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Evaluating the Safety and Therapeutic Effectiveness of Plasma Exchange in Pediatric Neuroimmunological Disorders

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Abstract

Therapeutic plasma exchange (TPE) is widely employed in managing various pediatric neuro-immunological disorders. This study aims to evaluate the safety profile and clinical effectiveness of TPE in children. We conducted a retrospective, single-center cohort study including pediatric patients who experienced neuro-immunological events and received TPE at a tertiary referral institution. A total of 81 patients (Guillain-Barre syndrome: 65; other polyneuropathies: 5; myasthenia gravis: 8; multiple sclerosis: 3) underwent 360 TPE sessions. Fresh frozen plasma (FFP) was used in 76.1% of procedures. Adverse events (AEs) occurred in 50% of TPE procedures involving FFP versus 39.5% in non-FFP sessions. The occurrence of two or more AEs was higher with FFP (24.5%) compared to procedures without FFP (8.1%). Allergic reactions were significantly more frequent in the FFP group (94.2% of TPEs with ≥1 AE) than in the non-FFP group (47.2%). Serious AEs were rare, accounting for 1.2% of procedures and 2.5% of patients. Clinical effectiveness assessed via a study-specific scale and the Hughes Functional Grading Scale revealed no pre-treatment differences between groups. Post-treatment, children with polyneuropathies displayed the most severe residual clinical status, while the greatest relative improvement was observed in the myasthenia gravis group. Filtration-based TPE is a safe and effective intervention for pediatric neuro-immunological disorders, with clinical benefits exceeding the risks of complications. Use of FFP increases the likelihood of AEs by 27% and substantially raises the risk of allergic and multiple adverse events.

Keywords: Therapeutic plasma exchange, Pediatric neuro-immunological disorders, Adverse events

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Introduction

Therapeutic plasma exchange (TPE) is a procedure in which a patient's plasma is replaced with either fresh-frozen plasma (FFP) and/or 5% human albumin (HA), and is a well-established intervention for various neurological disorders in both adults and children [1]. The therapeutic mechanism of TPE involves removing pathogenic immunomodulatory factors, including autoantibodies, immune complexes, and proinflammatory molecules such as complement components and coagulation factors, from the patient's circulation [2, 3]. In pediatric populations, TPE is indicated for a range of neuro-immunological conditions, including acute and chronic inflammatory demyelinating polyneuropathies, autoimmune encephalitis, paraneoplastic syndromes, and inflammatory cerebrovascular disorders [4].

Despite randomized trials supporting the use of TPE, its invasive nature in children and the potential for complications continue to present challenges for clinical decision-making. Moreover, the literature demonstrates considerable heterogeneity in outcome assessment methods for pediatric patients undergoing TPE for neurological disorders. To address this, our study aimed to develop and evaluate a practical outcome scale based on physical examination elements, providing a standardized approach for assessing neurological function in these patients.

The primary objective of this study was to assess the safety and clinical efficacy of TPE in pediatric patients with neuro-immunological diseases over a 25-year period at a single tertiary care center.

Materials and Methods

Study population

This retrospective, single-center study reviewed medical records of pediatric patients who underwent TPE for neuro-immunological conditions at the Department of Pediatric Nephrology and Hypertension, Cracow, Poland, between January 1, 1998, and December 31, 2022. Detailed data were extracted from patient charts, TPE procedure records, and outpatient documentation.

A total of 81 patients were included, categorized into four diagnostic groups:

1. Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP; Guillain-Barré syndrome, GBS) – 65 patients (80.2%)
2. Polyneuropathy (PN) – 5 patients (6.2%)
3. Myasthenia Gravis (MG) – 8 patients (9.9%)
4. Multiple Sclerosis (MS) – 3 patients (3.7%)

Anthropometric data including age, sex, weight, and height were recorded at the initiation of each TPE session. The indication for TPE was determined in accordance with the latest American Society for Apheresis (ASFA) guidelines [5].

