Technical Considerations for Renal Replacement Therapy in Children

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Summary: Provision of renal replacement therapy to the critically ill child entails numerous technical and prescriptive considerations because pediatric nephrologists and intensive care physicians are faced with patients ranging in size from 2-kg neonates to 200-kg adolescents or young adults. The current article focuses on the common technical and prescriptive issues that inform the care of children with acute kidney injury.
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For the patient conditions in the clinical cases presented by Symons and Picca in this issue,[1] local practices and resources will drive many of the technical therapeutic decisions to provide renal replacement therapy. The aims of this article are to highlight the practical and technical considerations inherent in providing renal replacement therapy (RRT) to children in terms of access, prescription, anticoagulation, and solution/dialysate bath selection. Each case is discussed independently with attention directed at key considerations. We have not advocated for one manufacturer or product over another, and by no means intend the prescriptions derived in this article to be considered definitive.

SEPSIS/MULTI-ORGAN DYSFUNCTION SYNDROME: CONTINUOUS RRT

Access

A functional vascular access is the most important technical component determining successful provision of continuous renal replacement therapy (CRRT). A wide variety of acute vascular catheters are available for the pediatric population.[2,3] A general acute catheter to patient size guideline is depicted in Table 1. Acute, uncuffed vascular access placement can be performed at the bedside by pediatric nephrologists, critical care physicians, or surgeons, semipermanent tunneled catheters should be placed by surgeons or interventional radiologists in an operating room. Catheter placement for CRRT may predispose blood vessels to blood vessel sclerosis or thrombosis and may be complicated by air emboli or hemorrhage. Future permanent access in the form of an arteriovenous graft or fistula for patients who develop chronic kidney disease may be compromised if acute access is placed in a subclavian vein. Clinicians must therefore consider the potential long-term vascular needs of patients who may be expected to develop chronic kidney disease. In terms of our septic patient,[1] a 10F to 14F double-lumen catheter placed in the internal jugular vein or femoral would allow optimal access while preserving subclavian vessels.

CRRT Prescription

Convective CRRT modality therapies may confer a survival advantage in patients with sepsis, although no randomized trial exists to compare the impact of diffusive versus convective CRRT modalities on survival. Functionally, convective therapy may be limited by an excessive filtration fraction, which is defined by the following equation:

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Table 1. Catheter and Patient Size Options

Patient Size	Catheter Size and Source	Site of Insertion
Neonate	Single-lumen 5F (Cook Medical, Bloomington, IN)	Femoral artery or vein
	Dual-lumen 7.0F (Cook/Medcomp, Harleysville, PA)	Internal/external jugular, subclavian, or femoral vein
3-6 kg	Dual-lumen 7.0F (Cook/Medcomp)	Internal/external jugular, subclavian, or femoral vein
	Triple-lumen 7.0F (Medcomp; Arrow, Reading, PA)	Internal/external jugular, subclavian, or femoral vein
6-30 kg	Dual-lumen 8.0F (Kendall, Mansfield, MA; Arrow)	Internal/external jugular, subclavian, or femoral vein
>15 kg	Dual-lumen 9.0F (Medcomp)	Internal/external jugular, subclavian, or femoral vein
>30 kg	Dual-lumen 10.0F (Arrow, Kendall)	Internal/external jugular, subclavian, or femoral vein
>30 kg	Triple-lumen 12F (Arrow, Kendall)	Internal/external jugular, subclavian, or femoral vein

$$\text{Filtration fraction} = \frac{\text{convective UF rate (mL/h)} + \text{fluid removal rate (mL/h)}}{\text{blood pump flow rate (mL/min)} \times 60\ \text{min/h}} \times 100\%$$

Higher filtration fractions (≥20%) may lead to increased blood viscosity in the hemofilter, which predisposes the filter to early clotting, thereby interrupting the continuous nature of CRRT delivery.[4] Data from the prospective pediatric CRRT Registry support this concern because circuits performing continuous venovenous hemofiltration or continuous venovenous hemofiltration and diafiltration showed a statistically shorter functional lifespan compared with circuits performing solely diffusive-based continuous venovenous hemodialysis.[1] Thus, the clinician must balance the theoretical therapeutic advantage of convection in sepsis with a shorter filter lifespan and more frequent therapy interruption.

