Therapeutic Plasma Exchange in Pediatric Intensive Care Unit: Single-center Experience

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Abstract

Aim: To examine the clinical characteristics, indications, and complications of patients undergoing therapeutic plasma exchange (TPE) in our pediatric intensive care unit (PICU).

Materials and methods: Patients who underwent therapeutic plasma exchange between January 2018 and January 2020 in the PICU were included in the study. Demographic, clinical, and laboratory data of patients were obtained retrospectively from medical records. A venous catheter was placed into subclavian, femoral, or jugular veins. The number of plasmapheresis sessions for each patient was determined by observing the course of the disease and clinical improvement. Patients were monitored for vital signs during the plasmapheresis process. Complications directly associated with TPE were recorded.

Results: During the 2-year study period, 105 TPE sessions were performed in 25 patients (15 male/10 female). The median age was 84 months (6–204), and the median body weight was 32 kg (8–75). Renal disorders and sepsis were the most common group, and about 48% of patients were in these groups. The most common diagnoses were sepsis with multiorgan dysfunction syndrome in seven patients and followed by hemolytic uremic syndrome (five patients) and Guillain–Barre syndrome (three patients). Nausea (6.7%) and hypocalcemia (6.7%) were the most common complications of patients associated with the procedure. Premature discontinuation of the procedure were not seen due to complications. Complications were treated with symptomatic therapy.

Conclusion: TPE is an effective treatment that can be safely used for pediatric patients with developments in PICUs. Nevertheless, TPE should be performed by experienced staff at a specialized center to minimize the risk of complications.

Keywords: Critically ill children, Hemolytic uremic syndrome, Pediatric intensive care, Plasma exchange.

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Introduction

Recent developments in pediatric intensive care have made it possible to use extracorporeal treatments for selected indications. Therapeutic plasma exchange (TPE) is an extracorporeal treatment that removes undesirable high molecular weight substances from the blood.[1,2] The removed plasma is replaced by an albumin solution, fresh frozen plasma (FFP), or crystalloid–colloid combinations; the (retained) blood cells are added, and the fresh (reconstituted) blood is given to the patient. TPE removes pathological intravascular autoantibodies, immunocomplexes, and high molecular weight substances such as cryoglobulin. TPE is now used to treat many diseases, including thrombotic microangiopathies, sepsis-related multiple organ failure, some drug poisonings, and neurological diseases (Guillain–Barre syndrome, acute disseminated encephalomyelitis, myasthenia gravis, multiple sclerosis, and Hashimoto encephalitis).[1–3]

In 2019, the American Society for Apheresis (ASFA) published a list of indications for therapeutic apheresis guided by the scientific data.[4] These guidelines are widely used when considering TPE for both pediatric and adult patients. Therefore, the number of diseases that can be treated in pediatric intensive care units (PICUs) is increasing day by day. However, data on TPE for pediatric patients remain limited, being usually in the form of case reports. Thus, protocols continue to be chosen by reference to adult studies. The TPE characteristics are technically identical for both adults and children, but differences in vascular access and extracorporeal volumes cause challenges when treating pediatric patients.

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Here, we examine the clinical characteristics, indications, and complications of patients undergoing TPE in our PICU.

Materials and Methods

With approval of the "Medical Research Local Ethics Committee" of Kayseri City Hospital, patients who underwent therapeutic plasma exchange between January 2018 and January 2020 in the PICU were included in the study. Demographic, clinical, and laboratory data of patients were obtained retrospectively from medical records and apheresis unit records. A form was created for each patient. Indications for plasma exchange, the number of procedures, complications associated with the procedure, and prognosis of patients were recorded.

Our patients were classified according to the ASFA classification as below:

Category I: TPE is a first-line treatment for the disease

Category II: Diseases in which TPE is second-line treatment (alone or in combination with other agents)

Category III: Diseases in which the optimal role of TPE cannot be precisely determined

Category IV: No benefit has been shown in current studies or harmful

A venous catheter was placed into subclavian, femoral, or jugular veins. TPE was performed by using Fresenius COM-TEC apheresis devices. We aimed to exchange 1 to 1.5 times the estimated plasma volume, resulting in a filtration rate of 10 to 50 mL/kg/hour over 1 hour. The plasma volume to be used was calculated using the blood volume formula estimated plasma volume (EPV), EPV = [0.07 × weight (kg)] × [1 − hematocrit]. Procedures were performed with FFP and/or albumin. Acid citrate dextrose (1:10–1:20 dilution) was used for anticoagulation of the system. Prophylactic calcium gluconate infusion (1 mg/kg) was administered through a separate vein during the procedure. All sessions were performed using the cell separator centrifuge method. The number of plasma exchange sessions for each patient was determined by observing the course of the disease and clinical improvement. Patients were monitored for vital signs during the plasma exchange process.