A TPE session was defined as a series of procedures performed on a patient with intervals of less than four weeks; procedures separated by four or more weeks were considered distinct sessions. Neurologists determined patient eligibility for TPE, while nephrologists and experienced surgeons collaborated on dual-lumen catheter placement and sizing. Catheters (8F–12.5F) were selected based on patient body weight and morphology according to literature recommendations [6, 7]. Pharmacotherapy was managed concurrently under neurologist supervision. Detailed TPE parameters, anticoagulation, fluid replacement, and medication protocols are provided in the Supplementary Data.

Blood pressure assessment was stratified for children under and over 16 years, considering sex, age, and height percentiles, as per current pediatric standards [8]. Comprehensive BP data during TPE sessions are available in Supplementary Table S1.

Table 1. Clinical characteristics of the studied group and therapeutic plasma exchange (TPE) procedures along with comparison of subgroups. Data are presented as medians and interquartile range (IQR)

Characteristics of Patients and TPE Procedures	1. GB (N=247)	2. PN (N=19)	3. MG (N=56)	4. MS (N=38)	Total (N=360)	p value (1 vs 2)	p value (1 vs 3)	p value (1 vs 4)	p value (2 vs 3)	p value (2 vs 4)	p value (3 vs 4)
Age [months]	112.0 (107.3)	142.0 (102.5)	192.0 (24.0)	186.0 (20.3)	166.0 (104.0)	NS	<0.001	<0.001	0.007	0.001	NS
Body Mass [kg]	26.8 (27.5)	33.0 (28.9)	53.0 (13.3)	49.0 (32.0)	44.5 (30.0)	NS	0.001	<0.001	NS	0.007	NS
Body Mass [percentiles]	27.5 (57.5)	67.0 (63.0)	50.0 (50.0)	18.0 (81.0)	29.0 (58.0)	NS	NS	NS	NS	NS	NS
Height [cm]	132.0 (51.5)	142.0 (43.0)	161.0 (10.3)	163.5 (4.5)	159.0 (46.0)	NS	0.001	<0.001	0.024	0.004	NS
Height [percentiles]	39.0 (57.0)	50.0 (63.0)	63.0 (65.0)	42.5 (30.0)	42.5 (42.0)	NS	0.125	NS	NS	NS	NS
Hospitalization [number of days]	26.0 (38.3)	40.0 (65.8)	27.0 (33.0)	7.0 (23.5)	24.0 (36.8)	NS	NS	<0.001	NS	0.019	0.003
Duration of Hospitalization to Start of TPE [days]	2.0 (2.3)	13.0 (20.5)	7.0 (9.5)	3.0 (1.5)	3.0 (3.0)	NS	<0.001	NS	NS	NS	0.007
QB [ml/kg/min]	2.3 (1.4)	2.2 (1.6)	1.8 (0.9)	1.4 (0.4)	2.00 (1.3)	NS	<0.001	<0.001	NS	<0.001	<0.001
Duration of TPE Procedure [min]	150.00 (80.00)	220.00 (77.5)	212.5 (110.00)	160.00 (45.00)	155.00 (90.00)	0.001	<0.001	NS	NS	0.002	0.011
Supplement Exchange Flow Rate [ml/kg/h]	31.6 (27.1)	19.5 (4.8)	20.00 (15.1)	21.6 (12.5)	28.3 (21.6)	0.001	<0.001	<0.001	NS	NS	NS

Serum Sodium After TPE [mmol/l]	140.0 (3.8)	137.2 (7.5)	141 (2.0)	140 (3.0)	140.0 (3.5)	0.011	0.031	NS	0.003	0.021	NS
Serum Ionized Calcium After TPE [mmol/l]	1.18 (0.15)	1.1 (0.17)	1.2 (0.16)	1.2 (0.2)	1.19 (0.16)	NS	NS	0.047	0.032	0.028	NS
No. of TPE in ICU (%) a	35 (14.2%)	12 (63.1%)	14 (25%)	0	61 (16.9%)	<0.001	0.041	0.005	0.004	<0.001	<0.001
No. of Patients Intubated During TPE (%) a	10 (4%)	8 (42.1%)	14 (25%)	0	32 (8.9%)	<0.001	<0.001	NS	NS	<0.001	<0.001
No. of Patients Intubated During TPE (%) b	2 (3.1%)	2 (40%)	3 (37.5%)	0	7 (8.6%)	0.023	0.008	NS	NS	NS	NS
Death Up to 3 Months After TPE b	0	1 (20%)	0	0	1 (0.3%)	NS	NS	NS	NS	NS	

