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Case Reports

Peritoneal Dialysis: An Alternative Modality of Fluid Removal in Neonates Requiring Extracorporeal Membrane Oxygenation after Cardiac Surgery

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Abstract: Extracorporeal membrane oxygenation (ECMO) is a lifesaving therapy for patients with cardiopulmonary failure after cardiac surgery. Fluid overload (FO) is associated with increased morbidity and mortality in this population. We present our experience using peritoneal dialysis (PD) as an adjunct for fluid removal in eight consecutive neonates requiring ECMO after cardiac surgery between 2010 and 2012. PD was added to FO management when fluid removal goals were not being met by hemofiltration (HF) or hemodialysis (HD). Percent FO was 36% at ECMO initiation; 88% (seven of eight) achieved negative fluid balance before discontinuation of ECMO. PD removed median 119 mL/kg/day (interquartile range [IQR], 70–166) compared with median 132 mL/kg/day (IQR, 47–231) removed by HF/HD. PD and HF/HD fluid removal were performed concurrently 38% of the time. Unlike HF/HD, PD was never stopped secondary to hemodynamic compromise. Median duration of ECMO was 155 hours (IQR, 118–215). Six of eight patients were successfully decannulated. These results suggest PD safely and effectively removes fluid in neonates on ECMO after cardiac surgery. PD may increase total fluid removal potential when combined with other modalities. **Keywords:** congenital heart disease, extracorporeal membrane oxygenation, fluid overload, peritoneal dialysis. *JECT. 2014;46:157–161*

Extracorporeal membrane oxygenation (ECMO) is a lifesaving therapy for patients with cardiopulmonary failure. Fluid overload (FO) often complicates cardiac ECMO and is associated with organ dysfunction, prolonged support times, and increased mortality (1–3). ECMO for neonates with postcardiopulmonary bypass (CPB) ventricular dysfunction involves temporary provision of full cardiac output to minimize ventricular wall stress and myocardial oxygen consumption. This period of cardiac rest is a crucial window of time to optimize the patient for separation from ECMO. Inotrope and vasopressor use is minimized, lung recruitment is maintained, and fluid removal is performed to ameliorate organ edema.

The optimal mode and rate of fluid removal during ECMO are unknown. Our center incorporates in-line hemoconcentrators into ECMO circuits for fluid removal and solute clearance through hemofiltration (HF) or hemodialysis (HD), whereas others use continuous renal replacement therapy (CRRT) machines and/or diuretics. Even in neonates with anasarca, fluid removal with these modalities may be limited in the setting of low or normal intravascular volume, because excess fluid removal may lead to diminished circuit "preload" resulting in decreased

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ECMO flow and exceedingly more negative venous return line pressures.

Since 2008, our center has routinely used peritoneal dialysis (PD) for postoperative fluid removal in neonates after cardiac surgery. It has proven to be very effective for fluid removal and is hemodynamically well tolerated (4); thus, we expanded our PD practice to augment fluid removal in neonates on cardiac ECMO. This case series represents our initial experience using PD in eight neonates supported with ECMO. PD proved to be well tolerated and contributed significantly to fluid removal in all cases.

METHODS

Eight consecutive neonates requiring ECMO after cardiac surgery at the University of Alabama at Birmingham between January 1, 2010, and December 31, 2012, were identified. Cases were reviewed and data from the medical record were abstracted. The study was approved by the Institutional Review Board. As a result of the retrospective nature of the study, the need for informed consent was waived.

Intraoperative Management

All patients in this series received a 39-cm single-cuffed silicone PD catheter (Pediatric Tenckhoff Curl Catheter; Tyco, Mansfield, MA) at the time of primary cardiac operation per institutional protocol. PD catheters were inserted into the abdominal cavity through a direct, tunneled periumbilical approach.

The CPB technique included cooling to 22°C (procedures involving aortic arch reconstruction) or 28°C (all others). Selective cerebral perfusion was used when possible during aortic arch reconstruction. Deep hypothermic circulatory arrest was required in three cases. During CPB, zero-balance ultrafiltration (UF) was performed. Patients not transitioned to ECMO from CPB received single-pass UF at the conclusion of CPB. The sternum was left open in all patients.