Complications directly associated with TPE were recorded. We recorded vomiting, nausea, allergic reactions, hypocalcemia and hypotension as well as procedural complications such as blood leakage, access problems, and filter clotting.

Statistical Analysis

All statistical analyses were performed in the Statistical Package for the Social Sciences 22.0 package program. In addition to descriptive statistical methods (mean, standard deviation [SD], median and interquartile range, frequency, and percentage), the Shapiro–Wilk test was applied to all variables to determine whether there was a normal or abnormal distribution. Variables with normal distribution were specified as mean ± SD and variables with abnormal distribution as median and interquartile range (IQR). $p < 0.05$ was considered significant.

Results

During the 2-year study period, 105 TPE sessions were performed in 25 patients (15 male/10 female). The median age was 84 months (IQR, 10–160), and the median body weight was 32 kg (IQR, 12–60). Characteristics of patients are shown in Table 1. Length of PICU stay in the TPE group is (12 days [IQR, 2–20]) longer than that of our standard PICU population (8 [IQR, 1–14]).

Our patients were classified into five groups according to their diagnosis: Renal disorders and sepsis were the most common group, and about 48% of patients were in these groups. The remaining patients had neurologic disorders, poisoning, and acute liver failure. The most common diagnoses were multiorgan failure (MOF) in seven patients and followed by HUS (five patients) and Guillain–Barre syndrome (three patients). According to the ASFA classification, the diagnosis of 6 patients (24%) was ASFA Category I, 6 patients (24%) in Category II, and 11 patients (44%) in Category III. Diagnosis and ASFA categories of patients are shown in Table 2. Total TPE sessions (31) and TPE sessions per patient (6.2) were higher in the neurologic disorder group.

FFP (70%) and 5% albumin (30%) were used in TPE sessions. The number of TPE sessions per patient was 4 (1–8), and patients with neurologic disorders had more TPE sessions (6.2) than others. Femoral (20%), internal jugular (68%), and subclavian (12%) veins were used for vascular access (Table 3).

Nausea (6.7%) and hypocalcemia (6.7%) were the most common complications of patients associated with the procedure. Premature discontinuation of the procedure was not observed due to complications. Complications were treated with symptomatic therapy (IV fluid bolus for hypotension, calcium therapy for hypocalcemia, etc.). Although no significant complications occurred that led to kidney or circulatory failure or chronic sequelae, when procedural and patient-related complications were taken together, we observed complications in 32 sessions (30.4%) (Table 4).

Table 1: Patient characteristics

Patient characteristics	*Median (IQR) n (%)*
Age (month)	84 (10–160)
Weight (kg)	32 (12–60)
Gender (male/female) *n* (%)	15/10 (60/40)
PRISM score at admission	27 (15–34)
PELOD score at admission	29 (12–33)
Ventilated (yes/no) *n* (%)	7/18 (28/72)
PICU stay (day)	12 (2–20)

PICU, pediatric intensive care unit; PRISM, pediatric risk of mortality; PELOD, pediatric logistic organ dysfunction

Table 2: Indication for TPE and ASFA categories

Clinical diagnosis	*Patients (n, %) n:25*	*Number of TPE sessions (n, %) n:105*	*ASFA category*	*Replacement fluid*
Renal				
STEC HUS	2 (8)	5 (4.8)	3	FFP
Atypical HUS	3 (12)	20 (19)	2	FFP
Neurologic				
ADEM	2 (8)	10 (9.6)	2	Albumin 5%
Guillain–Barre	3 (12)	21 (20)	1	Albumin 5%
Sepsis				
Sepsis + MODS	7 (28)	23 (21.9)	3	FFP
Liver diseases				
Acute liver failure	3 (12)	12 (11.4)	1	FFP
Poisoning				
Colchicine	2 (8)	5 (4.8)	3	FFP
Mushroom	1 (4)	4 (3.8)	2	FFP
Others				
Crimean–Congo hemorrhagic fever	2 (8)	5 (4.8)	n.c.	FFP

FFP, fresh frozen plasma; HUS, hemolytic uremic syndrome; ADEM, acute disseminated encephalomyelitis; MOF, multiorgan dysfunction syndrome; STEC, shiga toxin-producing *Escherichia coli*; TAMOF, thrombocytopenia associated multiorgan failure; n.c, not classified; MODS, multiorgan dysfunction syndrome

