

Effectiveness and Safety of Therapeutic Plasma Exchange in Intoxication Cases: A Single-Center Retrospective Study

 Sinan Mersin¹,  Pelin Aytan¹,  Seher Yontar²,  Semra Denizalp²,  Mahmut Bakır Koyuncu¹,
 Ayca Erkenekli¹,  Esin Oğuz Kozan³,  Enver Tekin¹,  Eyüp Naci Tiftik¹

¹ Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Mersin University, Mersin, Türkiye

² Department of Apheresis, Faculty of Medicine, Mersin University, Mersin, Türkiye

³ Adıyaman Training and Research Hospital, Adıyaman, Türkiye

*Correspondence: Sinan Mersin; sinanmersin86@msn.com

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Abstract

Objective: This study aimed to retrospectively evaluate clinical characteristics, procedural parameters, complication rates, and mortality-related factors in patients who underwent therapeutic plasma exchange (TPE) for intoxication. **Materials and Methods:** Twenty-five patients (30 sessions) who underwent TPE for intoxication were included. Demographic data, laboratory findings, procedural characteristics, and clinical outcomes were analyzed. Mann-Whitney U and Fisher's exact tests were used for intergroup comparisons; $p < 0.05$ was considered statistically significant. **Results:** Fifty-two percent of patients were female, with a mean age of 30.9 ± 15.6 years (range: 17–73). The most common diagnoses were amitriptyline intoxication ($n=7$, 28%) and intoxication with an unknown agent ($n=13$, 52%). Seventy-six percent of patients were followed in intensive care units. The mean volume of plasma exchanged was 2928 ± 530 mL and mean procedure duration was 111 ± 26 minutes. The complication rate was 3.3% (one Grade 3 event) and mortality rate was 16% (4/25). Hemoglobin, hematocrit, WBC, and platelet counts were significantly lower in the non-survivor group, while age was significantly higher (54.5 ± 23.8 vs. 26.4 ± 8.7 years; $p=0.037$). Age >40 years and thrombocytopenia ($PLT < 100 \times 10^3/\mu L$) were identified as significant risk factors for mortality ($OR=28.5$; $p=0.016$). **Conclusion:** TPE is an effective and safe modality in intoxication cases with a low complication rate. Advanced age and thrombocytopenia are the main risk factors requiring attention regarding mortality.

Keywords: Therapeutic plasma exchange; plasmapheresis; intoxication; drug poisoning; mortality

1. Introduction

Acute intoxication is a significant cause of morbidity and mortality worldwide, representing one of the most common reasons for emergency department (ED) visits and intensive care unit (ICU) admissions. Drug overdose, whether intentional or accidental, accounts for a substantial proportion of these cases. In Turkey, pharmaceutical agents —

particularly antidepressants, analgesics, and sedative-hypnotics — are among the most frequently reported causative agents in acute poisoning.^{1,2} Studies from various regions of Turkey have documented that antidepressant-related poisonings, including tricyclic antidepressants (TCAs), constitute a significant and clinically challenging subgroup.^{2,3}

The standard management of acute intoxication relies on supportive care, gastric decontamination, and when available, specific antidotes. However, in severe cases characterized by hemodynamic instability, altered consciousness, or multi-organ involvement, conventional measures are often insufficient, necessitating the use of extracorporeal elimination techniques.⁴ Among these, therapeutic plasma exchange (TPE) has emerged as a valuable modality for the removal of toxins that are not amenable to conventional dialysis-based methods.

TPE operates by replacing a patient's plasma — along with plasma-bound substances — with a substitute fluid such as fresh frozen plasma (FFP) or albumin, thereby facilitating the rapid clearance of protein-bound toxins and inflammatory mediators.⁵ The pharmacokinetic rationale for TPE in intoxication is primarily based on two key parameters: high plasma protein binding (>80%) and a relatively low volume of distribution. Substances meeting these criteria are largely confined to the intravascular compartment and are therefore more accessible to plasma exchange.⁶

Amitriptyline, a tricyclic antidepressant frequently implicated in intentional overdose, exemplifies such a profile: it exhibits plasma protein binding exceeding 90% and its circulating fraction remains highly protein-bound, making it a suitable candidate for TPE.^{6,7} TCA overdose may produce life-threatening cardiac arrhythmias, seizures, and refractory hypotension. The EXTRIP Workgroup has conducted a systematic review on extracorporeal therapies in TCA poisoning and provides evidence-based recommendations for their use in selected cases.⁷