Extracorporeal Membrane Oxygenation Circuit and Management

ECMO circuits were composed of centrifugal pumps (Terumo Capiox® SP 45, Tokyo, Japan), oxygenators (Quadrox iD Pediatric Oxygenator; MAQUET, Hirrlingen, Germany), and in-line hemoconcentrators (Minntech Hemocor® HPH Mini, Minneapolis, MN). Hemoconcentrators were placed into an existing shunt within the ECMO circuit, adding only 14 mL to ECMO circuit prime. Average blood flow through the shunt was 150 mL/min. Alaris IV (Carefusion, San Diego, CA) pumps were used to regulate dialysate flow and ultrafiltrate removal rate. When using HF/HD, volume infused from other sources (e.g., medications and blood products) was accounted for in the HF/HD volume removal to ensure prescribed fluid balance goals were met. All volume infused and removed was closely monitored and measured hourly using a SmartSite® Burette Infusion Set (Carefusion), a volumetric cylinder with accuracy measurements to 1 mL. For additional safety, desired hourly volumes were entered into the Alaris pumps so the devices would stop and require clinician intervention. Continuous HD was performed through a hemoconcentrator when increased solute clearance was desired. Normosol (Hospira, Inc., Lake Forest, IL) was used as a dialysate. Adjunctive therapy included high protein total parenteral nutrition and repletion of albumin, electrolytes, and serum immunoglobulins. Serum albumin was checked daily and oncotic pressure was maintained with 25% albumin infusions to keep serum albumin ≥3 g/dL.

Peritoneal Dialysis

PD was conducted using "Dialy-Nate" disposable PD delivery systems (Utah Medical Products, Midvale, UT) using a previously described protocol (4). In summary, standard dialysate solutions of 1.5%, 2.5%, and 4.25% dextrose (Baxter Healthcare Corporation, Deerfield, IL) were connected to enclosed system and warmed before infusion. Dialysis was initiated with 10 mL/kg fill volume of 1.5% dialysate. Hourly cycles consisted of a 10-minute fill, 40-minute dwell, and 10-minute drain. Dextrose concentration was titrated hourly to target fluid removal goals.

Fluid Management Protocol

HF/HD and PD were managed jointly by intensivists and nephrologists. Our institution practices a strategy of aggressive fluid removal for all postcardiotomy ECMO patients with a general goal to have a net even fluid balance by time of ECMO weaning trials (typically 48–72 hours postsurgery). Fluid removal through HF/HD started as soon as hemodynamics permitted, and PD was added when volume of fluid removal through HF/HD was inadequate to achieve the stated fluid removal goal. Removal rates were adjusted based on assessment of intravascular volume status, using physical examination, urine output, and laboratory tests including blood urea nitrogen and serum creatinine. When decreased urine output (UOP) was felt to be the result of hypovolemia and organ hypoperfusion based on the previously mentioned criteria, fluid removal rate was decreased. A limiting factor for HF/HD was almost always excessive negative pressure within the venous return line of the ECMO circuit or hypotension, at which time the HF/HD removal rate was decreased or intravenous colloid was administered at the intensive care unit attending physician's discretion. Diuretics were rarely used because fluid removal goals using HF/HD and PD were typically met.

Statistical Analysis

Normally distributed data were summarized as mean with standard deviation, whereas nonnormal data were summarized using median with interquartile range (IQR). SPSS 19 (SPSS Inc., Chicago, IL) was used for all statistical tests. The percent FO at a particular postoperative time point was calculated as: [(total fluid in from time of postoperative admission {mL} – total fluid out from time of postoperative admission {mL})/preoperative weight (grams)] × 100.

RESULTS

Eight consecutive neonates received PD while on ECMO. Median age at operation was 7 days (range, 5–30 days). Mean preoperative weight was 3.1 ± .4 kg. Five of eight patients were males. Surgical procedures included five Norwood operations, one arterial switch operation, and two aortic arch reconstructions. Median CPB time was 204 minutes (IQR, 163–263); aortic cross-clamp time was 77 minutes (IQR, 66–91). Four patients were transitioned from CPB directly to ECMO; it was initiated in the remaining four patients at a median of 10 hours (IQR, 7–20) after arrival to the cardiovascular intensive care unit (CVICU). Median duration of ECMO was 155 hours (IQR, 118–215). Six patients survived ECMO, one of whom was transitioned to a ventricular assist device (VAD) from ECMO. Both patients who died on ECMO experienced multiorgan failure.

