Pediatr Nephrol (2016) 31:2013–2015
DOI 10.1007/s00467-016-3423-4

EDITORIAL COMMENTARY

Neonatal extracorporeal renal replacement therapy—a routine renal support modality?

Leyat Tal[1] · Joseph R. Angelo[1] · Ayse Akcan-Arikan[1,2]

Received: 28 April 2016 / Accepted: 13 May 2016 / Published online: 6 June 2016

Abstract Peritoneal dialysis (PD) is generally considered the preferred extracorporeal therapy for neonates with acute kidney injury (AKI). However, there are situations when PD is not suitable, such as in patients with previous abdominal surgery, hyperammonemia and significant ascites or anasarca. Additionally, with a need to start PD soon after catheter placement, there is increased risk of PD catheter leak and infection. Extracorporeal continuous renal replacement therapy (CRRT) is challenging in severely ill neonates as it requires obtaining adequately sized central venous access to accommodate adequate blood flow rates and also adaptation of a CRRT machine meant for older children and adults. In addition, ultrafiltration often cannot be set in sufficiently small increments to be suitable for neonates. Although CRRT practices can be modified to fit the needs of infants and neonates, there is a need for a device designed specifically for this population. Until that becomes available, providing the highest level of care for neonates with AKI is dependent on the shared experiences of members of the pediatric nephrology community.

Keywords Extracorporeal continuous renal replacement therapy · Acute kidney injury · Neonates · nRIFLE · Continuous venovenous hemodiafiltration

✉ Ayse Akcan-Arikan
aysea@bcm.edu

1 Renal Section, Department of Pediatrics, Baylor College of Medicine, Houston, TX, USA

2 Section of Pediatric Critical Care Medicine, Department of Pediatrics, Baylor College of Medicine, 6621 Fannin Street, Houston, TX 77030, USA

In a recent article in *Pediatric Nephrology,* Lee and Cho review their continuous renal replacement therapy (CRRT) experience in 34 neonates with acute kidney injury (AKI) [1]. Although single center and retrospective, there are several noteworthy characteristics of this study. The authors standardize neonatal AKI using the neonatal RIFLE (nRIFLE) criteria to define and stratify severity of AKI. Of the 34 neonates included in the study, 44 % were born preterm (25–36 weeks), with 60 % of these preterm infants being either extremely or very low birth weight. All patients had AKI, and 24 patients met the nRIFLE class F (Failure) criterion. Survival was 50 %. Continuous venovenous hemodiafiltration (CVVHDF) with Prisma or Prismaflex (Gambro/Baxter Int., Lund, Sweden) dialysis machines and M10 (50 ml) or HF20 (55 ml) filters was used for all CRRT treatments. Access was via internal jugular 6.5-French (Fr) hemodialysis catheters. Mean filter life was 51.1 h. Similar to other studies in pediatric CRRT patients [2–4, 5], fluid overload (FO), defined by the percentage weight gain over weight at admission to the neonatal intensive care unit (NICU), was independently associated with mortality [6]. Neonatal studies have reported an FO of>15–20 % to be associated with poor outcome defined as need for CRRT, prolonged NICU stay, time to extubation or death within 30 days postcardiothoracic surgery [7, 8]. Interestingly, this study by Lee and Cho [1] reports a much higher FO cut-off of 30 % being associated with poor outcomes, including 100 % mortality for patients reaching an FO of >30 %. The authors propose higher body surface area, calorie consumption and insensible water loss in neonates as a possible explanation. They address this issue by using actual weight-based calculations to determine FO, as the higher insensible losses in NICU patients make the more commonly used (total fluid in − total fluid out)/admission weight formula potentially less reliable. In addition, as neonates have true weight gain over time, the comparison of fluid balance to NICU admission weight might overestimate overall fluid accumulation. Serial daily weights would have been more useful, but unfortunately these data are not available. Similar to data [9, 10] reported in adults, oliguria at both the start and at the end of CRRT was a poor prognostic factor and was associated with mortality.

CRRT was initiated without anticoagulation and heparin was started only if the initial CRRT filter life was <12 h. Despite this, mean CRRT filter life was quite good in this challenging patient population; one could possibly conceive that initiating anticoagulation routinely at the start of CRRT may have prolonged filter life even more.