Abbreviations: GB - Guillain-Barré syndrome; PN - Polyneuropathy; MG - Myasthenia Gravis; MS - Multiple Sclerosis; QB - blood flow; ICU – intensive care unit; NS – non significant.

[a]Percentages vs total number of TPEs.

[b]Percentages vs total number of patients.

Table 2. Clinical characteristics of patients during therapeutic plasma exchange (TPE) procedures. Data are presented as number and percentage

Patients' Clinical Status (Number and %)	1. GB (N=247)	2. PN (N=19)	3. MG (N=56)	4. MS (N=38)	p value (1 vs 2)	p value (1 vs 3)	p value (1 vs 4)	p value (2 vs 3)	p value (2 vs 4)	p value (3 vs 4)	Total (N=360)
Conscious	238 (93.4%)	7 (36.8%)	56 (100%)	38 (100%)	<0.001	NS	NS	<0.001	<0.001	NS	339 (94.2%)
Unconscious	9 (6.6%)	12 (63.2%)	0	0	CT	CT	CT	CT	CT	CT	21 (5.8%)
General Condition											
Good	164 (66.4%)	7 (36.8%)	36 (64.3%)	35 (92.1%)	0.011	NS	0.001	0.035	<0.001	0.002	242 (67.2%)
Moderate	66 (26.7%)	0	6 (10.7%)	3 (7.9%)	0.004	0.006	0.006	NS	NS	NS	75 (20.8%)
Serious	17 (6.9%)	4 (21.1%)	14 (25%)	0	NS	<0.001	NS	NS	0.010	<0.001	35 (9.7%)
Critical	0	8 (42.1%)	0	0	<0.001	NS	NS	<0.001	<0.001	NS	8 (2.3%)

Notes:

- GB, PN, MG, and MS likely represent different patient groups or conditions (e.g., Guillain-Barré syndrome, polyneuropathy, myasthenia gravis, multiple sclerosis), but specific definitions were not provided in the original table.
- NS indicates non-significant p-values.
- CT indicates that the p-value could not be calculated (likely due to zero values or insufficient sample size for statistical comparison).
- Values are presented as number (percentage) for categorical variables.

Evaluation methods

The impact of therapeutic plasma exchange (TPE) on neurological function was assessed by examining patients before starting the procedure and immediately after its completion. The Hughes Functional Grading Scale (HFGS) was used as a reference measure, assigning scores from 0 (normal neurological function) to 6 (death), with intermediate grades reflecting varying levels of motor impairment, assistance needs, or ventilatory support [9].

In parallel, a novel semi-quantitative tool (Author's Scale, AS) was developed for this study to capture nuanced neurological changes. For the Guillain-Barré syndrome (GBS; n = 65) and polyneuropathy (PN; n = 5) groups, the AS incorporated assessments of muscle strength and tone (0–2 per limb), deep tendon reflexes (0–2, hyperreflexia scored as −1), gait patterns (0–1), required supine positioning (0 or −1), bulbar involvement (0 to −2), sensory deficits or pain (0 or −1), and respiratory compromise (0 or −1), generating total scores from −7 to +15 (Supplementary Table S2).

For the myasthenia gravis (MG; n = 8) group, the AS additionally evaluated hypophonia, ocular manifestations (ptosis or diplopia), positive response to the ice pack or muscle weakness tests, and respiratory function, with the same −7 to +15 scoring range (Supplementary Table S3).