Net fluid balance (including data from the operating room) at ECMO initiation was median positive 360 mL/kg (IQR, 230–560; 36% FO). Seven of eight patients reached negative fluid balance before removal from ECMO (the remaining patient transitioned to VAD with net positive fluid balance). FO at onset of ECMO in patients successfully decannulated was 25% compared with 37% in others.

Median times to initiation of HF and PD were 5 hours (IQR, 1–11) and 16 hours (IQR, 11–59), respectively. Median output per day by modality was: HF/HD 132 mL/kg/day (IQR, 47–231), PD catheter 119 mL/kg/day (IQR, 70–166), chest tube 24 mL/kg/day (IQR, 11–73), and UOP 22 mL/kg/day (IQR, 7–39). Passive peritoneal drainage accounted for 21% of fluid removal through the PD catheter. Cumulative fluid removal by modality over time is illustrated in Figure 1. There were no incidents of PD malfunction, peritonitis, or hemoperitoneum.

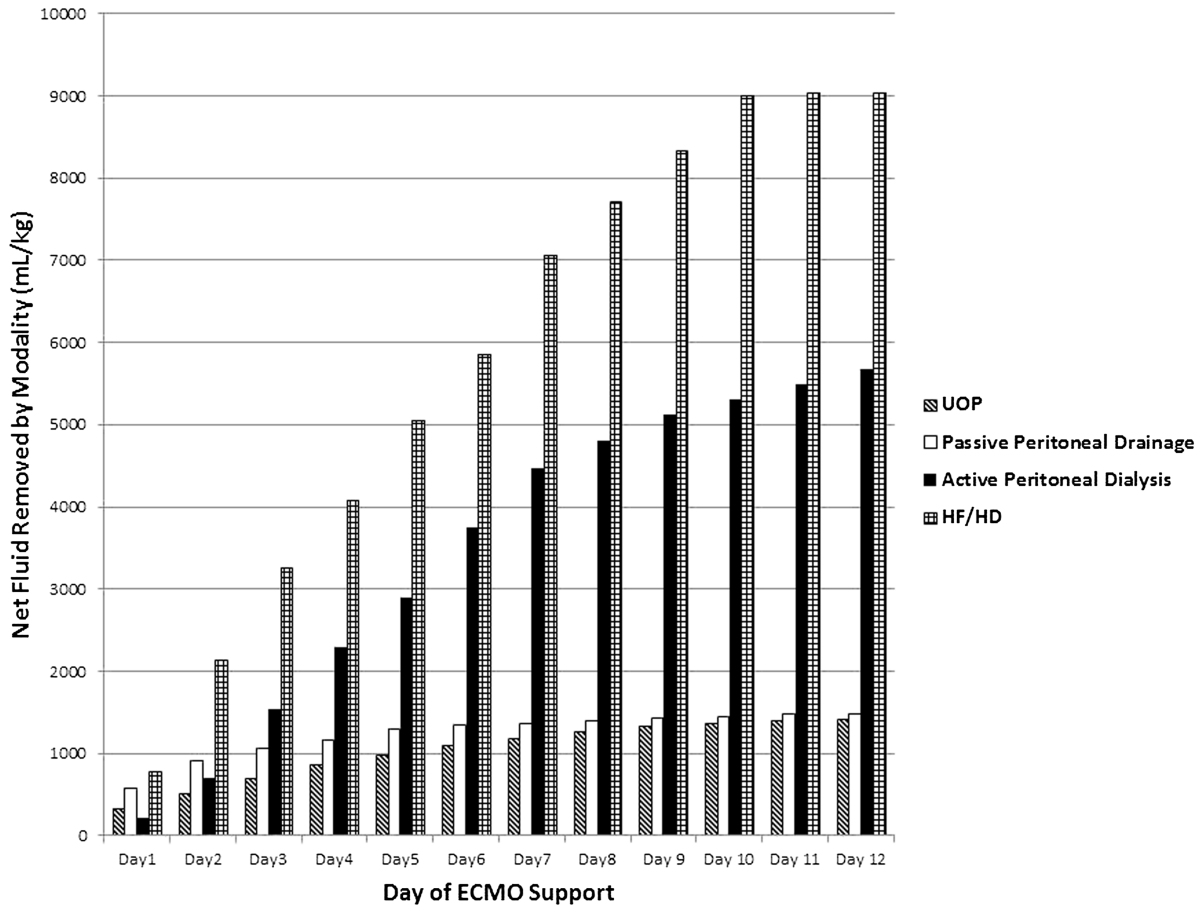

Figure 1. Cumulative fluid removed by modality for all patients. UOP, urine output; HF/HD, hemofiltration/hemodialysis.