This study brings to light a larger issue: we have a unique subset of smaller and younger patients that require renal replacement therapy, but lack the ideal tools to manage them. CRRT machines available for use are currently approved by the Federal Drug Administration for patients weighing >25 kg; however, these are frequently used off label for patients weighing <20 kg. This presents several challenges to provide CRRT to the neonate, such as frequent blood exposure with blood prime due to the large extracorporeal volume, high blood flow rate and smaller vascular access that has been shown to be associated with increased risk of filter clotting [2]. Westrope et al. described their experience using <7-Fr dialysis catheters in neonates using FH22 and HF07 filters with pediatric lines [(extracorporeal volume (ECV) 78 ml and 119 ml, respectively)] which was associated with a median CRRT circuit survival of 40 h [11]. The present study by Lee and Cho [1] reports longer filter life even in the absence of anticoagulation.

Although there are CRRT filters with small ECV, such as the one used in the study of Lee and Cho [1] these are often AN 69 filters that have been associated with bradykinin release syndrome leading to hemodynamic instability at the initiation of CRRT. Widespread availability of the polyarylethersulfone filters, such as HF20, could improve the safety profile in hemodynamically fragile neonates.

Several new machines are currently in development or being modified to provide small extracorporeal sizes that address the needs of the neonate and small infants with AKI. The Miniaturized Cardio-Renal Pediatric Dialysis Emergency Machine (CARPEDIEM) developed by Ronco et al. [12] has a reduced ECV of 27 ml and a built-in syringe pump for heparin infusion with sensitive built-in scales for infusion and effluent bags as well as ultrafiltration; the ultrafiltration accuracy is consistently within 1 g/h and fluid pump imprecision is ±7.5 %. The authors recently described their first successful trial on a 3-day-old neonate with 63 % FO using a 4-Fr 5-cm dual lumen hemodialysis catheter placed in the femoral vein [13].

The Newcastle infant dialysis and ultrafiltration system (NIDUS) has been designed to provide CVVHD to patients weighing between 800 g and 8 kg [14]. Coulthard et al. [14] described their experience dialyzing nine babies weighing between 1.8 and 5.9 kg using a single lumen vascular access without the need for blood priming (ECV <10 ml). Patients on NIDUS were found to have consistently higher clearances of urea, creatinine and phosphate compared to peritoneal dialysis with an ultrafiltration precision of <0.25 %.

The Aquadex FlexFlow system (Gambro), which was designed for the purpose of ultrafiltration in adults with congestive heart failure refactory to diuretic therapy, has been adapted for renal replacement therapy by Askenazi et al. [15]. Reported complications were related to hypothermia and anticoagulation with heparin; however, six of 12 infants lived to discharge. Although the ECV of 33 ml makes it an attractive option, there is no pump to provide countercurrent dialysis, so only CVVHF can be done by prefilter replacement fluid and heparin infusions external to the device that do not communicate directly with the Aquadex circuit. The blood pump accuracy is +15–20 % and the ultrafiltration accuracy is ±10 %, ranges which can have huge implications for smaller patients.

There remains a great need for precise CRRT machines with small ECVs that can provide adequate and safe dialysis to neonates. Although the aforementioned CRRT machines are promising, they are not yet readily available clinically, which necessiates the use of what is available, and not necessarily what is ideal, to treat this unique group of patients. As technology continues to advance, CRRT equipment designed specifically for neonates is likely to become more accessible to those providing care to critically ill newborns. The development and implementation of this powerful tool would advance the field of neonatal AKI and stands to significantly influence outcomes for one of our most vulnerable patient populations. As with most innovative medical devices, the clinical application of these emerging neonatal CRRT circuits to an individual patient should involve multidisciplinary discussions which consider the risks and benefits of the therapy, treatment goals and endpoints, comorbidities, long-term survival prognosis and respect for parental views regarding the quality of life they desire for their child. Dialytic treatment remains a palliation, not cure, to end-stage renal disease (ESRD). Survival of more neonates with AKI and resultant chronic kidney disease or ESRD could lead to a change in the topography of the pediatric ESRD population with emerging long-term comorbidities and changing demands on resources.

Acknowledgments Administration assistance was provided by Theresa Leftely (email: tleftel@texaschildrens.org; office telephone: +1-832-8266291.

Compliance with ethical standards

Conflict of interest disclosure AAA has provided consultancy to Baxter Inc in the calendar year of 2015. The other authors have no conflicts of interest.

