findings highlight the need for individualized TPE protocols based on disease-specific plasma dynamics. Further multi-center studies are warranted to refine evidence-based guidelines for optimal TPE outcomes.

Keywords: Therapeutic plasma exchange (TPE), neurological disorders, immunological diseases, plasma volume.

Introduction

Therapeutic plasma exchange (TPE) is an extracorporeal blood purification technique that has evolved over more than a century of practice.[1] At its core, TPE targets the removal of harmful plasma constituents, such as lipoproteins, autoantibodies, and immune complexes, that contribute to various disease processes. In this procedure, a patient's blood is drawn and circulated through an apheresis device, where the plasma is separated from the cellular elements. The removed plasma, often laden with pathogenic substances, is discarded, while the remaining cells are reinfused into the patient alongside replacement fluids like fresh frozen plasma or albumin, tailored to the clinical scenario.[2]

Initially applied in the early 1950s to manage hyperviscosity in multiple myeloma, TPE demonstrated its capability to significantly alter plasma protein concentrations through the use of membrane plasma separators. Fundamentally, the technique operates by filtering out high-molecular-weight proteins as blood traverses through a specialised circuit. During this process, the plasma is segregated from the cellular components, and after discarding the affected plasma, the cells are combined with an appropriate fluid replacement.[3]

Two principal methods are employed to perform plasmapheresis: centrifugation and filtration. In centrifugation-based apheresis, centrifugal forces separate whole blood into distinct fractions based on density differences, effectively isolating the plasma from red cells, white cells, and platelets.[4] In contrast, the filtration method uses a membrane with a defined pore size to remove plasma components while retaining the cellular elements selectively.[5] Filtration-based plasma exchange is particularly useful in clinical settings such as nephrology and intensive care, where it can be performed in tandem with other modalities like continuous veno-venous hemodialysis, thereby enhancing overall patient management.[6]

The technical process of TPE is generally broken down into several key steps: installation and priming of the apheresis kit, active separation of the plasma, reinfusion of the cellular components along with the replacement fluid, and finally, the removal of the apheresis circuit.[7] One of the notable clinical advantages of using fresh frozen plasma in this context is its capacity to restore essential plasma proteins, for instance, replenishing ADAMTS13 in patients with thrombotic thrombocytopenic purpura. Moreover, TPE is frequently employed in critical care scenarios, such as in the management of severe sepsis or hypertriglyceridemia-induced pancreatitis, because it has the potential to remove a broad spectrum of pro-inflammatory cytokines, although further data to support some of these applications are still awaited.[8]

TPE is particularly appropriate for conditions where disease pathology is driven by toxic molecules with relatively high molecular masses (typically above 15,000 Daltons).[9] The historical refinement of plasmapheresis techniques—especially during the formative years of modern TPE in the 1960s—has cemented its role in clinical practice by continually enhancing its technical precision and therapeutic effectiveness. According to ASFA 2023 guidelines, TPE is considered first-line treatment in Guillain-Barré Syndrome, Goodpasture Syndrome, Myasthenia Gravis, TTP, Acute liver failure etc.[10]

Materials and Methods

This retrospective analysis was conducted in the Department of Immunohematology & Blood Transfusion at a tertiary care hospital in Ahmedabad, Gujarat, India, from 1st January to 31st December 2024. All patients for whom TPE was indicated by the treating physician

and subsequently admitted to the hospital were included in the study. Comprehensive clinical and laboratory evaluations, including complete blood counts, electrolytes, serum proteins, coagulation profiles, and vital signs, were systematically performed. Informed consent was obtained from each patient or their relative and was duly documented.

TPE procedures were executed using a double-lumen hemodialysis catheter, establishing venous access (via central or femoral routes) and utilizing a continuous cell separator (Spectra Optia, Terumo BCT or COMTEC, Fresinius Kabi). Sessions were typically scheduled on alternate days for 8 to 12 days. Plasma separation was achieved by centrifugation, with anticoagulation maintained using citrate at ratios ranging from 1:12 to 1:14. The volume and type of replacement fluid, be it fresh frozen plasma or a combination of FFP or Normal Saline, were administered based on individual patient requirements. As part of the protocol, prophylactic intravenous calcium gluconate was routinely infused.

Data Collection

A systematic record was maintained for each procedure, documenting the clinical indication for TPE, number of cycles performed, volume of plasma exchanged and the corresponding volume of replacement fluid administered and the patient's response to the treatment.

Patient details were retrieved from the blood centre's records, which included the apheresis register, apheresis files, requisition forms, and laboratory results. Specifically, data collected included Demographic details (name, age, sex, height, and weight), clinical diagnosis and indication for TPE, the referring department, the number of cycles required, Blood group, and key laboratory values such as hemoglobin, hematocrit, serum calcium and serum albumin.

