



Original Contribution

Therapeutic plasma exchange in poisoning: 8 years' experience of a university hospital



Nezihat Rana Dişel, MD ^{a,*}, Ayça Açıklan Akpınar, MD ^a, Ahmet Sebe, MD ^a, Emre Karakoç, MD ^b, Selen Sürer, MD ^a, Ferda Tekin Turhan, MSc ^c, Selçuk Matyar, MD ^d

^a Department of Emergency Medicine, Çukurova University Faculty of Medicine, Adana, Turkey

^b Intensive Care Unit, Department of Internal Medicine, Çukurova University Faculty of Medicine, Adana, Turkey

^c Balcali Hospital, Hemapheresis, Stem Cells and Cryopreservation Unit, Çukurova University School of Medicine, Adana, Turkey

^d Biochemistry Division of Central Laboratory, Çukurova University Faculty of Medicine, Adana, Turkey

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ABSTRACT

Introduction and Aim: This study examined the extracorporeal methods for the elimination of toxic substances in poisoned patients that are used by clinicians taking care of such patients. Here we present our experience in the use of therapeutic plasma exchange (TPE). To the best of our knowledge, this is the largest number of poisoning cases ever reported in a study.

Patients and Methods: This is a retrospective study conducted at the Çukurova University Faculty of Medicine, Department of Emergency Medicine, with the permission of the ethical committee of the medical faculty. The study includes patients who had undergone TPE because of poisoning between January 2007 and May 2015. We summarize the clinical data and outcomes of the patients with available files.

Results: A total of 36 cases among the 42 patients who underwent TPE in this 8-year period were included in the study. More than 20 identified toxic substances, most of which were pesticides, were found to be the causes of poisoning. Twenty-three healthy discharges and 12 deaths are discussed in the study.

Conclusion: We believe that our study reports the largest ever number of poisoning cases treated with TPE in the literature. When applicable, TPE may be a promising extracorporeal elimination and treatment technique in poisoned patients when performed in selected cases.

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1. Introduction

Several extracorporeal methods for the decontamination of poison have promise in emergency care settings. The toxicants themselves, or their active metabolites, can be removed from circulation by means of hemodialysis, hemoperfusion, hemofiltration, and apheresis. In addition, toxicant-containing blood can be filtrated to separate the plasma and replace the fluids and various blood products to ensure the removal of the toxicants. Therapeutic plasma exchange (TPE) is one method that is recommended mainly for neurologic, rheumatologic, and hematologic diseases; the method has also recently been used for sepsis and multiorgan failure patients to remove immune complexes. In addition to these diseases, mushroom poisoning and envenomations are listed as indications in apheresis guidelines as second-line therapies, or in individual experiences in selected cases with low quality of evidence [1]. Toxicants and substances with high protein-binding affinity are good candidates for plasma removal or exchange treatments. Reports of the application of TPE in poisoning cases include such toxicants.

In this study, we share our 8-year experience with the largest number of cases ever reported, with the use of TPE in poisoning at the emergency medicine department (ED) of a tertiary care university hospital. We discuss our findings in how TPE was successfully used in poisoning cases.

2. Patients and methods

This retrospective study was performed with permission of the Ethical Committee of the Medical School of Çukurova University. The list of patients who had undergone TPE was obtained from the Apheresis Unit of the Çukurova University School of Medicine Hospital between January of 2007 and May of 2015. The study included adult patients who had been diagnosed as being poisoned and who had undergone TPE in the ED and/or intensive care unit (ICU). Patients who had undergone TPE for indications other than poisoning (ie, thrombotic thrombocytopenic purpura or isolated septicemia unrelated to poisoning), who were younger than 18 years, or whose records were absent were excluded from the study. We reviewed the patients' medical histories, demographic data, exposure to drugs/toxicants, ICU admissions, conditions due to poisoning, and outcomes by using hospital registration and medical records after recording these in a study sheet.

* Corresponding author. Department of Emergency Medicine, Çukurova University Faculty of Medicine, 01260, Adana, Turkey. Tel.: +90 5332416405; fax: +90 3223387140.
E-mail address: ranalpay@gmail.com (N.R. Dişel).