The American Society for Apheresis (ASFA) publishes regularly updated, evidence-based guidelines classifying apheresis indications into four categories (I–IV). In the most recent ninth edition published in 2023, ASFA categorizes and grades indications for therapeutic apheresis across a wide variety of diseases, providing structured guidance for clinicians considering TPE.⁸ For most intoxications, TPE is generally considered a Category II or III indication — used as a second-line or individualized intervention in cases where conventional management has failed.^{5,8}

Despite growing clinical experience with TPE in intoxication, published data from single-center series remain limited, particularly from Turkey. Dişel et al. reported one of the largest poisoning series treated with TPE, describing 36 cases over 8 years at a university hospital, with more than 20 identified toxic substances, emphasizing the potential of TPE as an extracorporeal elimination technique in selected cases.⁹

The aim of this study was to retrospectively evaluate the clinical characteristics, procedural parameters, complication rates, and mortality-related factors in patients who underwent TPE for intoxication at our center.

2. Materials and Methods

2.1. Study Design and Patient Selection

This retrospective, observational, single-center study was conducted at a university hospital hematology department. Patients who underwent therapeutic plasma exchange (TPE) due to intoxication between 2000 and 2020 were screened. Of these, 25 patients (30 sessions) with complete medical records were included in the final analysis. Patients with incomplete data were excluded. The study was approved by the institutional ethics committee and all procedures were carried out in accordance with the ethical principles of the Declaration of Helsinki.

2.2. Data Collection

Demographic data (age, sex, height, weight), clinical information (diagnosis, causative agent, ward of admission, length of hospital stay, outcome), laboratory parameters at the time of the first TPE session (hemoglobin, hematocrit, white blood cell count [WBC], platelet count [PLT]), and procedural details (device used, anticoagulation, replacement fluid type and volume, vascular access, procedure duration, inlet flow rate, number of sessions) were retrieved from patient files.

2.3. Procedure

All TPE procedures were performed in accordance with ASFA guidelines⁸ by experienced apheresis teams. Procedures were carried out using Fresenius, Baxter, Optia, or Spectra Optia continuous-flow centrifugation devices. Anticoagulation was achieved with ACD-A (acid citrate dextrose formula A) solution in all sessions. Replacement fluids included FFP, hydroxyethyl starch (3–4% HES), 4% albumin, or combinations thereof. Vascular access was established via a double-lumen hemodialysis catheter (11.5 Fr) in the majority of cases, or via peripheral venous access when central catheterization was contraindicated or not feasible. The volume of plasma exchanged per session was calculated as approximately 1–1.5 times the estimated plasma volume. Complications occurring during or within 24 hours of the procedure were graded according to the ASFA adverse event classification system (Grade 1–4).⁸

2.4. Causative Agent Classification

Cases with a clearly documented causative agent were classified by the specific agent. Cases involving more than one agent were classified as 'mixed drug intoxication'. Cases in which no toxic agent could be identified were classified as 'unknown agent intoxication'.

2.5. Outcome Assessment

The primary outcome was in-hospital mortality. Patients were categorized as survivors or non-survivors based on their discharge status. Secondary outcomes included procedural complication rates and length of hospital stay.

2.6. Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics (version 26.0; IBM Corp., Armonk, NY, USA). Continuous variables are expressed as mean $\pm$ standard deviation (SD) or median (interquartile range) as appropriate. Categorical variables are expressed as numbers and percentages. Normality was assessed using the Shapiro-Wilk test. The Mann-Whitney U test was used for non-parametric continuous variables, and Fisher's exact test for categorical variables. Odds ratios (OR) with 95% confidence intervals (CI) were calculated for binary outcomes. A p-value of <0.05 was considered statistically significant.

3. Results

3.1. Demographic and Clinical Characteristics

A total of 25 patients (13 female, 12 male; 52% / 48%) underwent 30 TPE sessions during the study period. Twenty patients received a single session, while 5 patients required two sessions, resulting in a mean of 1.2 sessions per patient. The mean age was 30.9 ± 15.6 years (range: 17–73), with the majority of patients falling within the young adult age group; however, non-survivors were notably older (mean 54.5 ± 23.8 years). Baseline hemoglobin was 12.0 ± 2.6 g/dL, WBC $11.5 \pm 7.5 \times 10^3/\mu\text{L}$, and PLT $190 \pm 103 \times 10^3/\mu\text{L}$. The mean length of hospital stay was 13.2 ± 15.5 days (median: 7 days, range: 1–62). Demographic and clinical characteristics are summarized in Table 1.