The multiple sclerosis (MS; n = 3) cohort exhibited diverse, non-repeating symptoms; thus, a simplified

categorical approach was used post-TPE: complete recovery (no neurological deficits), partial recovery (improvement without full resolution), and no improvement (status unchanged). Evaluated features included visual disturbances, nystagmus, tongue deviation, ataxia, hyperreflexia, Babinski or Rossolimo signs, limb pain, diminished abdominal reflexes, balance disorders, headache, and vertigo.

Safety monitoring focused exclusively on adverse events (AEs) directly related to TPE and the interventions undertaken to manage them. Device- or catheter-related technical complications were excluded from the analysis.

Statistical analysis

Data analysis was performed using MATLAB (R2022b, v9.13.0). Continuous variables were summarized as means ± standard deviation or medians with interquartile ranges, based on normality assessed by the Shapiro-Wilk test. Group comparisons were conducted using Student's t-test, Wilcoxon rank-sum test, Fisher's exact test, or Pearson correlation as appropriate. Multivariable modeling employed a generalized linear model (GLM) with backward elimination. Statistical significance was defined as $p < 0.05$.

Ethical considerations

The study protocol was approved by the local ethics committee (ref. 118.6120.187.2023). Informed consent was waived given the retrospective design. All procedures adhered to the principles of the Declaration of Helsinki and its subsequent amendments.

Results

The study population consisted of 81 children undergoing a total of 360 TPE procedures. In the GBS cohort (AIDP, ASFA Category I), 65 patients underwent 65 sessions comprising 247 individual TPE treatments, averaging 3.8 treatments per patient. The PN cohort (2 with ADEM, ASFA Category II; 3 with MMN, ASFA Category IV) underwent 5 sessions with 19 treatments, averaging 3.8 per patient. The MG cohort (ASFA Category I for acute therapy, Category II for long-term management) included 8 children undergoing 13 sessions with 56 procedures, averaging 7 treatments per patient. The MS cohort (ASFA Category II acute relapse, Category III chronic course) included 3 patients with 24 sessions totaling 38 treatments, averaging 12.7 per patient.

Patients in the GBS and PN groups were younger than those in the MG and MS cohorts, while age within each group was consistent. Body mass and height followed the same pattern. Percentile analyses confirmed that all children were within normal growth ranges. Key demographic and procedural data are presented in **Table 1**, **Table 2**, and Supplementary Table S4.

Results

The study included 81 pediatric patients who collectively underwent 360 therapeutic plasma exchange (TPE) procedures. The cohort of children with acute inflammatory demyelinating polyradiculoneuropathy (AIDP; Guillain-Barré syndrome, GBS) comprised 65 patients who underwent 65 sessions encompassing 247 procedures, averaging nearly four procedures per patient. The polyneuropathy (PN) group included five children, two with acute disseminated encephalomyelitis (ADEM) and three with multifocal motor neuropathy (MMN), who underwent a total of 19 procedures across five sessions. The myasthenia gravis (MG) cohort consisted of eight children who participated in 13 sessions and 56 procedures, averaging seven procedures per patient. The multiple sclerosis (MS) group comprised three children who underwent 24 sessions and 38 procedures, averaging over 12 procedures per patient.

Patients in the GBS and PN groups were significantly younger than those in the MG and MS groups, although no age differences were observed within the respective disease cohorts. Similar trends were noted for body mass and height, while percentile analyses confirmed that all patients exhibited growth parameters within the expected range. Across the MS cohort, hospital stays were notably shorter, whereas patients in the PN group were more frequently treated in intensive care settings, often intubated or unconscious, reflecting a higher baseline severity of illness. One death occurred in the PN cohort, accounting for an overall mortality of 0.3%. Blood pressure readings remained within the normal range throughout TPE procedures.

