CHAPTER 206

Renal Replacement Therapy for the Critically Ill Infant

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Objectives

This chapter will:

1. Explain special issues related to use of renal replacement therapy for infants.
2. Identify specific risks and complications of renal replacement therapy in infants.
3. Highlight advantages and disadvantages of different renal replacement modalities for the critically ill infant.

The expanding role of renal replacement therapy (RRT) in the care of critically ill children extends to the smallest pediatric patients. Infants with oliguria, volume overload, multi-organ dysfunction, and metabolic disorders can be treated successfully with techniques that have been established in larger children and adults. RRT for infants presents special challenges. Data regarding dialysis support for infants in the intensive care unit (ICU) are limited and recommendations often are based on clinical experience. Overall, the need is relatively uncommon, but dialysis is potentially lifesaving when circumstances warrant. Careful preparation, communication, and coordination between various hospital specialists, including nephrologists, neonatologists, surgeons, nurses, nutritionists, and pharmacists, can maximize the likelihood of success for these critically ill infants.

RENAL FAILURE AND OTHER INDICATIONS FOR RENAL REPLACEMENT THERAPY

Indications for RRT in the critically ill infant parallel those seen in older children and adults (Box 206.1). Acute kidney injury (AKI) is a common complication seen in the neonatal period and has been reviewed recently.[1,2] Causes for AKI in the newborn period can include urinary obstruction, so-called prerenal conditions with diminished perfusion, and complications of intrinsic renal diseases including congenital abnormalities. A majority of infants with AKI experience recovery without the need for therapy beyond supportive care. When conservative measures fail, RRT can be considered for the newborn with renal dysfunction. Renal replacement in this setting provides the parallel needs of metabolic control and fluid balance, identical to that required by an older child or adult with AKI. Rarely, an infant patient will require RRT for chronic kidney disease. Indications are similar to those for older children or adults with the additional need to begin treatment in the setting of suboptimal growth or inability to provide sufficient nutrition to the infant because of fluid limitations. Acute intoxication, either with endogenous toxins as seen with inborn errors of metabolism or exogenous toxins resulting from iatrogenic events, represents another clinical scenario that may require treatment by dialysis. Hemodialysis can remove toxins rapidly and is often the preferred therapy for severe intoxication in older children and adults. For infants, hemodialysis is similarly more efficient than peritoneal dialysis in this setting and should be considered for the treatment of intoxication.[3,4]

The concept of "renal support" has been applied to older patients[5] to describe the use of renal replacement therapies before the development of absolute indications such as fluid overload or uremia. Fluid restriction as part of conservative management for a patient with mild renal dysfunction potentially may lead to reduced nutrition. RRT can reduce the total fluid burden related to daily fluid input and also permit maximal medical support. The infant with renal dysfunction can benefit from this approach as well; RRT should be considered early in the course of AKI.

BOX 206.1

Potential Indications for Renal Replacement Therapy in Infants

Volume overload or metabolic/electrolyte abnormalities related to decreased kidney function
- Diminished effective circulating volume ("prerenal" states):
  - Volume depletion
  - Hemorrhage/blood loss
  - Fluid redistribution ("third-space")
  - Diminished cardiac output (e.g., congenital heart disease)
  - Hypotension/shock (e.g., sepsis syndrome)
- Urinary obstruction ("postrenal" states):
  - Bladder outlet obstruction (e.g., posterior urethral valves)
  - Bladder dysfunction (e.g., neurogenic bladder)
  - Obstructing tumor or mass
  - Congenital obstruction of ureters
  - Solitary functioning kidney with obstruction
- Intrinsic renal disease or injury ("intrarenal" states)
  - Ischemic injury
  - Tubular toxicity (e.g., drugs, myoglobin)
  - Vascular thrombosis
  - Hemolytic uremic syndrome
  - Congenital renal diseases (e.g., renal dysplasia)
  - Multi-organ dysfunction

Intoxication
- Endogenous intoxication (e.g., hyperammonemia of the newborn)
- Exogenous intoxication (e.g., drug intoxication)

Renal support
- Suboptimal kidney function limiting delivery of nutrition and medical therapy

PERITONEAL DIALYSIS

Despite technologic improvements that have opened the possibility of use of all modalities of RRT in the critically ill infant, peritoneal dialysis (PD) remains an effective renal replacement modality and may represent a superior alternative for infants.[6] Even the most experienced centers may have difficulty achieving vascular access in infants, limiting options for the use of hemodialysis and continuous RRT. Children with vascular abnormalities, certain types of cardiac disease, or hemodynamic issues may be suboptimal candidates for extracorporeal perfusion. In such circumstances PD can be the best choice for RRT.

Indications

PD is an effective method for achieving metabolic control and fluid balance in the infant with renal failure. The technique is relatively straightforward, and protocols for therapy in the newborn are well established. PD often is considered the preferred method of management for infants who have undergone cardiac surgery and can be a useful adjunct to maintaining fluid balance in those patients who have low cardiac output.[7–9]

Technique

To perform PD, a dialysis catheter must be placed in the infant's abdomen. These catheters come in various sizes; smaller catheters are available for use in the newborn and small infant. Either a surgically placed catheter or percutaneously inserted temporary catheters may be used. Some evidence suggests fewer complications with surgically placed catheters.[10] Local practice often determines who will insert the catheters when they are needed; the procedure requires expertise to ensure proper function of the catheter. Peritoneal dialysate comes in standardized concentrations that are available commercially. These formulations usually are acceptable for use in the critically ill infant. In the United States, peritoneal dialysate is available in standard dextrose concentrations of 1.5%, 2.5%, and 4.25%, with lactate used as the base; similar dextrose concentrations are available elsewhere.