References

1. Lee ST, Cho H (2016) Fluid overload and outcomes in neonates receiving continuous renal replacement therapy. Pediatr Nephrol. doi:10.1007/s00467-016-3363-z

2. Askenazi DJ, Goldstein SL, Koralkar R, Fortenberry J, Baum M, Hackbarth R, Blowey D, Bunchman TE, Brophy PD, Symons J, Chua A, Flores F, Somers MJ (2013) Continuous renal replacement therapy for children ≤10 kg: a report from the prospective pediatric continuous renal replacement therapy registry. J Pediatr 162:587–592
3. Foland JA, Fortenberry JD, Warshaw BL, Pettignano R, Merritt RK, Heard ML, Rogers K, Reid C, Tanner AJ, Easley KA (2004) Fluid overload before continuous hemofiltration and survival in critically ill children: a retrospective analysis. Crit Care Med 32:1771–1776
4. Sutherland SM, Zappitelli M, Alexander SR, Chua AN, Brophy PD, Bunchman TE, Hackbarth R, Somers MJ, Baum M, Symons JM, Flores FX, Benfield M, Askenazi D, Chand D, Fortenberry JD, Mahan JD, McBryde K, Blowey D, Goldstein SL (2010) Fluid overload and mortality in children receiving continuous renal replacement therapy: the prospective pediatric continuous renal replacement therapy registry. Am J Kidney Dis 55:316–325
5. Hayes LW, Oster RA, Tofil NM, Tolwani AJ (2009) Outcomes of critically ill children requiring continuous renal replacement therapy. J Crit Care 24:394–400
6. Goldstein SL, Currier H, Cd G, Cosio CC, Brewer ED, Sachdeva R (2001) Outcome in children receiving continuous venovenous hemofiltration. Pediatrics 107:1309–1312
7. Hazle MA, Gajarski RJ, Yu S, Donohue J, Blatt NB (2013) Fluid overload in infants following congenital heart surgery. Pediatr Crit Care Med 14:44–49
8. Piggott KD, Soni M, Decampli WM, Ramirez JA, Holbein D, Fakioglu H, Blanco CJ, Pourmoghadam KK (2015) Acute Kidney injury and fluid overload in neonates following surgery for congenital heart disease. World J Pediatr Congenit Heart Surg 6:401–406
9. Kellum JA, Sileanu FE, Murugan R, Lucko N, Shaw AD, Clermont G (2015) Classifying AKI by urine output versus serum creatinine level. J Am Soc Nephrol 26:2231–2238
10. Prowle JR, Liu Y-L, Licari E, Bagshaw SM, Egi M, Haase M, Haase-Fielitz A, Kellum JA, Cruz D, Ronco C, Tsutsui K, Uchino S, Bellomo R (2011) Oliguria as predictive biomarker of acute kidney injury in critically ill patients. Crit Care 15:R172
11. Westrope C, Morris KP, Kee CY, Farley M, Fleming S, Morrison G (2016) Experience of circuit survival in extracorporeal continuous renal replacement therapy using small-calibre venous cannulae. Pediatr Crit Care Med. doi:10.1097/PCC.0000000000000677
12. Ronco C, Garzotto F, Ricci Z (2012) CA.R.PE.DI.E.M. (Cardio-Renal Pediatric Dialysis Emergency Machine): evolution of continuous renal replacement therapies in infants. A personal journey. Pediatr Nephrol 27:1203–1211
13. Ronco C, Garzotto F, Brendolan A, Zanella M, Bellettato M, Vedovato S, Chiarenza F, Ricci Z, Goldstein SL (2014) Continuous renal replacement therapy in neonates and small infants: development and first-in-human use of a miniaturised machine (CARPEDIEM). Lancet 383:1807–1813
14. Coulthard MG, Crosier J, Griffiths C, Smith J, Drinnan M, Whitaker M, Beckwith R, Matthews JN, Flecknell P, Lambert HJ (2014) Haemodialysing babies weighing <8 kg with the Newcastle infant dialysis and ultrafiltration system (NIDUS): comparison with peritoneal and conventional haemodialysis. Pediatr Nephrol 29:1873–1881
15. Askenazi D, Ingram D, White S, Cramer M, Borasino S, Coghill C, Dill L, Tenney F, Feig D, Fathallah-Shaykh S (2016) Smaller circuits for smaller patients: improving renal support therapy with Aquadex™. Pediatr Nephrol 31:853–860