Treatment efficacy, assessed using both the Hughes Functional Grading Scale (HFGS) and the author-developed semi-quantitative scale (AS), indicated no significant baseline differences across the cohorts. After completing TPE, PN patients demonstrated the most severe residual neurological deficits, whereas MG patients experienced the greatest improvement. Specifically, over half of the GBS cohort exhibited moderate-to-significant improvement, and more than 80% of MG patients showed substantial recovery. In contrast, most PN patients demonstrated minimal or no improvement. Among MS patients, complete clinical recovery was observed in less than one-third of sessions, with partial recovery documented in the remainder. Assessment via HFGS revealed similar baseline scores across groups, with MG patients achieving the most favorable post-treatment outcomes. Notably, there was a strong negative correlation between pre- and post-treatment scores in the GBS cohort, suggesting consistent improvements at the individual patient level.

Adverse events and safety

Adverse events (AEs) associated with TPE were evaluated independently of symptoms attributable to the underlying neurological disorders. Overall, AEs were recorded in 80.6% of procedures, with 88% occurring in sessions where fresh frozen plasma (FFP) was administered, compared to 57% in procedures without FFP, indicating a 54% higher incidence when FFP was used. Multiple AEs were also more frequent in the FFP group. Anxiety and agitation were observed more often in non-FFP procedures, whereas allergic manifestations, including chills, hypotension, and skin reactions, were more common when FFP was included.

The occurrence of allergic adverse events (AAEs), encompassing chills, hypotension, skin reactions, nausea, vomiting, and dyspnea, varied across the disease cohorts. Overall, AAEs were observed in approximately 40% of procedures, with nearly half of the FFP-associated procedures affected, compared to less than 20% of non-FFP procedures. When considering only procedures in which at least one AE occurred, AAEs accounted for more than 90% of events in the FFP group but less than half in the non-FFP group. Excluding anxiety and agitation reduced the overall AE frequency from 80.6% to 60.8%, with the FFP group maintaining a more than twofold higher rate compared to the non-FFP group. Procedures with at least one AE were categorized as mild, moderate, or severe, with the latter requiring early termination in a very small fraction of cases.

Medical interventions to manage AEs were more frequently required in the FFP group, particularly antihistamines and glucocorticoids, whereas sedatives and hydroxyzine were more often used in non-FFP procedures. No significant differences were noted for other interventions. Baseline patient status and levels of consciousness were comparable between the FFP and non-FFP groups, and the occurrence of TPE in unconscious patients was similarly low in both groups. Electrolyte measurements, including sodium and ionized calcium, remained within normal ranges, suggesting that observed AEs were not attributable to electrolyte disturbances. In total, 68 of the 81 patients experienced at least one AE, although no life-threatening events occurred.

Multivariable regression analysis identified age as a consistent protective factor, with older children demonstrating a lower likelihood of experiencing AEs. The use of FFP increased the odds of multiple and allergic AEs. Membership in the PN or MS cohorts did not influence AE risk, whereas younger GBS patients were more susceptible to any or moderate-to-severe AEs, and MG patients were comparatively less at risk. Higher baseline severity increased the likelihood of most AEs, while procedures performed in the ICU were associated with reduced AE risk, likely due to sedation. Correlation analyses supported these findings, revealing a strong positive association between age and body mass and negative associations between age and both any AE and moderate/severe AEs, as well as between body mass and any AE occurrence.

Table 3. Assessment of Therapeutic Plasma Exchange (TPE) Effectiveness in Selected Patient Groups Using the Author's Scale (AS) and Hughes Functional Grading Scale (HFGS). *Data are presented as medians and interquartile range (IQR)*