An initial blood pump rate should target 3 to 5 mL/kg/min, which corresponds to 200 mL/min.[5] A reasonable approach to CRRT dose (ie, small solute clearance) would be to provide this 50-kg child with roughly 35 to 50 mL/kg/h (roughly 2,000-3,000 per 1.73 m^2/h), which yields a targeted clearance of 2 to 2.5 L/h. In addition, because this patient is severely fluid overloaded, initial net target ultrafiltration (UF) rates could aim for 1% to 3% of the patient's blood volume per hour (35-105 mL/h). If we used solely convective clearance, the resulting filtration fraction would be as follows:

$$\frac{2{,}000\ \text{mL/h} + 35\ \text{mL/}}{200\ \text{mL/min} \times 60\ \text{min/h}} \times 100\% = 17\%$$

Fluid Composition

Recently, the Food and Drug Administration approved bicarbonate-based solutions for both diffusive and convective clearance.[6] Bicarbonate-based solutions are available in multiple formulations, with and without calcium added; commercially available solutions are listed in Table 2. Extemporaneously pharmacy-based solutions carry a risk for formulation error and attendant adverse events.[6] Thus, a strict quality-assurance program should be in place to guarantee the composition of pharmacy-prepared CRRT solutions.

Because patients with sepsis and multiorgan function disorder (MODS) often have a metabolic acidosis, the initial solution should contain the highest bicarbonate concentration available in the brand selected by the program. Because citrate regional circuit anticoagulation has become more widely used in pediatric CRRT and is associated with fewer adverse events when compared with heparin,[7] a calci-

Table 2. Commercially Available CRRT Solutions

		PrismaSate (D) PrismaSol (FRF)				
Electrolyte	**Normocarb**	**BK0/3.5**	**BKK2/0**	**B25GK4/0**	**ACCUSOL**	**Duosol**
Na, mEq/L	140	140	140	140	140	140
Ca, mEq/L	0	3.5	0	0	3.5	3
K, mEq/L	0	0	2	4	0-4	0-4
Mg, mEq/L	1.5	1	1	120.5	1.0-1.5	
Cl, mEq/L	107	109.5	108	120.53	109.5-116.3	109-113
Phos, mmol/L	0	0	0	0	0	0
L-lactate, mEq/L	0	3	3	3	0	0
Bicarb, mEq/L	25/35	23/32	23/32	22	30-35	35
Glucose, mg/dL	0	0	110	110	0-100	

Normocarb, Dialysis Solutions, Incorporated, Whitby, Ontario, Canada; PrismaSate and PrismaSol, Gambro Renal Products, Lakewood, CO; Accusol, Baxter, Inc, McGaw Park, IL; Duosol, B Braun Inc, Bethlehem, PA.
D, dialysis fluid; FRF, filter replacement fluid; Phos, phosphate; Bicarb, bicarbonate.

um-free hemofiltration solution should be chosen if citrate anticoagulation is used.

Anticoagulation

Standardized protocols have been well established for both heparin and regional citrate anticoagulation. Heparin and citrate-based anticoagulation protocols have been shown to confer equitable filter survival in pediatric CRRT, and the use of either is clearly supported over schemes without anticoagulation.[6] The main advantage of citrate anticoagulation is the prevention of systemic pharmacologic anticoagulation of the patient, which can be an issue in patients with multiorgan failure and sepsis. Calcium is a requisite cofactor in both the intrinsic and extrinsic coagulation cascades. Citrate functions by binding free calcium, thereby inhibiting coagulation in both the intrinsic and extrinsic coagulation pathways. The most frequently studied pediatric citrate protocol[6] uses anticoagulant dextrose solution A (ACD-A; Baxter Healthcare, McGaw Park, IL), prescribed based on the following blood flow rate: ACD rate (mL/h) = blood pump rate (mL/min × min/hour) × 1.5.

The ACD-A is infused via a stopcock at the catheter-CRRT circuit connection leading to the CRRT machine. Because our prescribed blood pump flow is 200 mL/min, the resulting ACD-A rate would be 300 mL/h. The second aspect of the citrate protocol provides prevention of citrate-induced systemic hypocalcemia by providing a calcium chloride continuous infusion (8 g calcium chloride/1 L normal saline) to the patient via a central line. The calcium chloride rate also is based on the following blood pump rate: calcium chloride (mL/h) = blood pump rate (mL/min × min/h) × 0.6.

Thus, the calcium chloride rate for our patient would be 120 mL/h. It is important to remember that pumps independent of the CRRT machine infuse both ACD-A and calcium chloride, so the fluid removal rate must account for these additional infusions. As a result, our filtration fraction will now increase to 20.4% ([2,000 + 35 + 300 + 120 mL/h]/[200 mL/min × 60 min/h]), which is still acceptable.