Table 1. Demographic and clinical characteristics of patients

Characteristic	n / Mean $\pm$ SD	% / Range
Total patients	25	—
Total sessions	30	—
Female / Male	13 / 12	52% / 48%
Age (years)	30.9 $\pm$ 15.6	17–73
Height (cm)	166 $\pm$ 8	—
Weight (kg)	68 $\pm$ 12	—
Hemoglobin (g/dL)	12.0 $\pm$ 2.6	7.2–17.4
Hematocrit (%)	35.3 $\pm$ 7.3	21.1–50.0
WBC ($\times 10^3/\mu\text{L}$)	11.5 $\pm$ 7.5	0.3–32.0
PLT ($\times 10^3/\mu\text{L}$)	190 $\pm$ 103	11–465
Length of hospital stay (days)	13.2 $\pm$ 15.5	1–62

3.2. Diagnosis Distribution and Ward of Admission

The most common diagnostic category was intoxication with an unknown causative agent (n=13, 52%), reflecting cases in which the ingested substance could not be identified from the available clinical records. Among patients with a documented causative agent, amitriptyline (Laroxyl) was the most frequently identified drug (n=7, 28%), followed by mixed drug intoxication (n=2, 8%). Organophosphate poisoning, venomous snakebite, and mushroom intoxication each accounted for one case (4% each). The diagnosis distribution is presented in Table 2.

Table 2. Distribution of diagnoses

Diagnosis	n	%
Drug intoxication — Amitriptyline (Laroxyl)	7	28.0
Drug intoxication — Mixed agents	2	8.0
Drug intoxication — Unknown agent	13	52.0
Organophosphate intoxication	1	4.0
Venomous snakebite	1	4.0
Mushroom intoxication	1	4.0
Total	25	100

The vast majority of patients (n=19, 76%) were admitted to the reanimation unit or an intensive care unit (ICU) at the time of the TPE procedure. The remaining patients were followed in neurology, surgical ICU, nephrology, gastroenterology ICU, and emergency service wards.

3.3. TPE Procedural Characteristics

The mean procedure duration was 111 $\pm$ 26 minutes (range: 75–180 minutes), and the mean volume of plasma exchanged per session was 2928 $\pm$ 530 mL (range: 1850–4000 mL). The most frequently used replacement fluid was FFP, administered in 16 sessions (53.3%), either alone or in combination. Hydroxyethyl starch (HES) was the second most common replacement choice (20.0%), followed by 4% albumin (10.0%) and combination regimens. Vascular access was established via hemodialysis catheter (11.5 Fr) in 26 sessions (86.7%), with peripheral venous access used in 4 sessions (13.3%). The most frequently used

apheresis device was Fresenius (60.0%), followed by Spectra Optia (20.0%), Optia (13.3%), and Baxter (6.7%). Procedural details are presented in Table 3.

Table 3. TPE procedural characteristics

Parameter	n / Mean $\pm$ SD	% / Range
Procedure duration (minutes)	111 $\pm$ 26	75–180
Inlet flow rate (mL/min)	67 $\pm$ 66	40–412
Volume of plasma exchanged (mL)	2928 $\pm$ 530	1850–4000
Single session / Two sessions	20 / 5 patients	80% / 20%
Replacement fluid		
Fresh frozen plasma (FFP)	16	53.3
Hydroxyethyl starch 3–4% (HES)	6	20.0
4% Albumin	3	10.0
Albumin + FFP combination	3	10.0
HES + Albumin combination	2	6.7
Vascular access		
Hemodialysis catheter (11.5 Fr)	26	86.7
Peripheral vein	4	13.3
Apheresis device		
Fresenius	18	60.0
Spectra Optia	6	20.0
Optia	4	13.3
Baxter	2	6.7

3.4. Complications and Mortality

The overall complication rate was 3.3% (1 out of 30 sessions). The single complication observed consisted of nausea, vomiting, and abdominal pain, classified as Grade 3 according to the ASFA adverse event grading system.⁸ The procedure was managed conservatively and completed without interruption. No Grade 1, 2, or 4 complications were recorded in any session.

