



Case Report

# Plasma Exchange Therapy in an Infant: Proposing a New Anticoagulation Protocol

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## Introduction

Infants with liver failure require Therapeutic Plasma Exchange (TPE) for support of synthetic liver functions. Renal dysfunction in the form of Acute Kidney Injury (AKI) can develop and renal support therapy may be necessary. This is challenging on many aspects, from vascular access to anticoagulation, to monitoring and to therapy end-point. We briefly describe a 2 week-old infant with liver failure caused by Rh-isoimmunization leading to coagulopathy and AKI, requiring both TPE and renal support therapy. We are proposing a novel anticoagulation protocol for TPE in patients with coagulopathy.

## Case Presentation

Infant male born full-term by repeat C/section to a G2P2 mother, had an Apgar score of 5<sup>1</sup>-7<sup>5</sup>, a birth weight of 3.79 kg, was limp, pale and apneic, with perinatal depression and hematocrit of 13%. He required early ventilator assistance. His blood type was A+, his mother’s blood type was A- and she did not receive Rhogam. Diagnosis of Rh iso-immunization was also supported by positive antibody titer with severe hepatomegaly. An exchange transfusion was performed in the first 12 hours of life, for a rapid rise of serum total bilirubin. He required surfactant and nitric oxide for Persistent Pulmonary Hypertension of the Newborn (PPHN), milrinone for cardiac dysfunction and diuretics for oliguria. On ultrasound, kidneys were echogenic, without obstruction, and eGFR (estimated glomerular function rate, based on bedside

modified Schwartz’ formula) was 20 mL/min/1.73m<sup>2</sup> on second Day of Life (DOL2), improved on DOL7 to eGFR of 41 mL/min/1.73m<sup>2</sup>. Work-up for infectious diseases was negative. Head ultrasound revealed grade I Intraventricular Hemorrhage (IVH), later associated with ventriculomegaly, improved over time. Hemolysis continued, Plasma Free Hemoglobin (PFH) reaching 230, total bilirubin peaked at 19.2 mg/dL on DOL5 due to cholestasis and ischemia.

TPE was initiated for acute liver failure. Head ultrasound was performed prior to initiation of Therapeutic Plasma Exchange (TPE). Plasma volume of 200 mL was replaced with FFP. Because of coagulopathy, citrate use needed to be minimized, as both pRBC and FFP contain citrate. As such, we thought of using a higher blood:citrate ratio than customary (15:1). However, we noticed that the time to establish the interface was much delayed, plasma exchange starting only after ~1 hour. On subsequent runs, we titrated the citrate as in Table 1. During that first run, maximum inlet flow rate was 5 mL/min, on subsequent runs it reached 14 mL/min. The rinse back volume was based on end-of-treatment hematocrit. For anasarca due to hydrops fetalis, aquapheresis using the Aquadex FlexFlow<sup>R</sup> (CHF Solutions, Inc., Eden Prairie, MN 55344, USA) was initiated on DOL9, via a 7Fr right internal jugular dialysis catheter, without heparin because of the severe coagulopathy. On DOL12, when his eGFR declined to 13 mL/min/1.73m<sup>2</sup> convection was added for six more days for renal support therapy, as described by Askenazi DJ, et al. [1].

Run	Priming solution	Replacement solution	Time to interface	Ca infusion	BP start	BP end	iCa start	iCa mid-Rx	iCa end	Blood: citrate ratio at start	Blood: citrate ratio after interface established	Blood: citrate ratio once plasma exchange started
1	pRBC	FFP	60 min	10 mg/kg/h	81/46	85/47	1.41	1.13	1.44	40:1	15:1	40:1
2	pRBC	FFP	20 min	20 mg/kg/h	72/34	79/40	1.28	1.26	1.39	15:1	25:1	40:1
3	pRBC	FFP	10 min	20 mg/kg/h	79/41	70/35	1.20	1.11	1.34	15:1	25:1	40:1
4	pRBC	FFP	10 min	20 mg/kg/h	88/58	87/59	1.43	1.32	1.38	15:1	25:1	40:1

**Table 1:** TPE details of priming, replacement solution, calcium infusion, ionized calcium (iCa) values as well as citrate titration.

Liver biopsy was not diagnostic for Gestational Alloimmune Liver Disease (GALD), and no further TPE treatments were performed after DOL24, as hyperbilirubinemia improved. In addition to improvement in his liver function, his acute kidney injury resolved, eGFR being 77 mL/min/1.73m<sup>2</sup> on DOL20 and 113 mL/min/1.73m<sup>2</sup> on DOL35. He was discharged home on DOL35 with a serum total bilirubin of 5.4 mg/dL, which at 7 months of age was 0.3 mg/dL (normal 0.1-0.7 mg/dL).

## Discussion

Originally described by John Abel and Leonard Rowntree of Johns Hopkins Hospital in 1913 [2], developed by Dr. José A. Grifols Lucas in 1950-1951 [3], first use of TPE was in a patient with thrombotic Thrombocytopenic Purpura (TTP) in 1959 [4]. Since then, TPE was performed in prospective mothers with severe Rh disease and expected fetal loss [5] with Aminco Cell Separator from 20 weeks gestation onwards until the severity of fetal hemolysis decreased. Bambauer and colleagues [6,7] reported the feasibility and outcomes of single-needle TPE in newborns with severe Rh-erythroblastosis who failed exchange transfusion and phototherapy, using umbilical and femoral veins for vascular access, and heparin for anticoagulation. The mean blood flow was 5.3 ml/min and an average plasma volume of 192.4 ml was exchanged per treatment. Serum bilirubin was reduced from 15.6±4.8 to 7.3±3.2 mg/dl after 1-10 sessions.

Apheresis equipment was modified over time to be more accurate, reduce re-circulation, allow citrate anticoagulation and 40-45 mL plasma/kg to be replaced [7]. Citrate anticoagulation was reported by Magen et al [8] in a 2-month-old infant with idiopathic atypical HUS, successfully treated with a 1-month course of plasmapheresis using Spectra machine version 5.1 (COBE Lakewood, CO) (CSP). Our intention was to prevent bleeding, and as such, after the first session, blood:citrate ratio was set at 15:1, increased to 25:1 once interface was established, and once plasma exchange started after ~15 more minutes, blood:citrate ratio was

increased to 40:1 until completion of therapy (total ~3 hours for the first treatment, less than 2 hours, subsequently) (Table 1).

Feasibility of TPE in infants notwithstanding, it remains challenging due to access size and coagulopathy, especially in patients with liver dysfunction. Singer, et al. [9] used a Gambro cell separator in 49 patients with acute liver failure for 243 treatments. Following a randomized, non-blinded, paired (crossover) pivotal trial, Tormey CA, et al. [10] described advantages of Optia (SPO), reason for its use in our patient. We propose a new protocol for citrate anticoagulation in cases of coagulopathy and present what we believe to our knowledge to be the youngest patient undergoing TPE with Optia centrifugal system. This approach allowed us to establish the interface faster, did not alter the circuit flows, and did not worsen the IVH.

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