Metric	1. GB (N=247)	2. PN (N=19)	3. MG (N=56)	p value (1 vs 2)	p value (1 vs 3)	p value (2 vs 3)	Total (N=360)
AS Score (−7 to 15) a							
Before TPE	4.0 (4.0)	1.0 (11.3)	2.0 (8.5)	NS	NS	NS	4.0 (5.0)
After TPE	9.0 (5.0)	6.0 (11.5)	9.0 (4.3)	0.041	NS	0.029	9.0 (5.0)
Difference (Points)	4.0 (5.3)	0.0 (2.0)	7.0 (6.3)	0.017	0.016	0.004	4.0 (6.0)
HFGS Score (6–1) a							
Before TPE	4.0 (2.0)	4.0 (1.3)	4.0 (2.0)	NS	NS	NS	4.0 (2.0)
After TPE	3.0 (1.0)	4.0 (2.0)	2.0 (2.0)	0.017	0.013	0.006	3.0 (1.0)
Difference (Points)	−1.0 (2.0)	0.0 (0.3)	−2.0 (2.0)	0.021	0.047	0.005	−1.0 (2.0)
Number of Sessions (Assessed by AS)	1. GB (N=65)	2. PN (N=5)	3. MG (N=13)	p value (1 vs 2)	p value (1 vs 3)	p value (2 vs 3)	
No Improvement/Worsening [−1 to 0 difference]	4 (6.2%)	3 (60%)	0	0.006	NS	0.012	
Minor Improvement [1–3 point difference]	27 (41.5%)	1 (20%)	2 (15.4%)	NS	NS	NS	
Moderate Improvement [4–8 point difference]	25 (38.5%)	1 (20%)	6 (46.1%)	NS	NS	NS	
Significant Improvement [>9 point difference]	9 (13.8%)	0	5 (38.5%)	NS	0.050	NS	

Abbreviations: GB - Guillain-Barré syndrome; PN - Polyneuropathy; MG - Myasthenia Gravis; NS - Non-significant. a Detailed descriptions of AS and HFGS scoring are provided in the 'Materials and Methods' section.

Table 4. Overall Assessment of Safety and Adverse Events (AE) During Therapeutic Plasma Exchange (TPE) in the Study Population, Grouped by Procedures With and Without Fresh Frozen Plasma (FFP). *Data are presented as number and percentage*

Metric	FFP1 Cohort (N=274)	FFP0 Cohort (N=86)	p value	Total Population (N=360)
TPE with at Least 1 AE	137 (50%)	34 (39.5%)	NS	171 (47.5%)
TPE with at Least 1 AE (Excluding Anxiety/Agitation)	128 (46.7%)	20 (23.3%)	<0.001	148 (41.1%)
TPE with More Than 1 AE	67 (24.5%)	7 (8.1%)	0.001	74 (20.6%)
TPE with More Than 1 AE (Excluding Anxiety/Agitation)	15 (5.5%)	3 (3.5%)	NS	18 (5%)
TPE with at Least 1 Allergic AE	129 (47.1%)	16 (18.6%)	<0.001	145 (40.3%)
Total AEs vs Total TPE (%)	241 (88%)	49 (57%)	<0.001	290 (80.6%)
Total AEs vs Total TPE (%) (Excluding Anxiety/Agitation)	192 (70.1%)	27 (31.4%)	<0.001	219 (60.8%)

Abbreviations: FFP0 - Without fresh frozen plasma; FFP1 - Using fresh frozen plasma; NS - Non-significant.

Table 5. Assessment of Safety and Adverse Events (AE) During Therapeutic Plasma Exchange (TPE) in the Study Population, Grouped by Procedures With and Without Fresh Frozen Plasma (FFP). *Data are presented as number and percentage vs number of TPE with AE*

Adverse Event	FFP1 Cohort (N=137)	FFP0 Cohort (N=34)	p value
Total Allergic AEs	129 (94.2%)	16 (47.2%)	<0.001
Anxiety/Agitation	49 (35.8%)	22 (64.7%)	0.002
Shivers/Sensation of Coldness	40 (29.2%)	1 (2.9%)	<0.001
Blood Pressure Decrease/Hypotension	36 (26.3%)	3 (8.8%)	0.020
Skin Allergic Reaction	32 (23.4%)	2 (5.9%)	0.014
Nausea/Vomiting	14 (10.2%)	6 (17.6%)	NS
Dyspnea	7 (5.1%)	4 (11.8%)	NS
Extremities Pain	13 (9.5%)	7 (20.6%)	NS
Abdominal Pain	7 (5.1%)	1 (2.9%)	NS
Increased Blood Pressure	6 (4.4%)	0	NS
Numbness of Extremities/Face	6 (4.4%)	0	NS
Sensation of Heat	5 (3.6%)	0	NS
Back Pain	5 (3.6%)	0	NS
Headache	4 (2.9%)	1 (2.9%)	NS
Paleness	8 (5.8%)	1 (2.9%)	NS
Tachycardia	3 (2.2%)	0	NS
Fever	1 (0.7%)	1 (2.9%)	NS
Others a	5 (3.6%)	0	NS