Statistical Analysis

Data was organized and analyzed using Microsoft Excel and IBM SPSS Statistics 26 software. The chi-square test was employed to evaluate statistical significance, with the threshold for significance set at $p < 0.01$.

Results

Within the study period, 723 therapeutic plasma exchange (TPE) procedures were performed on 181 patients. Indications for TPE were broadly categorized into three clusters (Figure 1).

- Neurological Disorders (83.4%): This cluster included predominantly Guillain–Barré syndrome (GBS, 62.5%), followed by transverse myelitis (11%) and neuromyelitis optica (3.3%).
- Immunological Diseases and Vasculitis (14.4%): Cases in this group were mostly due to myasthenia gravis (11%), with smaller proportions attributed to thrombotic thrombocytopenic purpura (TTP, 1.2%) and systemic lupus erythematosus (SLE, 0.96%).
- Other Conditions (2%): This included acute liver failure (1.5%) and mixed connective tissue disorder (MCTD, 0.69%).

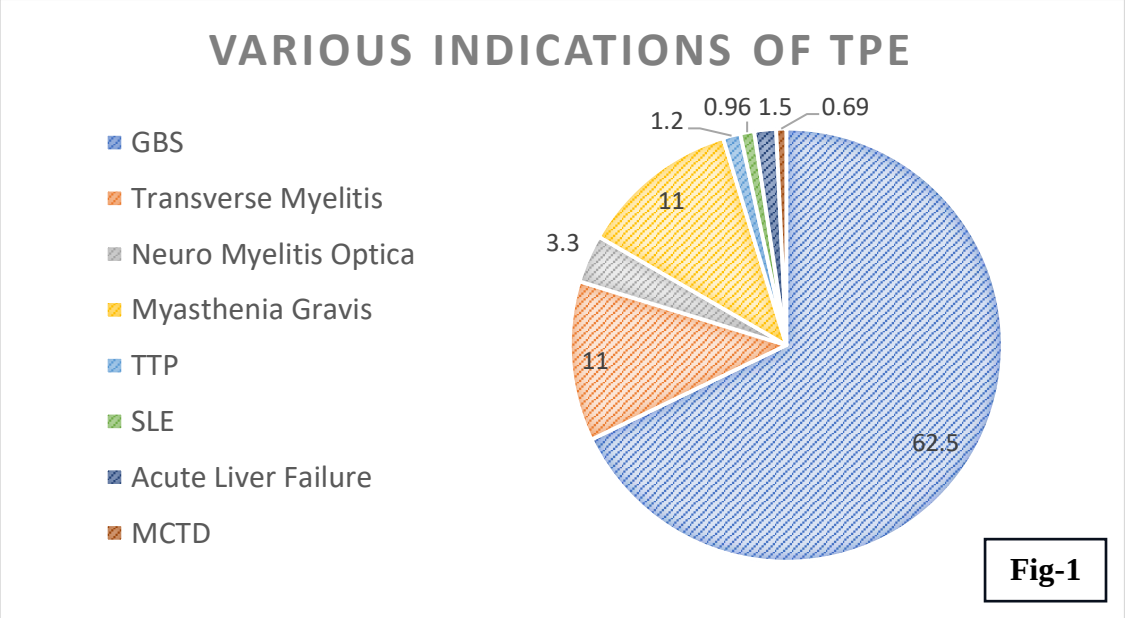

Figure 1: Various indications of TPE

A total of 181 patients undergoing therapeutic plasma exchange (TPE) were analyzed (Table 1). The overall median age was 47.0 years [interquartile range (95% CI): 35.0–59.0]. When stratified by clinical indication, patients with neurological conditions (n = 151) had a median age of 48.0 years [95% CI: 34.0–62.0], those diagnosed with immunological diseases and vasculitis (n = 26) had a median age of 44.0 years [95% CI: 34.0–54.0], and the remaining group (n = 4) had a median age of 46.5 years [95% CI: 34.0–52.0]. The cohort comprised 112 males and 69 females overall. Notably, the neurological group had a male-to-female ratio of 95:56, whereas the immunological/vasculitis group exhibited a relative predominance of females (11 males vs. 15 females), and the "others" group was equally distributed (2 males and 2 females).