3. Results

A total of 42 patients were found to have undergone TPE. Two patients' records were absent, and 3 patients had undergone TPE for indications other than poisoning (2 patients for septicemia and 1 patient for thrombotic thrombocytopenic purpura), and 1 patient was a 4-year-old boy with pesticide poisoning. The remaining 36 patients (22 men and 14 women), with single or combined drug or toxicant exposures, were included in the study. The mean age of the patients was 46.11 ± 21.43 years (range, 17–83 years). The drugs and toxicants that the study patients had been exposed to mainly included pesticides (organophosphates [OPs], organochlorines, and paraquat). Twenty-six patients, one of whom also had a methyl alcohol overdose, were hospitalized for OP poisoning. Other toxicants (in the remaining 10 patients) included paracetamol, antidepressants (mianserin), sedative-hypnotics (carbamazepine), antipsychotics (olanzapine, quetiapine), cardiovascular drugs (amlodipine), nonsteroidal antiinflammatory drugs (ibuprofen, flurbiprofen), rodenticides (super warfarin), inorganic phosphorus (yellow phosphorus), an unknown type of mushroom, and a heavy metal (bismuth). The OPs that were identified and recorded in the patient files were diazinon and chlorpyrifos. Five patients (2 poisoned with yellow phosphorus, 1 with paracetamol, 1 with paraquat, and 1 by mushrooms) had undergone TPE to maintain homeostasis. Hepatic failure and multiorgan failures were indications of TPE in these patients. Thirty-one patients had undergone TPE to remove toxicants. None of the patients had envenomation. Seventeen patients of this study group were subjects of a previously reported study, which investigated the effectiveness of TPE in intermediate syndrome OP poisoning [2].

All of the poisoned patients in our study were evaluated in the ED according to their complaints, drug and/or toxicant intakes, and clinical situations. The appropriate decontamination techniques (gastric lavage, bowel irrigation, etc) and antidote administration (when available and/or applicable), symptomatic treatment, and supportive care measures were performed on all patients. Fresh-frozen plasma and albumin in isotonic saline at a calculated dose (according to the patient's body weight and baseline serum albumin and hemoglobin levels) were used as replacement fluid in all patients. Cooperating patients who had 2 large (minimum 18-gauge green catheter) peripheral venous cannulas were treated with TPE via their peripheral veins. Patients who did not cooperate and those without suitable peripheral access were inserted with femoral catheters to perform TPE. The TPE procedure was performed by a trained nurse from the Therapeutic Apheresis Unit with an automatic device (Spectra Optia Apheresis System; CaridianBCT, Lakewood, CO or Fresenius-AS-TEC 204; Fresenius Hemocare, Redmon, WA), either in the ED or in the ICU. Therapeutic plasma exchange was administered in cases where (1) clinical improvement could not be achieved, despite supportive and antidotal treatments in drug or toxicant poisonings, which are known to bind plasma proteins; (2) the replacement with fresh plasma, which was rich in depleted factors or enzymes (such as cholinesterases), was needed due to clinical worsening, despite all conventional treatment modalities; or (3) hepatic or multiorgan failure due to poisoning was diagnosed during treatment.

Therapeutic plasma exchange was performed in the first 24 hours after admission in 3 patients and after 24 hours in 33 patients. Among those 33 patients, the leading situations indicating the need for TPE included uncontrolled and ongoing toxidrome symptoms, despite conventional treatment modalities; respiratory depression; the need for prolonged endotracheal intubation and mechanical ventilatory support; and the occurrence of intermediate syndrome in patients with OP poisoning. Twelve patients died (due to multiorgan failures, septicemia, pulmonary thromboembolism, pneumonia, gastrointestinal bleeding, or complications from tracheostomy) and 33 were discharged. One patient left the ward without permission after the TPE procedure was performed, and the outcome is unknown. Five patients underwent both hemodialysis and TPE due to metabolic acidosis and uremia.

Twelve patients underwent multiple sessions of TPE (6 patients had 2 sessions, 4 had 3 sessions, 1 had 4 sessions, and 1 had 5 sessions). The demographic and clinical data of the patients are summarized in Table.

4. Discussion

Researchers are currently studying several extracorporeal methods for the elimination of toxic substances to enhance detoxification and to achieve quicker clinical improvement in poisoned patients. Choosing the best method for extracorporeal elimination depends on the properties of the toxic substances, as well as the availability of the appropriate method. The deciding factors include protein-binding capacities, water solubility, the volume of the toxicant's distribution in the body, and ways of elimination. Hemodialysis, hemoperfusion, hemofiltration, and apheresis are procedures that require trained personnel and specific devices for the extracorporeal elimination of toxicants. Plasmapheresis is a procedure in which less than 15% of total plasma is removed, and it is not replaced. In TPE, on the other hand, the separated plasma is replaced with albumin and/or fresh-frozen plasma and crystalloids [1].

The terms “plasmapheresis” and “TPE” identify different procedures, but they cause confusion and are frequently misused in the literature. Many articles in the toxicology field misuse the term plasmapheresis, when what is meant is TPE. Plasmapheresis is often used to remove immune complexes. Therapeutic plasma exchange is also used for the same purpose, but is preferred when very large amounts of plasma have to be removed and therefore need to be replaced.