The goals of regional citrate anticoagulation are to maintain the circuit-ionized calcium between 0.2 and 0.4 mmol/L and the patient's systemic ionized calcium in the normal physiologic range (1.1-1.3 mmol/L). The circuit-ionized calcium concentration is managed by adjustment of the citrate rate, whereas the patient's systemic ionized calcium concentration is managed by adjustment of the calcium chloride rate.

INFANTS WITH INBORN ERRORS OF METABOLISM OR AFTER CONGENITAL HEART SURGERY

Similar technical considerations apply to all infants requiring extracorporeal dialytic thera-

pies. The technical considerations for providing acute peritoneal dialysis are addressed in detail in their respective case discussion articles in this issue of *Seminars in Nephrology*.

Access

A double-lumen, 7F, 10-cm catheter should be placed in the internal jugular or the subclavian or femoral vein. Umbilical vessels and single-lumen 5F catheters should be avoided if possible because they may not provide adequate and reliable flow.[1] This is especially important because adequate outcomes in neonates with inborn errors of metabolism correlate with the duration and level of hyperammonemia. Careful consideration of dialysate bath/CRRT solution components is paramount in the treatment of children/neonates with inborn errors of metabolism because the child being treated may not have acute renal failure. In such circumstances, the dialysis bath/CRRT solution will need to be supplemented with potassium and phosphorus to prevent depletion and electrolyte derangement.

Hemodialysis

If hemodialysis is the initial modality chosen, the dialysate bath should include a standard calcium concentration of 2.5 mmol/L, a potassium concentration of 4 to 5 mEq/L, and a physiologic phosphorous concentration between 4.5 and 5.5 mg/dL. If phosphorus supplementation is not available, an intravenous infusion of phosphate may be initiated. The blood pump flow rate should be prescribed at 8 to 10 mL/kg/min (30-35 mL/min), with a dialysate flow rate of 500 mL/min and a net ultrafiltration would be zero. Hemodialysis membranes can have an obligatory ultrafiltration of 100 mL/h, so the infant warmer may need to be placed on a scale to guide a saline infusion provided to the patient to offset this ultrafiltration and keep the patient's fluid balance neutral. The temperature of the hemodialysis should be turned up to 38°C or 39°C to offset temperature loss from the extracorporeal circuit. Heparinization would be in order for anticoagulation during this period of time.

CRRT

CRRT can be used initially or immediately after intermittent hemodialysis, the choice usually is dependent on the ammonia levels and the patient circumstance. The CRRT circuit blood flow rate should be targeted at 8 to 10 mL/kg/min (30-35 mL/min), and CRRT can be prescribed either as continuous venovenous hemodialysis or continuous venovenous hemodialysis, with a bicarbonate-based replacement or dialysis solution supplemented with potassium and phosphorus. The circuit extracorporeal volume likely will be greater than 15% of an infant's blood volume, so a blood prime of the circuit may be required. The bradykinin release syndrome often is observed with blood priming of AN-69 CRRT circuit membranes, and is manifested by acute hypotension with CRRT initiation.[7] The bradykinin release syndrome is potentiated by the acidotic nature of the blood prime; a number of maneuvers have been reported to normalize the pH of the blood prime or bypass the blood prime of the AN-69 circuit. Another strategy involves avoidance of the AN-69 membrane in nonsepsis situations because the main advantage of the AN-69 membrane is in superior cytokine removal characteristics.

As opposed to intermittent hemodialysis, CRRT clearance of small solutes is determined by the replacement/dialysis fluid rate; a rate of 4,000 to 8,000 mL/1.73 m^2/h will lead to rapid clearance of ammonia. The circuit should receive regional anticoagulation using the protocol described earlier for the patient with sepsis. However, because hepatic metabolism of citrate may not be mature in neonates, the ACD-A rate should be started at 50% of the rate used in patients older than 1 year of age. Thus, if the blood flow rate is 30 mL/min, the ACD-A rate should be initiated at 50% of 45 mL/h, or 22 mL/h. Circuit and patient systemic ionized calcium levels should be sent hourly to allow for frequent adjustment until the desired ranges are achieved (circuit, 0.2-0.4 mmol/L; systemic, 1.1-1.3 mmol/L) and stable.

STEM CELL TRANSPLANT RECIPIENT

The technical considerations for this patient are similar for the patient with MODS and sepsis

described earlier. An in-depth discussion of renal replacement therapy timing, modality choice, and dose is provided in the article by DiCarlo and Alexander found in this issue (p. 481).

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