Table 1: Different Parameters of the TPE procedures

Parameter	**All (n=181)**	**Neurological (n=151)**	**Immunological disease and Vasculitis (n=26)**	**Others (n=4)**
Age	47.0 [35.0 - 59.0]	48.0 [34.0-62.0]	44.0 [34.0 - 54.0]	46.5 [34.0-52.0]
Sex (M/F)	112/69	95/56	11/15	2/2
BMI (kg/m^2)	22.14 [20.9-23.3]	22.24[20.3-24.18]	21.22[20.6-21.84]	22.98[20.8-25.1]
Hct	37.8 [34.2-41.4]	40.2 [37.3-43.1]	35.7 [32.1-39.3]	37.2 [35.4-39.2]
PV_{calc} (ml)	2560[2343-2900]	2376[2078-2872]	2728[2491-3138]	2576[2462-2690]
PV_{ex} (ml)	2165[1864-2466]	2186[1928-2444]	2101[1856-2346]	2209[1963-2455]
PV_{ex}/PV_{calc}	0.84 [0.73-0.94]	0.92 [0.72-1.1]	0.77 [0.69-0.82]	0.85 [0.79-0.91]

Treatments (n)		5 [3-5]	5 [5-5]	5 [3-5]	5 [3-5]
Exchange Fluid (%)	FFP	20.5%	0%	61.5%	0%
	FFP & NS	79.5%	100%	38.5%	100%

The overall median body mass index (BMI) was 22.14 kg/m² [95% CI: 20.9–23.3]. Group-specific median BMIs were 22.24 kg/m² [95% CI: 20.3–24.18] for neurological disorders, 21.22 kg/m² [95% CI: 20.6–21.84] for immunological/vasculitis cases, and 22.98 kg/m² [95% CI: 20.8–25.1] for others. Hematocrit (Hct) values varied among the groups, with an overall median Hct of 37.8% [95% CI: 34.2–41.4]. The neurological group exhibited a higher median Hct of 40.2% [95% CI: 37.3–43.1] compared with 35.7% [95% CI: 32.1–39.3] in the immunological/vasculitis group and 37.2% [95% CI: 35.4–39.2] in the others category.

Technical parameters related to plasma volumes were also assessed. The overall calculated plasma volume (PVcalc) had a median of 2560 ml [95% CI: 2343–2900 ml]. Patients in the immunological/vasculitis group had a higher median PVcalc of 2728 ml [95% CI: 2491–3138 ml] compared to 2376 ml [95% CI: 2078–2872 ml] in those with neurological conditions (p value <0.01) and 2576 ml [95% CI: 2462–2690 ml] in the other group (p value <0.01). The overall median exchange volume (PVex) was 2165 ml [95% CI: 1864–2466 ml]. In terms of efficiency, expressed as the ratio of plasma exchanged to the calculated plasma volume (PVex/PVcalc), the overall median was 0.84 [95% CI: 0.73–0.94]. The neurological group achieved a slightly higher median ratio (0.92 [95% CI: 0.72–1.1]) compared with 0.77 [95% CI: 0.69–0.82] in the immunological/vasculitis group (p value <0.01) and 0.85 [95% CI: 0.79–0.91] in the others (p value <0.01).

Regarding treatment protocols, the median number of cycles administered was 5 [95% CI: 3–5] for the overall cohort. Notably, neurological patients consistently received 5 cycles (95% CI: 5–5), whereas the immunological/vasculitis and others groups had a slightly wider variation (95% CI: 3–5). Replacement fluids during the TPE procedures also varied significantly by indication. Overall, 20.5% of the procedures utilized fresh frozen plasma (FFP) exclusively, while 79.5% administered a combination of FFP and normal saline (NS). In the neurological subgroup, 100% of cases employed a combination of FFP & NS, with no procedures using FFP alone. In contrast, the immunological/vasculitis group predominantly used FFP alone in 61.5% of cases, with the combination applied in the remaining 38.5%. The small “others” group also exclusively received the FFP & NS combination (100%).

Discussion

This retrospective analysis of 723 TPE procedures in 181 patients over a one-year period provides important insights into how patient-specific factors can influence treatment parameters and outcomes in therapeutic plasma exchange.

Demographic and Baseline Characteristics:

The median ages across the groups ranged from 44 to 48 years, with a comparatively higher median in the neurological group. A male predominance (112 males vs. 69 females) was observed overall; however, the immunological/vasculitis subgroup demonstrated a reverse trend (11 males vs. 15 females). These findings are in agreement with previous epidemiological studies that report a higher prevalence of certain autoimmune and vasculitic conditions in females, while many neurological conditions, such as Guillain–Barré syndrome (GBS), are more frequently observed or more severe in males.[11] Recognising

these demographic disparities is crucial, as they may not only affect clinical presentation but also influence the physiological response to TPE.