Today, TPE is a promising treatment modality in poisoning cases because it has several advantages over hemodialysis and hemoperfusion. It is faster; it is independent of the size of the toxicant molecules under consideration (the molecular weight of the substance to be cleared by hemodialysis and hemoperfusion must be 100–40000 kDa, with a maximum 50000 kDa for hemofiltration); and it can be performed via 2 large peripheral veins instead of via central catheters. Therapeutic plasma exchange is effective in eliminating substances with high plasma protein-binding capacity (>80%) and low distribution volume (<0.2 l/kg body weight) [3]. Many case reports advocate the effectiveness of plasmapheresis or TPE in different poisoning cases, including amitriptyline [4,5], theophylline [6], carbamazepine [7], phalloid mushroom [8], diltiazem [9], verapamil [10], amlodipine [11], propranolol [12], L-thyroxine [13], and heavy metals such as mercury [14]. In these reports, the protein-binding capacity of the toxicants/drugs makes the use of TPE logical for reducing plasma levels, as well as for treating poisoning symptoms.

Ibrahim and Balogun [15] reviewed another group of medications—including chemotherapeutics, antibiotics, and miscellaneous drugs—according to case reports, in order to discuss additional loading doses that are needed after TPE is performed for reasons other than poisoning, because these medications are removed in the process. Nenov et al [6] claimed in their study that plasmapheresis is not helpful for OP poisoning; the authors could not detect any decrease in dimethoate concentrations in the plasma in their study. We suggest that the desired results of TPE may include not only the elimination of OPs but also the replacement of cholinesterase by fresh-frozen plasma in patients with prolonged poisoning symptoms, such as respiratory depression. Güven et al [16,17] reported clinical improvement in patients with OP poisonings after plasmapheresis performed for sepsis. There have been many other reports on the use of plasmapheresis in OP poisoning [18,19]. Seventeen of the patients in our study were also the subjects of a prospective study previously held in our clinic. Patients having intermediate syndrome due to OP poisoning were included in that study, in which the effectiveness of TPE was reported [2]. That study concluded that TPE is an effective method of treatment for intermediate syndrome because 13 patients showed clinical improvement after undergoing TPE.

A total of 26 patients with OP poisoning had undergone TPE over the course of 8 years in our clinic. Including the previously reported 17 cases, all had prolonged cholinergic symptoms that were resistant to pralidoxime and atropine (all of them received >250 mg/kg daily