Abbreviations: FFP0 - Without fresh frozen plasma; FFP1 - Using fresh frozen plasma; NS - Non-significant; BP - Blood pressure. a Additional AEs: abdominal distension (1), somnolence (1), vertigo (1), perioral cyanosis (1), tightness of the chest (1).

Table 6. Assessment of Safety and Adverse Events (AE) During Therapeutic Plasma Exchange (TPE) in the Study Population, Grouped by Procedures With and Without Fresh Frozen Plasma (FFP). *Data are presented as number and percentage vs total number of AEs*

Adverse Event	FFP1 (N=241; 83.1%)	FFP0 (N=49; 16.9%)	p value
Total AEs (Excluding Anxiety/Agitation)	192 (66.2%)	27 (9.3%)	0.001
Anxiety/Agitation	49 (16.9%)	22 (7.6%)	0.001
Shivers/Sensation of Coldness	40 (13.8%)	1 (0.3%)	0.003
Blood Pressure Decrease/Hypotension	36 (12.4%)	3 (1%)	NS
Skin Allergic Reaction	32 (11%)	2 (0.7%)	0.047
Nausea/Vomiting	14 (4.8%)	6 (2.1%)	NS
Dyspnea	7 (2.4%)	4 (1.4%)	NS
Extremities Pain	13 (4.5%)	7 (2.4%)	0.034
Abdominal Pain	7 (2.4%)	1 (0.3%)	NS
Increased Blood Pressure	6 (2.1%)	0	NS
Numbness of Extremities/Face	6 (2.1%)	0	NS
Sensation of Heat	5 (1.7%)	0	NS
Back Pain	5 (1.7%)	0	NS

Headache	4 (1.4%)	1 (0.3%)	NS
Paleness	8 (2.8%)	1 (0.3%)	NS
Tachycardia	3 (1%)	0	NS
Fever	1 (0.3%)	1 (0.3%)	NS
Others a	5 (1.7%)	0	NS

Abbreviations: FFP0 - Without fresh frozen plasma; FFP1 - Using fresh frozen plasma; NS - Non-significant; BP - Blood pressure. a Additional AEs: abdominal distension (1), somnolence (1), vertigo (1), perioral cyanosis (1), tightness of the chest (1).

Discussion

This study analyzed four pediatric cohorts affected by distinct neuro-immunological disorders: Guillain-Barré syndrome (GBS), polyneuropathies (PN), myasthenia gravis (MG), and multiple sclerosis (MS). GBS, an acute neuropathic condition, typically presents with symmetric ascending paralysis resulting from peripheral nerve inflammation. The PN group, heterogeneous in nature, included patients with acute disseminated encephalomyelitis and multifocal motor neuropathy. MG represents an autoimmune disorder in which antibodies target acetylcholine receptors or muscle-specific kinase at the neuromuscular junction, while MS is the most prevalent chronic inflammatory demyelinating disease affecting the central nervous system.

The heterogeneity of these disorders, coupled with variable follow-up protocols, complicates the direct comparison of TPE efficacy across groups. To address this challenge, a semi-quantitative neurological assessment scale was developed specifically for the study population. While established tools such as the Hughes Functional Grading Scale (HFGS) and the Expanded Disability Status Scale (EDSS) provide generalized measures of motor function, they do not capture disease-specific symptoms. The tailored scale integrates key components of the physical examination consistently documented in patient records, enabling a more precise evaluation of treatment outcomes. Given the retrospective design, these findings remain preliminary and should be validated in prospective studies.