Mean serum creatinine before and during ECMO was .6 ± .2 mg/dL and .6 ± .1 mg/dL, respectively. Mean creatinine after decannulation through time of intensive care unit discharge was .7 ± .4 mg/dL. For the first 72 hours after decannulation, median UOP was .58 mL/kg/h (IQR, .13–.80). Only one of the six patients successfully decannulated was anuric (the patient died 1 week after decannulation secondary to pulmonary hypertensive crisis). PD was continued in all patients after decannulation.

DISCUSSION

Given the association between FO and prolonged ECMO duration with morbidity and mortality, our institution has adopted an aggressive approach to fluid removal whereby we aim to quickly achieve preoperative weight to facilitate successful decannulation. Through gained experience, we learned we were often unable to achieve our goal with HF/HD alone, leading to the addition of PD to our fluid removal management. We describe our experience using PD for fluid removal in eight neonates on ECMO after cardiac surgery. As illustrated in Figure 1, PD accounted for 40% of total fluid removal in our cohort. It was well tolerated and combined with HF/HD, PD helped facilitate resolution of FO in the majority of patients by the time of decannulation.

The concept of FO as an important therapeutic target during cardiac ECMO has gained recognition as knowledge about its deleterious effects has grown. Several recent studies of FO in critically ill children have found an association with poor clinical outcomes (5–7). Judicious rather than liberal resuscitation and early fluid removal through renal replacement therapy have been proposed as management strategies addressing FO. All of our patients had severe FO at ECMO initiation as a result of resuscitation, deleterious effects of CPB, and systemic inflammation/capillary leak. Early initiation of aggressive fluid removal should benefit the neonate through reduction of organ edema and decreasing ECMO duration as long as critical organ perfusion is maintained. Further investigation into optimal methods of preventing and treating FO during ECMO is needed.

Although HF or HD through an inline hemoconcentrator is our primary source of fluid removal during ECMO, we often find our aggressive volume removal goals are limited by hypotension or excessive negative pressure within the venous side of the ECMO circuit. This is especially true early in the course, when high ECMO flow requirements necessitate generous intravascular volume to provide adequate preload to the ECMO circuit, complicated further by the reduction in intravascular volume caused by systemic inflammation and capillary leak seen in neonates. Therefore, volume administration or decreasing fluid removal rate is often necessary to maintain the intravascular volume needed for full ECMO flow and to minimize side effects related to excessive negative return line pressure such as hemolysis and air embolism. Fluid removal through PD may have less of an immediate effect on ECMO circuit preload because it involves fluid exchange in peritoneal membrane capillary beds in contrast to HF/HD, which removes fluid directly from the macrocirculation. This is supported by the fact that we were often able to add PD to HF/HD management, even when increasing fluid removal through a hemoconcentrator was previously not tolerated. Because the addition of PD rarely required cessation of HF/HD, the combination of the two modalities typically increased net fluid removal.

PD may have multiple benefits for neonates requiring cardiac ECMO, including ease of use, safety, and efficiency in fluid removal. An additional benefit of PD is continued availability after decannulation. The incidence of acute kidney injury (AKI) in this population exceeds 70% in some series and vascular access options for hemodialysis or CRRT are often limited (8,9). PD was used in all decannulated patients for continued fluid removal and metabolic AKI management. Similar to that seen in post-CPB neonates (4), PD use during ECMO was hemodynamically well tolerated and contributed to attainment of aggressive fluid removal goals. PD was never stopped as a result of clinical instability.

The removal of proinflammatory cytokines by PD (4,10) may be particularly important in this population because the heightened inflammatory state triggered by cardiac surgery and CPB may be sustained or even intensified as a result of ongoing exposure to foreign material within extracorporeal circuits. Inflammatory cytokines can have a direct effect on endothelial cell integrity and thus may worsen FO by potentiating interstitial edema (11). Although the clinical significance of cytokine removal has not been fully delineated, data from a recent study suggest that it may be associated with hemodynamic stability and other improved clinical outcomes (4).