Table

The demographic and clinical data of the patients

P. no.	Age (y)	Sex	Drug/Toxicant	Diagnose	Initial GCS score	ETI	MV	Tr. to ICU	Day of ICU tr.	Total day of hosp.	TPE indication	No. of TPE	Day of TPE(s)	Weaning after TPE	Post-TPE day of hosp.	Concomitant problems during hosp.	Outcome
1	83	M	OP (diazinon)	Alzheimer, psychosis, poisoning	7	+	+	+	10.	35	Poisoning	2	15,17	—	18	Arrhythmia, intermediate syndrome	Death
2	59	M	Mianserin	DM, hypoglycemia, HT, poisoning	7	—	—	+	2.	20	Poisoning	5	3, 4, 5, 7, 8	—	12	Stroke, urinary tract infection	Discharge
3	20	M	Carbamazepine, baclofen, superwarfarin	Spinocerebellar ataxia, hemiplegia, epilepsy, poisoning	3	+	+	+	2	27	Poisoning	1	3	—	24	Hyponatremia	Discharge
4	53	M	OP (undetermined)	Poisoning	7	+	+	—	—	7	Poisoning	1	1	+	6	Intermediate syndrome	Discharge
5	53	F	OP (undetermined)	HT, Hemiplegia, poisoning	15	+	+	+	6	41	Poisoning	1	5	—	40	Intermediate syndrome, bilateral pneumothorax, CPA, tracheostomy	Death
6	21	M	Paracetamol, ethyl alcohol	Toxic hepatitis, poisoning	15	—	—	—	—	3	Hepatic Failure	1	1	—	2	—	Unauthorized leave-escape
7	51	F	OP (undetermined)	Poisoning	15	+	+	—	—	33	Poisoning	1	7	+	26	Intermediate syndrome	Discharge
8	17	F	Amlodipine, bepridil, atorvastatin, ibuprofen, flurbiprofen metoclopramide	Poisoning	10	+	+	—	—	12	Poisoning	2	1, 2	+	10	Shock, Intra-aortic balloon pump, peritonitis, abdominal and pleural effusion	Discharge
9	63	M	OP (diazinon)	Poisoning	4	+	+	+	9	47	Poisoning	2	12, 13	+	34	Intermediate syndrome	Discharged earlier than planned (patient's own decision)
10	41	M	OP (diazinon)	Poisoning	7	+	+	—	—	30	Poisoning	4	5, 6, 7, 12	+	18	Intermediate syndrome	Discharge
11	22	F	OP (undetermined)	Poisoning	8	+	+	—	—	21	Poisoning	2	7, 18	+	3	Intermediate syndrome	Discharge
12	67	M	OP (chlorpyrifos)	Poisoning	7	+	+	+	18	95	Poisoning	3	2, 5, 9	—	86	Tracheostomy, gastrointestinal bleeding	Death
13	61	F	OP (diazinon)	Poisoning	6	+	+	—	—	28	Poisoning	1	25	+	3	DM, DVT	Discharge
14	18	F	OP (undetermined)	Poisoning	11	+	+	—	—	14	Poisoning	1	2	+	12	Intermediate syndrome, intra-abdominal free fluid	Discharge
15	72	M	OP (undetermined)	Poisoning	6	+	+	+	5	22	Poisoning	1	3	—	19	Acute AF, pneumonia, septicemia, intermediate syndrome	Death
16	63	M	OP (diazinon)	Poisoning	7	+	+	+	5	13	Poisoning	1	6	—	7	Post-CPR on admission	Death
17	29	M	OP (undetermined)	Poisoning	6	+	+	—	—	15	Poisoning	1	2	+	13	—	Discharge
18	81	F	Seroquel	Poisoning	12	—	—	—	—	6	Poisoning	1	2	—	4	DM, HT, chronic renal failure, HD	Discharged earlier than planned (patient's own decision)
19	50	M	OP (undetermined)	Poisoning	12	+	+	—	—	13	Poisoning	1	6	+	7	Intermediate syndrome	Discharge
20	32	M	OP, toxic alcohol (methyl alcohol)	Poisoning	3	+	+	—	—	18	Poisoning	1	10	+	8	First HD for toxic alcohol, then TPE for OP, intermediate syndrome	Discharge
21	22	F	OP (undetermined)	Poisoning	10	+	+	+	4	16	Poisoning	1	5	—	11	ARDS, septicemia, pneumonia	Death
22	76	M	OP (diazinon)	Poisoning	6	+	+	+	7	41	Poisoning	3	13, 15, 19	+	22	HT, glaucoma, cataract, intermediate syndrome	Discharge
23	23	M	OP (chlorpyrifos)	Poisoning	8	+	+	—	—	21	Poisoning	2	3, 8	+	13	Intermediate syndrome	Discharge

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Table (continued)

P. no.	Age (y)	Sex	Drug/Toxicant	Diagnose	Initial GCS score	ETI	MV	Tr. to ICU	Day of ICU tr.	Total day of hosp.	TPE indication	No. of TPE	Day of TPE(s)	Weaning after TPE	Post-TPE day of hosp.	Concomitant problems during hosp.	Outcome
24	65	M	OP (undetermined)	Poisoning	8	+	+	+	10	18	Poisoning	3	4, 5, 10	—	8	HT, Intermediate syndrome	Death
25	26	M	Yellow phosphorus	Poisoning	15	—	—	+	2.	15	Hepatic failure	3	2, 3, 4	—	9	Hepatic failure, liver Tx	Discharge
26	28	M	OP (chlorpyrifos)	Poisoning	8	+	+	—	—	15	Poisoning	1	8	+	7	—	Discharge
27	34	F	Bismuth	Poisoning	14	—	—	—	—	24	Poisoning	1	3	—	21	ARF	Discharge
28	21	F	OP (chlorpyrifos)	Poisoning	15	+	+	—	—	10	Poisoning	1	3	+	7	Intermediate syndrome	Discharge
29	65	F	OP (diazinon)	Poisoning	12	+	+	—	—	8	Poisoning	1	4	+	4	Intermediate syndrome	Discharge
30	19	F	Paraquat	Poisoning	15	+	+	—	—	13	Poisoning	2	3, 10	—	3	ARDS, ARF, pancreatitis, hyperbilirubinemia	Death
31	22	M	Yellow phosphorus	Poisoning, psychosis	15	—	—	+	3	18	Poisoning, hepatic Failure	2	4, 6	—	12	Hepatic failure, liver Tx	Discharge
32	61	F	OP (undetermined)	Poisoning	8	+	+	—	—	17	Poisoning	2	4, 7	—	10	Massive pulmonary thromboembolism	Death
33	51	M	OP (undetermined), antipsychotic (undetermined),	Poisoning	5	+	+	—	—	6	Poisoning	1	3	—	3	DM, AF, psychosis, pneumonia, tracheostomy	Death
34	49	F	OP (undetermined)	Poisoning	10	+	+	+	4	10	Poisoning	1	2	+	8	Psychosis, aspiration pneumonia	Discharge
35	81	M	Mushroom	Poisoning	15	+	+	+	3	11	Poisoning, hepatic failure	1	8	—	3	HD first, hepatic and renal failure	Death
36	61	M	OP (diazinon)	Poisoning	8	+	+	+	6	38	Poisoning	1	5	—	33	Intermediate syndrome, DM, pulmonary thromboembolism (?), hypernatremia, HD, pneumonia, septicemia	Death