The in-hospital mortality rate was 16% (4 out of 25 patients). Comparison of clinical parameters revealed that while hemoglobin, hematocrit, WBC, and platelet counts were significantly lower in the non-survivor group, age was significantly higher (54.5 $\pm$ 23.8 vs. 26.4 $\pm$ 8.7 years; $p=0.037$). Age >40 years and thrombocytopenia (PLT <100 $\times 10^3/\mu\text{L}$) were each identified as significant risk factors for mortality (OR=28.5; $p=0.016$ for both). Length of hospital stay showed a trend toward prolongation in the non-survivor group (27.2 $\pm$ 18.0 vs. 10.6 $\pm$ 13.9 days; $p=0.068$). Female sex, number of sessions, and leukopenia (WBC <4 $\times 10^3/\mu\text{L}$) were not significantly associated with mortality. A detailed comparison is provided in Table 4.

Table 4. Comparison of clinical parameters between non-survivors and survivors

Parameter	Non-survivor (n=4) Mean $\pm$ SD	Survivor (n=21) Mean $\pm$ SD	p	OR
Age (years)	54.5 $\pm$ 23.8	26.4 $\pm$ 8.7	0.037*	—
Hemoglobin (g/dL)	9.4 $\pm$ 2.0	12.7 $\pm$ 2.5	0.028*	—

Parameter	Non-survivor (n=4) Mean $\pm$ SD	Survivor (n=21) Mean $\pm$ SD	p	OR
Hematocrit (%)	27.9 $\pm$ 5.5	37.6 $\pm$ 7.0	0.022*	—
WBC ($\times 10^3/\mu\text{L}$)	5.5 $\pm$ 1.5	13.7 $\pm$ 7.7	0.006*	—
PLT ($\times 10^3/\mu\text{L}$)	80.6 $\pm$ 88.4	214.0 $\pm$ 88.3	0.015*	—
Length of hospital stay (days)	27.2 $\pm$ 18.0	10.6 $\pm$ 13.9	0.068	—
Age >40 years, n (%)	3/4 (75%)	2/21 (10%)	0.016*	28.5
PLT <100 ($\times 10^3/\mu\text{L}$), n (%)	3/4 (75%)	2/21 (10%)	0.016*	28.5

Mann-Whitney U and Fisher's exact tests were used. * $p < 0.05$. OR: Odds ratio.

4. Discussion

In this single-center retrospective study, we evaluated the clinical characteristics, procedural parameters, complication rates, and mortality-related factors of 25 patients who underwent TPE for intoxication. Our findings demonstrate that TPE can be performed safely in this patient population, with a low overall complication rate of 3.3%. Advanced age and thrombocytopenia were identified as the most significant risk factors associated with in-hospital mortality.

The pharmacokinetic rationale for TPE in intoxication rests primarily on two properties of the causative agent: high plasma protein binding (>80%) and a low volume of distribution, which together limit the drug's removal by conventional hemodialysis or hemoperfusion.^{5,10} In our series, amitriptyline — a tricyclic antidepressant with plasma protein binding exceeding 90% — was the most frequently documented causative agent (n=7, 28%). This is consistent with previously published series from Turkey and other countries.^{6,9} The substantial proportion of cases with an unidentified causative agent (52%) reflects the real-world challenge of toxicological identification in acute poisoning, particularly in patients who are unconscious or unable to provide a history. In such cases, the decision to initiate TPE is based primarily on clinical deterioration and failure to respond to conventional supportive measures.¹⁰

The overall complication rate in our cohort (3.3%, Grade 3) is notably low and compares favorably with rates reported in the general TPE literature. Schutt et al. highlighted that TPE is generally well tolerated in poisoned patients, with procedural adverse events occurring in a minority of cases.¹⁰ Similarly, a pediatric intoxication series reported no TPE-related mortality or major complications in 14 patients.¹¹ This favorable safety profile underscores the viability of TPE as an adjunctive treatment strategy in selected intoxication cases, even in critically ill patients who may already have compromised physiological reserves.