Conclusions derived from this case review are limited by its retrospective data collection and limited sample size; thus, we cannot make definitive comment about the impact of PD on the morbidity and mortality associated with postcardiotomy ECMO in neonates. We acknowledge that a strategy of aggressive fluid removal through renal replacement therapy to enhance chances of early, successful decannulation has not been rigorously tested. Despite a general CVICU strategy of aggressive fluid removal in this patient population, lack of a stringent fluid removal protocol and strict criteria for PD initiation may have led to practice variation with regard to timing of initiation and titration of each modality. In addition, we acknowledge that failure to remove fluids to achieve our goals with HF/HD may have improved if different removal rates

were used, although these data suggest that the use of both PD and HF/HD may be the best option. As a result of the limitations of this study, it is not possible to determine if PD alone would have been superior to the described technique applied to this patient population. Although diuretics were not routinely used as a result of our practice patterns, their use for fluid removal on ECMO is described and warrants further investigation (12).

Based on the clinical experience gained during this case series, we have developed a protocol for neonatal post-cardiotomy ECMO FO management. Components include early initiation of PD after ECMO support if fluid removal goals are not being met with use of hemoconcentrator, CRRT device, and/or diuretics (within 24 hours). Our surgeons will place a PD catheter if one was not placed during the primary procedure. Titration of fluid removal will be achieved by continuation of PD in the background with hourly manipulations of fluid removal rate through HF/HD to achieve fluid balance goals. Overall goals include achievement of preoperative weight as quickly as tolerated to minimize the child's exposure to ECMO while ensuring continued organ perfusion as followed by surrogates like UOP. Further prospective studies are greatly needed to determine optimal fluid removal modalities, timing, and goals that will improve outcomes in this population.

CONCLUSION

FO in neonates requiring ECMO is associated with organ dysfunction and may delay successful decannulation, increasing the likelihood of ECMO morbidity and mortality. Use of PD for fluid removal during neonatal ECMO was well tolerated and effective, helping achieve near euvolemia before decannulation. Concomitant use of PD and HF/HD may remove more fluid than can be achieved through either modality in isolation. Prospective evaluation of PD and our FO management protocol is needed to determine if it can decrease duration of ECMO support.

REFERENCES

1. Heiss K, Pettit B, Hirschl R, et al. Renal insufficiency and volume overload in neonatal ECMO managed by continuous ultrafiltration. ASAIO Trans. 1987;33:557–60.
2. Kelly R, Phillips J, Foglia R, et al. Pulmonary edema and fluid mobilization as determinants of the duration of ECMO support. J Pediatr Surg. 1991;26:1016–22.
3. Swaniker F, Kolla S, Moler F, et al. Extracorporeal life support outcome for 128 pediatric patients with respiratory failure. J Pediatr Surg. 2000;35:197–202.
4. Sasser W, Dabal R, Askenazi D, et al. Prophylactic peritoneal dialysis following cardiopulmonary bypass in children is associated with decreased inflammation and improved clinical outcomes. Congenit Heart Dis. 2014;9:106–15.
5. Hazle M, Gajarski R, Yu S, et al. Fluid overload in infants following congenital heart surgery. Pediatr Crit Care Med. 2013;14:44–9.
6. Selewski D, Cornell T, Blatt N, et al. Fluid overload and fluid removal in pediatric patients on extracorporeal membrane oxygenation requiring continuous renal replacement therapy. Crit Care Med. 2012;40:2694–9.
7. Sutherland S, Zappitelli M, Alexander S, et al. Fluid overload and mortality in children receiving continuous renal replacement therapy: The prospective pediatric continuous renal replacement therapy registry. Am J Kidney Dis. 2010;55:316–25.
8. Smith A, Hardison D, Worden C, et al. Acute renal failure during extracorporeal support in the pediatric cardiac patient. ASAIO J. 2009;55:412–6.
9. El Masri K, Jackson K, Borasino S, et al. Successful continuous renal replacement therapy using two single-lumen catheters in neonates and infants with cardiac disease. Pediatr Nephrol. 2013;12:2383–7.
10. Dittrich S, Aktuerk D, Seitz S, et al. Effects of ultrafiltration and peritoneal dialysis on proinflammatory cytokines during cardiopulmonary bypass surgery in newborns and infants. Eur J Cardiothorac Surg. 2004;25:935–40.
11. Boyle E, Pohlman T, Johnson M, et al. Endothelial cell injury in cardiovascular surgery: The systemic inflammatory response. Ann Thorac Surg. 1997;63:277–84.
12. van der Vorst M, Wildschut E, Houmes R, et al. Evaluation of furosemide regimens in neonates treated with extracorporeal membrane oxygenation. Crit Care. 2006;10:R168.