Abbreviations: ARF, acute renal failure; ARDS, acute respiratory distress syndrome; CPA, cardiopulmonary arrest; CPR, cardiopulmonary resuscitation; DM, diabetes mellitus; DVT, deep venous thrombosis; ETI, endotracheal intubation; F, female; GCS, Glasgow Coma Scale; Hosp., hospitalization; HD, hemodialysis; HT, hypertension; M, male; MV, mechanical ventilation; P, patient; TPE, total plasma exchange; Tr., transfer; Tx, transplantation.

atropine), and all were mechanically ventilated. One patient had dermal exposure to OPs; the patient's decontamination could not be achieved by washing due to wrinkled skin. One other patient was poisoned with bismuth, which binds to plasma proteins. Four patients had no enzyme regeneration with prolonged respiratory depression and the need for ventilator support, which indicated tracheostomy. The paraquat poisoning patient had multi-organ failure and the 2 patients with inorganic phosphorus poisoning had hepatic failure. All the 3 patients had undergone TPE because of hyperbilirubinemia, and TPE was used for clearance of bilirubin. The patients with inorganic phosphorus poisoning were candidates for liver transplantation. Therapeutic plasma exchange was used as a supportive care measure and successful healing was achieved in both patients after transplantation. Five patients had undergone both hemodialysis and TPE due to metabolic acidosis and uremia. Twelve patients had multiple sessions of TPE (6 patients had 2 sessions, 4 had 3 sessions, 1 had 4 sessions, and 1 had 5 sessions).

Of the 12 fatalities, 10 were related to OP poisoning. Nine of these patients were older than 50 years, and many of them had chronic diseases like hypertension, arrhythmia, and diabetes. Five of these patients were diagnosed as having intermediate syndrome. Although fatalities occurred after concomitant problems, intermediate syndrome may be said to be the leading cause of these 5 fatalities because of prolonged hospitalization. Three of these patients had pneumonia-related septicemia, and 2 had pneumonia. One other patient with OP poisoning was resuscitated before admission and had neurologic dysfunction. Multiorgan failure was the leading cause of death in the 2 patients with mushroom and paraquat poisonings, for whom TPE was used for

supportive care. The patient with paraquat poisoning had ingested a lethal amount of paraquat (nearly 100 mg), and she had persistent hypoxemia due to respiratory failure and mental alteration due to hepatic and renal failures. Massive pulmonary thromboembolism was diagnosed and intra-arterial cannulation and thrombolysis were performed in 1 patient with OP poisoning, but she died of hypoxemia due to hemoptysis.

5. Limitations

The main limitation of this study is that it was retrospective. Nearly half of the study patients were subjects of a prospective study that had been previously reported. Therapeutic plasma exchange was performed according to sample cases reported in the literature, or as a last-chance treatment option for many study patients. Some types of poisonings are represented by only 1 patient in the study. The clearance of the toxicants was not proven in all patients by biochemical assays, so effectiveness of TPE may be questioned. Furthermore, the ineffectiveness of TPE for poisoning treatment in patients who died cannot be concluded also, because of the visible reasons of death in many of them.

6. Conclusion

Extracorporeal methods for the elimination of toxicants in poison management are helpful for improving the clinical status of selected patients. The decision to use the right method may have prognostic value in suitable patients. These modalities are expensive, and they require

trained personnel and specific devices. We suggest the use of TPE in toxicology clinics to manage extraordinary and serious cases of certain patients who are suffering from poison and/or toxicant ingestion, especially when clinical worsening occurs despite conventional treatments. Among a total of 36 seriously poisoned patients in our study, 23 were discharged in a healthy condition (2 were discharged by their personal decisions earlier than planned), which may enlighten new indications of TPE in poisoning. Further studies are needed to support the use of TPE.

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