Body mass index (BMI) values were closely clustered across all groups, suggesting that dosing and volume estimates based on body mass remain reliable across these populations. In contrast, hematocrit (Hct) values differed significantly; the neurological group exhibited a higher median Hct (40.2%) compared to the immunological/vasculitis group (35.7%). As hematocrit is known to affect blood viscosity and the efficiency of plasma separation, these differences likely necessitate adjustments in procedural parameters to optimize pathogenic substance removal while maintaining hemodynamic stability. Similar observations regarding the impact of hematocrit on plasma volume calculations have been reported in prior studies.[12]

Plasma Volume and Exchange Parameters

One of the key technical findings was that the median calculated plasma volume (PVcalc) was higher in the immunological/vasculitis group (2728 mL) compared to the neurological group (2376 mL), a statistically significant difference ($p < 0.01$). This suggests that patients with immunological conditions might have unique plasma dynamics or body composition characteristics that require a higher base volume for an effective exchange.[13] Despite these differences in calculated volume, the exchanged plasma volume (PVex) remained within a comparable range among groups. The overall ratio of exchanged to calculated plasma volume (PVex/PVcalc) was 0.84, with the neurological group reaching a higher median ratio of 0.92 compared to 0.77 in the immunological/vasculitis group. This higher ratio in neurological patients may reflect a more aggressive removal strategy aimed at clearing the pathogenic molecules specific to conditions such as GBS, transverse myelitis, and neuromyelitis optica.[14]

Previous investigations have emphasized that achieving a higher proportion of plasma exchange might enhance the removal of circulating autoantibodies and inflammatory mediators, thereby improving clinical outcomes.[13] Our findings support this concept while also raising the possibility that even lower-than-recommended exchange volumes can be clinically beneficial, a notion corroborated by the significant improvements observed in almost all patients despite the suboptimal PVex/PVcalc ratios.

Treatment Cycles and Replacement Fluid Strategies

The median number of TPE cycles was consistently about five across all groups. In the neurological group, there was minimal variation (all patients received five cycles), which likely reflects a protocol-driven approach based on established clinical guidelines and desired therapeutic endpoints.[10] This degree of standardization enhances the reliability of attributing clinical outcomes to procedural variables.

The choice of replacement fluid varied notably between groups. In all neurological procedures, a combination of fresh frozen plasma (FFP) and normal saline (NS) was employed. In contrast, within the immunological/vasculitis group, 61.5% of cases utilized FFP exclusively, with the remainder receiving the combined approach. This disparity likely reflects differing therapeutic goals: patients with immunological disorders may benefit more from the exclusive use of FFP, aimed at replenishing vital plasma proteins such as clotting factors and immune-modulatory proteins, whereas neurological conditions may require a balance between efficient clearance of pathogenic substances and the maintenance of circulatory volume.[15] The American Society for Apheresis (ASFA) has previously emphasized the importance of tailoring replacement fluid strategies to individual patient needs, and our data further support this individualized approach.[10]

Clinical Implications

Despite the observed lower-than-recommended exchanged plasma volumes, significant clinical improvement was noted in almost all patients. This outcome suggests that there may exist a therapeutic threshold for plasma exchange beyond which additional volume does not necessarily confer greater clinical benefit. These observations are in line with a Cochrane review which indicated that even partial plasma exchange can have a significant impact on disease outcomes, particularly in conditions such as GBS.[16]

Furthermore, our study reinforces the concept that TPE protocols should be customized according to the patient's underlying condition, plasma dynamics, and individual risk factors. The differences in PVcalc and PVex/PVcalc ratios between neurological and immunological/vasculitis groups underscore the necessity of adjusting exchange volumes and replacement fluid compositions to optimize the removal of pathogenic mediators while ensuring safety. These findings provide a framework for future prospective studies aimed at correlating technical parameters with long-term clinical outcomes, and they highlight the potential for protocol refinement that could improve therapeutic efficiency in diverse clinical scenarios.

Conclusion

This study reinforces the importance of tailoring therapeutic plasma exchange (TPE) protocols to individual patient characteristics and disease profiles. The findings demonstrate that the clinical benefits of TPE can be successfully achieved even with lower exchanged plasma volumes than those recommended by conventional guidelines, provided that treatment is customized according to patients' plasma dynamics and underlying pathologies.

These observations have significant implications for clinical practice, as they suggest that a one-size-fits-all approach may not be optimal when managing diverse patient groups. Instead, personalizing TPE, including adjustments in the exchange volume and replacement fluid composition, could enhance treatment efficacy and safety while potentially reducing procedural risks and resource utilization.

Looking forward, it is essential to conduct prospective, multi-centre studies that further refine these individualized TPE parameters. Future research should focus on optimizing exchange volumes based on real-time assessments of plasma dynamics and on developing standardized criteria for replacement fluid selection. Additionally, incorporating biomarkers to monitor therapeutic response and safety could pave the way for adaptive TPE protocols that dynamically adjust to patient needs.

Ultimately, establishing an evidence-based framework for personalized TPE will not only improve clinical outcomes but also provide a more efficient and cost-effective approach to managing complex disorders. This will help in moving toward a more nuanced, patient-centered model of care in plasmapheresis procedures.

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