

Therapeutic Plasmapheresis using Membrane Plasma Separation

Aditi Sinha · Anand Narain Tiwari ·
Rahul Chanchlani · V. Seetharamanjaneyulu ·
Pankaj Hari · Arvind Bagga

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Abstract The authors present their experience with therapeutic plasmapheresis (TPE) using membrane filters at the pediatric dialysis unit of a referral center. Between January 2006 and December 2010, 486 sessions of TPE were performed in 39 patients (range 6–17 y), chiefly for atypical hemolytic uremic syndrome (HUS, $n=22$), crescentic glomerulonephritis ($n=8$) and focal segmental glomerulosclerosis ($n=5$). Satisfactory response was noted in 32 patients, particularly with HUS ($n=22$) or crescentic glomerulonephritis ($n=6$). Adverse effects included chills or urticaria ($n=8$ sessions), hypocalcemia ($n=6$) and hypotension ($n=5$). The present findings highlight the safety, efficacy and feasibility of TPE using membrane filtration.

Keywords Plasma exchange · Hemodialysis

Introduction

Therapeutic plasma exchange (TPE) or plasmapheresis is indicated for treatment of several systemic diseases [1]. The procedure is done using either centrifugation devices or membrane filters [2]. The former, using cell separators, has limited application in children due to high costs, and need for large extracorporeal fractions and high blood flow rates [2, 3]. Plasma filtration, using highly permeable membranes with standard hemodialysis equipment, is equally efficacious and

technically easier [3, 4]. In view of scarce reports on membrane filtration-based TPE, particularly from our country, the authors report their experience emphasizing its feasibility, safety and efficacy [5, 6].

Material and Methods

Records of all TPE procedures performed at the Pediatric Hemodialysis Unit, from 2006 through 2010, were reviewed for indications, details of procedure and outcomes. TPE was conducted on 4008S hemodialysis machines (Fresenius, Hamburg, Germany) in isolated ultrafiltration mode [2]. Vascular access was through a double-lumen 8–12 French catheter placed in the femoral or internal jugular vein. Blood was filtered across a polysulfone membrane filter (PlasmaFlux, Fresenius) with surface area 0.3–0.6 m²; separated plasma was collected in graduated cylinders. An equivalent volume was replaced with 5 percent albumin and/or fresh frozen plasma through the venous end. Blood flow rate was 80–120 mL/min and transmembrane pressure was below 100 mm Hg. Heparin (loading dose 50 U/kg IV, followed by boluses of 25 U/kg/h) was titrated to maintain activated coagulation time of 120–150 s [7]. Plasma filters were reused thrice following manual sterilization with Renalin (Minntech Systems, Minneapolis, MN).

The indications and prescription for TPE were based on criteria of American Society for Apheresis [1] and disease specific guidelines (Table 1) [2, 3]. Concomitant therapies and/or hemodialysis were dictated by underlying disease.

Results

Thirty nine patients (29 boys) with median age 9.5 y (range 6–17 y) and weight 27.6 kg (17–56 kg) underwent 486 sessions of

A. Sinha · A. N. Tiwari · R. Chanchlani ·
V. Seetharamanjaneyulu · P. Hari · A. Bagga (✉)
Division of Nephrology, Department of Pediatrics,
All India Institute of Medical Sciences,
Ansari Nagar,
New Delhi 110029, India
e-mail: arvindbagga@hotmail.com

Table 1 Schedule for therapeutic plasma exchange (TPE) [1, 2]

Disease	Schedule ^a	Response
Hemolytic uremic syndrome	1.5-volume TPE daily till hematological remission; then alternate days for 2 wk; twice weekly and once-weekly for 2 wk each	Remission: platelets >150,000/mm ³ ; absence of hemolysis; LDH <300 U/L
Pauci-immune crescentic glomerulonephritis	1.5–2 volume TPE for 3 d; then on alternate days for 4 sessions	Normal urine output, serum creatinine and ANCA titers
Focal segmental glomerulosclerosis (pre-transplant)	1.5 TPE on alternate days for 6 sessions in the fortnight preceding transplantation	Lack of proteinuria
Guillain-Barre syndrome with respiratory distress	1–1.5 TPE daily for 3 d; then on alternate days	Improved muscle strength and motor performance

^a The preferred replacement fluid in hemolytic uremic syndrome was fresh frozen plasma, and albumin in focal segmental glomerulosclerosis

^a Plasma volume: $0.065 \times \text{weight in kg} \times (1 - \text{hematocrit})$

TPE. The median number of TPE per patient was 13.3 (4–36); each session lasted 45–90 min. Venous access was through the internal jugular vein ($n=27$, 69.2 percent patients), femoral vein (4) and either route (8). Median plasma volume exchanged was 974 (650–1,900) ml; this was replaced with fresh frozen plasma ($n=25$), albumin (3) or a combination (11).