Evaluation using both the HFGS and the semi-quantitative scale revealed consistent results. Baseline clinical status was comparable across the cohorts. Following TPE, patients in the PN group exhibited the most severe residual neurological deficits and minimal improvement, whereas the MG cohort demonstrated the most substantial recovery. Moderate to significant improvements were observed in over half of GBS patients and in the majority of MG patients, while most PN patients showed minimal or no clinical change. Comparison with previously published pediatric studies is challenging due to heterogeneity in patient populations and outcome measures. Nonetheless, reported TPE efficacy in children with neuro-immunological disorders ranges from 60% to 90%. Published studies demonstrate a spectrum of outcomes, with some cohorts exhibiting high response rates, while others show only modest improvements, suggesting that our results are consistent with existing literature and support the reliability of the semi-quantitative scale in evaluating TPE outcomes.

Safety profile

Overall, 84% of patients experienced at least one adverse event (AE), a figure broadly consistent with published pediatric cohorts, although higher than some reports citing rates of 4.9%–7%. Approximately half of TPE procedures involved at least one complication, with a higher incidence observed in sessions using fresh frozen plasma (FFP). Anxiety and agitation were common, reflecting the pediatric population, particularly among younger patients with GBS. Excluding these symptoms, AE rates remained significantly higher in FFP-associated procedures, indicating that FFP contributes to both the frequency and severity of TPE-related complications.

Severe complications necessitating early termination of TPE occurred in a small fraction of procedures, consistent with literature-reported rates of 0.4%–3% per procedure. Commonly observed AEs in this study included anxiety/agitation, chills or cold sensation, hypotension, allergic skin reactions, extremity pain, and nausea or vomiting. The higher frequency of AEs compared with some previous reports may reflect intensive bedside monitoring, early interventions, and the inclusion of historical procedures performed with less biocompatible technology, such as 6% hydroxyethyl starch, which is no longer in use.

Multivariable analysis indicated that older age and higher body mass were protective against AEs, whereas younger patients, particularly in the GBS cohort, were more susceptible. FFP use significantly increased the odds of multiple and allergic AEs, whereas baseline severity raised the likelihood of most AEs, with the exception of allergic events. Procedures conducted in the ICU were associated with reduced AE frequency, likely due to sedation and closer monitoring. Overall, no life-threatening complications occurred, and electrolyte levels remained within normal ranges, indicating that observed AEs were unrelated to electrolyte imbalances.

Comparisons with intravenous immunoglobulin (IVIg) suggest that both modalities effectively reduce disease severity, although TPE may confer advantages in critically ill pediatric patients, such as shorter mechanical ventilation and PICU stays. Potential nephrotoxicity associated with sucrose-containing IVIg preparations should also be considered. Selection of patients for TPE

should follow current ASFA guidelines, recognizing GBS and acute short-term MG as Category I indications. Treatment should be individualized based on patient characteristics and center expertise.

Limitations

This study's retrospective, single-center design imposes inherent limitations. Treatments span a 25-year period during which diagnostic precision, particularly for heterogeneous polyneuropathies, was variable. Documentation practices evolved over time, potentially leading to underreporting of complications. Nonetheless, adverse events during TPE are generally well-documented due to the necessity of procedural adjustments and pharmacologic interventions. Despite these limitations, this cohort represents the largest pediatric TPE database from a single tertiary referral center in Central and Eastern Europe, providing a comprehensive evaluation of safety and efficacy. The author-developed neurological assessment scale offers a practical tool for evaluating clinical outcomes and may be utilized in future prospective studies of GBS, PN, and MG.

Conclusions

Therapeutic plasma exchange administered via filtration is a safe and effective intervention for pediatric neuro-immunological disorders, with clinical benefits substantially outweighing risks. Anxiety and agitation were the most commonly observed adverse events. The use of FFP increases the likelihood of TPE-related complications, particularly allergic and multiple AEs, and even after excluding anxiety and agitation, complication rates remain approximately twice as high compared with procedures without FFP. The semi-quantitative neurological assessment scale provides a structured approach for evaluating patient status before and after TPE and may support standardized outcome assessments in future prospective studies.

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