The in-hospital mortality rate in our cohort was 16% (4/25). This figure is higher than rates reported in general ICU intoxication populations, where mortality typically ranges from 2% to 6%.^{12,13} However, this difference is not unexpected, given that patients in our series represented a highly selected subgroup with severe or refractory intoxication, the majority of whom (76%) required intensive care unit admission. In a similarly selected series, Dişel et al. reported a mortality rate of 33% among 36 cases receiving TPE for poisoning over 8 years, further illustrating the severe clinical profile of patients in whom extracorporeal therapy is deemed necessary.⁹

A key finding of this study is the significant association between thrombocytopenia (PLT <100 $\times 10^3/\mu\text{L}$) and in-hospital mortality (OR=28.5; $p=0.016$). Thrombocytopenia is well recognized as an independent predictor of mortality in critically ill patients. Vanderschueren et al. demonstrated in a prospective ICU cohort that thrombocytopenic patients had a crude odds ratio of 5.0 for ICU mortality compared to those with normal

platelet counts.¹⁴ Furthermore, the degree of platelet count reduction has been shown to correlate in a dose-dependent manner with mortality risk.¹⁵ In our series, three of four non-survivors had platelet counts below $100 \times 10^3/\mu\text{L}$ at the time of TPE initiation, and the one young non-survivor presented with severe thrombocytopenia (PLT: $23 \times 10^3/\mu\text{L}$), suggesting that thrombocytopenia may carry prognostic significance regardless of age. These findings support the use of platelet count as a readily accessible and clinically meaningful prognostic marker in intoxicated patients undergoing TPE.

Advanced age (>40 years) was also significantly associated with mortality in our cohort (OR=28.5; $p=0.016$), with non-survivors being markedly older than survivors (54.5 ± 23.8 vs. 26.4 ± 8.7 years; $p=0.037$). This is consistent with the broader literature on acute poisoning outcomes. Mühlberg et al., in a retrospective analysis of 5,883 patients in a toxicological ICU, identified age as a significant risk factor for higher mortality and prolonged ICU stay following acute poisoning.¹⁶ Similarly, Liisanantti et al. found that clinical severity scores on admission — which inherently incorporate age-related physiological reserve — were among the strongest predictors of hospital mortality in drug-poisoned ICU patients.¹² The reduced physiological reserve and higher prevalence of comorbidities in older patients likely account for the disproportionate impact of toxic insult in this age group.

Notably, WBC count was significantly lower in the non-survivor group (5.5 ± 1.5 vs. $13.7 \pm 7.7 \times 10^3/\mu\text{L}$; $p=0.006$). While leukocytosis is a common physiological response to acute toxin exposure, its absence — manifesting as a relatively low WBC — may indicate underlying immunosuppression, bone marrow suppression, or early sepsis. This finding underscores the importance of monitoring hematological parameters when making decisions regarding TPE.

The length of hospital stay showed a non-significant trend toward prolongation in the non-survivor group (27.2 ± 18.0 vs. 10.6 ± 13.9 days; $p=0.068$). The apparent paradox of non-survivors having longer hospital stays may be explained by late deterioration following initial stabilization, consistent with what has been described in delayed hepatotoxicity (as in mushroom intoxication) or prolonged multiorgan dysfunction.

The present study has several limitations. Its retrospective design and single-center nature limit the generalizability of the findings. The relatively small sample size ($n=25$) restricts the statistical power of the analyses, particularly for multivariate modeling. The heterogeneity of the patient population introduces confounding that cannot be fully controlled. Furthermore, the absence of a control group makes it impossible to determine the direct contribution of TPE to clinical outcomes independent of other supportive measures. Moreover, the study spans a long period from 2000 to 2020, during which intensive care practices, apheresis technology, and general supportive care evolved substantially. These temporal changes may have influenced clinical outcomes independently of TPE itself, as patients treated in more recent years may have benefited from overall improvements in critical care rather than from the procedure alone. This potential temporal confounding should be taken into account when interpreting the results. These findings should therefore be regarded as hypothesis-generating and warrant validation in larger, prospective multicenter studies.

5. Conclusion

Therapeutic plasma exchange is a safe and effective extracorporeal treatment option in patients with severe intoxication refractory to conventional management. In our single-center series of 25 patients, the overall procedural complication rate was 3.3%, confirming the favorable safety profile of TPE even in critically ill patients. The in-hospital mortality rate of 16% reflects the severity of the underlying clinical condition rather than the procedure itself.

Advanced age and thrombocytopenia at the time of TPE initiation were identified as the most significant risk factors associated with in-hospital mortality, each carrying an odds ratio of 28.5. These parameters are readily accessible at the bedside and may serve as clinically meaningful prognostic indicators to guide risk stratification in intoxicated patients considered for TPE.

Given the retrospective and single-center nature of this study, these findings should be regarded as hypothesis-generating. Larger, prospective, multicenter studies are needed to establish standardized indications, optimal procedural protocols, and evidence-based prognostic models for TPE in intoxication.

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