Indications and Outcome

Indications for TPE included atypical hemolytic uremic syndrome (HUS, $n=22$), pauci-immune crescentic glomerulonephritis ($n=8$) and refractory focal segmental glomerulosclerosis (FSGS, $n=5$) (Table 2). Sequential hemodialysis was required for patients with HUS ($n=20$), crescentic

glomerulonephritis ($n=8$) and lupus nephritis. These patients also received immunosuppressive medications. Table 2 shows satisfactory short-term outcome in most patients with HUS and crescentic GN. Two patients with refractory or recurrent FSGS showed worsening kidney function. Favorable outcome was noted in three patients with neurological illnesses.

Complications

Chills, rigors and urticaria (8 sessions) responded to IV diphenhydramine and hydrocortisone. Other complications were hypocalcemia ($n=6$), hypotension (5) and abdominal pain (3). Six patients required change of vascular access for catheter-related bloodstream infection (4) and thrombosis (2).

Table 2 Indications for plasmapheresis ($n=39$), categorized according to American Society for Apheresis (ASFA) criteria [1], and patient outcomes

Indication	ASFA category	Number of patients	Follow up, mo	Outcome	
				Short term	Long term
Hemolytic uremic syndrome	I	22	14 (2–39)	Hematological remission, $n=22$; off dialysis, $n=14$	ESRD, $n=6$; stage 2 hypertension and normal renal function, $n=12$; no sequelae, $n=4$
Rapidly progressive glomerulonephritis	I	8	24.5 (12–26)	Off dialysis, $n=6$	ESRD, $n=2$; stage 2 hypertension and normal renal function, $n=4$; CKD stage 2, $n=2$
Focal segmental glomerulosclerosis (FSGS)					
Refractory nephrotic syndrome	–	1	18	No response	CKD stage 3
Prevent transplant recurrence	II	3	9 (2–12)	No recurrence	No proteinuria
Therapy of recurrent FSGS	I	1	24	No response	ESRD
Systemic lupus erythematosus	II	1	0.5	Remission of thrombotic microangiopathy; persistent neurological dysfunction	
Guillain Barre syndrome	I	2	9, 16	Incomplete recovery of motor function	Complete recovery
Acute demyelinating encephalomyelitis	II	1	13	Major neurological deficits	Impaired cognitive function; spasticity

CKD Chronic kidney disease; ESRD End stage renal disease

Discussion

The authors' experience suggests that plasmapheresis using membrane-filtration is an effective and safe extracorporeal therapy in children with atypical HUS, pauci-immune crescentic glomerulonephritis and for preventing recurrent FSGS in the allograft. The underlying diseases are accepted indications for plasmapheresis [1–3]. The procedure was an adjunct to standard management, and the overall outcomes were satisfactory. Most patients were sequentially hemodialyzed, for deranged renal function, using the same vascular access. The procedure was well tolerated with minor adverse events [5, 6].

The chief indication for TPE was atypical HUS secondary to anti-factor H antibodies; 70 percent patients recovered renal function after its initiation and other therapies. TPE is the standard of care for patients with atypical HUS; improved outcomes depend on prompt initiation of therapy [1, 3, 8]. This procedure is also recommended for patients with pauci-immune crescentic glomerulonephritis with plasma creatinine levels exceeding 2.8 mg/dL [9]. While the efficacy of TPE in refractory or recurrent FSGS is unclear, most centers prefer a few sessions of plasmapheresis before renal transplantation [1].

Pediatric literature on plasmapheresis from developing countries is scant. A recent report described the outcomes of centrifugation-based TPE in 195 adults and children [6]. Centrifugation-based TPE is utilized infrequently due to limited availability of equipment, reliance on blood bank services, need for high blood flow rates and risk of hypovolemia [2–4]. Since this center has a dedicated pediatric hemodialysis facility, the authors find membrane filtration feasible and convenient. Multiple studies show that the latter is as safe and effective as centrifugal plasmapheresis [2, 4, 5]. When equipment costs are discounted, the cost for TPE/session is lower with membrane filters (Rs. 2,500–3,000) than centrifugation-based procedures (Rs 5,000–6,000) [2].

Hemodialysis services are available in pediatric or adult units at most referral centers, and existing capabilities can be conveniently used to provide membrane-based TPE. Since many patients also require hemodialysis, this can follow

TPE without the need for additional equipment or training of staff. With minor innovation, both procedures can be done simultaneously (tandem hemodialysis-plasma exchange), reducing procedure time and costs [10].

Conflict of Interest None.

Role of Funding Source None.

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