Table 3: Technical details of TPE sessions

Technical details	**Median (IQR)**
Sessions per patient	4 (1–8)
Blood flow volume (mL/min)	35 (10–50)
Exchange volume (mL/kg)	51.7 (30–78)
Replacement fluid	**n (%)**
Albumin 5%	31 (30)
FFP	74 (70)
Vascular access	**n (%)**
Femoral	5 (20)
Jugular	17 (68)
Subclavian	3 (12)

Table 4: Complications

Complications	*n/105 (%)*
Patient	
Nausea	8 (6.7)
Vomiting	7 (6.7)
Hypotension	6 (5.7)
Hypocalcemia	8 (7.6)
Procedure	
Access malfunction	2 (1.9)
Circuit clotting	1 (0.9)

Discussion

The increased numbers of PICUs in our country and of trained pediatric intensive care specialists have enhanced the applicability of special procedures such as TPE. Although recent advances have been encouraging, evidence-based data are lacking.[1–6] TPE should be performed only by experienced staff and only in specialist centers to minimize the risk of complications.

Although TPE indications in single-center pediatric reports often depend on the specific subspecialties of the centers, sepsis is one of the most common indications in these centers. In our study (unlike the literature), sepsis (28%) was the most frequent indication for TPE. In the multicenter study of Paglialonga et al.,[6] 67.2 and 20.9% of TPEs (respectively) were performed to treat hematological and neurological diseases. Hematological centers report various proportions, but hematological and neurological disorders are the most frequent indications.[7] The World Apheresis Registry found that neurological disorders were most commonly treated.[8] Similar to our study, Sık et al.,[9] in a single-center study, reported that sepsis with multiorgan dysfunction syndrome (MODS) (44.4%) was the most frequent indication for TPE. This is because both studies were conducted in PICUs. Center-specific subspecialities may explain the differences in TPE indications. Of our patients, 6 (24%) had ASFA category I, 7 (28%), category II, and 10 (40%), category III diagnoses, comparable to the figures of a multicenter European analysis.[6]

In our study, TPE was most commonly used to treat patients with sepsis-MODS. The ASFA considers this to be a category III diagnosis (it is unclear whether TPE is the optimal treatment).[11] Sepsis-related MOF is associated with high mortality and morbidity despite improvements in antibiotics and hemodynamic support. TPE eliminates thrombogenic and antifibrinolytic molecules and replaces missing anticoagulants and profibrinolytic molecules (thus ensuring normal hemostasis); it also removes cytokines and other mediators of organ failure.[11] In adults, TPE was associated with decreased mortality from disseminated intravascular coagulation, sepsis, and sepsis-related MODS.[12–14] Early TPE reduced mortality from sepsis-related MOF in otherwise healthy pediatric patients.[15] Şık et al. showed that the sepsis survival rate was 75% in critically ill pediatric patients.[9] Our rate was 71.4%; five of seven patients who underwent TPE because of sepsis-related MODS survived.

The utility of TPE to treat pediatric poisoning remains unclear. The ASFA TPE indicators include mushroom poisonings and drug overdoses, especially the latter (drugs bind to plasma proteins). We used TPE to treat two patients with colchicine intoxication and one with mushroom poisoning. Early TPE can be life-saving for the former patients; colchicine can be lethal at even low doses. The patients responded well, consistent with the literature.[10]

Crimean–Congo hemorrhagic fever (CCHF) is a viral disease that has become increasingly common in our country in recent years and has a high mortality rate. Despite advances in pediatric intensive care and antiviral agents, CCHF is often fatal. New treatments are needed; there is no approved vaccine or therapy. Although the ASFA has not considered CCHF, several adult case series found that TPE was an effective treatment.[16–18] We treated two pediatric patients with CCHF via TPE. This is a rare example of the use of TPE to treat pediatric patients with CCHF.

Complications developing during plasma exchange include catheter blockage, circuit clotting, vascular malfunction, allergic reactions, rash, bradycardia, hypotension, nausea, vomiting, and dizziness.[11,19] Complications are usually associated with vascular access, the replacement solution, and the process. The pediatric TPE complication rate ranges from 1 to 40%.[19] We recorded no serious complication. Nausea (6.7%) and hypocalcemia (6.7%) were the most common complications (32% in total, similar to the literature value of 30.4%).

The limitations of our study is the retrospective design in a single center. Despite these limitations, data on pediatric TPE are very limited; we believe that our contribution is useful.

TPE is effective and safe for pediatric patients in specialized intensive care units with experienced staff. More prospective, randomized controlled trials are needed to standardize pediatric indications and procedures.

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