Lactate absorption can lead to complications in critically ill infants. The hospital pharmacy may have to specially prepare dialysate with bicarbonate, although in our experience standard lactate-based dialysate is usually acceptable. Outside of the United States bicarbonate-based peritoneal dialysate is available commercially. Peritoneal dialysate should be warmed to body temperature before use in infants to prevent hypotension associated with cold dialysate infusion. Initial exchanges with a newly placed PD catheter should use relatively lower volumes of 10 to 20 mL/kg (200–500 mL/m^2) of dialysate to limit the chance of leak from the catheter insertion site. Low-volume PD can be an effective method in the infant, successfully achieving ultrafiltration goals.[11] Exchanges of dialysate can be performed throughout the day in the ICU, thereby increasing time on dialysis compared with that typical when PD is performed in the ambulatory setting. This more frequent exchange helps achieve metabolic balance even with the use of lower dialysate volume. For those patients who require greater mass transfer after successful initiation, fill volumes may increase gradually to 1000 to 1100 mL/m^2. Shorter dwell times often are used for infants in the critical care setting. Although longer dwell periods provide more time for equilibration of dialysate and for ultrafiltration, shorter dwell periods may permit more dialysis and ultrafiltration in a 24-hour period by allowing more exchanges per day. Initial dwell periods of 15 to 30 minutes in the newborn can be adjusted later based on clinical status.

Programming limitations may prevent the use of a cycler for infants who require very small fill volumes or very short dwell times. In such circumstances PD must be performed manually. Premade tubing systems for hand dialysis in the neonate are available commercially, or caregivers familiar with the modality may assemble extemporaneously a system using intravenous tubing. In either case, bedside care providers must be careful to maintain sterility through a closed system.

Disadvantages and Complications in the Infant

This modality requires placement of a peritoneal catheter and a sufficiently maintained intraabdominal status for success. Infants who have undergone abdominal surgery or have had abdominal complications or abnormalities, such as diaphragmatic hernia, omphalocele, or necrotizing enterocolitis, may be poor candidates for PD.

Dialysate can fail to fill or drain through the dialysis catheter as a result of kinking, fibrin plugs, omental obstruction, or catheter malposition. The catheter can perforate abdominal or pelvic structures, either during placement or later.[12] Although perforation is a relatively uncommon event, significant morbidity can result.

Fluid leak is seen with dwell volumes that are too large, especially in the period immediately after catheter placement.[13] This is of particular concern in the critically ill patient and in the newborn. Fluid leak into the thorax can compromise respiration. External fluid leak around the catheter increases infection risk. Peritonitis is a significant complication and can prove fatal in the critically ill infant receiving PD. Careful attention to sterile technique reduces the likelihood of infection. Infants on PD can lose protein into the dialysate and may require increased nutritional support over that needed in older children and adults. The high dextrose concentrations in the dialysate can cause hyperglycemia, necessitating administration of insulin. Indwelling dialysate causes increased intraabdominal pressure that can complicate care of the critically ill patient by limiting diaphragmatic excursion and compromising pulmonary mechanics, reducing venous return or causing gastroesophageal reflux. Low-volume PD with frequent exchanges, as often performed in the infant, can lead to diminished sodium transport despite apparently adequate ultrafiltration ("sodium sieving").[14] This problem potentially may result in volume overload and hypernatremia. Adjustment of the sodium in the dialysate to lower concentrations (e.g., 127 mmol/L compared to 132 mmol/L) can improve sodium extraction while maintaining ultrafiltration.

INTERMITTENT HEMODIALYSIS

The technique for intermittent hemodialysis (IHD) for pediatric patients is well established.[15] IHD offers the advantages of high efficiency for rapid metabolic correction and fluid removal. Hemodialysis for infants is particularly challenging: the majority of devices and materials are designed for larger patients and special techniques are required. Successful treatment can be achieved but requires experienced personnel and careful attention to detail.[16,17]

Indications

Hemodialysis usually is considered the best modality for rapid particle removal because of its high efficiency, making it a good choice for the treatment of toxic ingestions, many serious drug overdoses, and metabolic derangements that lead to the overproduction of endogenous toxins such as ammonia.[18–22] Consequently, IHD is an important modality to consider in the treatment of hyperammonemia of the newborn, in whom rapid reduction of ammonia levels is essential to preserving neurologic outcome.[3,23]

The hemodialysis system can perform ultrafiltration more rapidly than any other renal replacement modality, making it the best choice for the treatment of critical volume overload. Profound metabolic imbalance, such as seen with critical hyperkalemia, can be corrected most quickly with IHD.

Technique

Successful hemodialysis requires a functional vascular access. This remains a significant obstacle to the use of this modality in small patients. Physical limitations of small blood lines greatly limit the rate of blood flow for dialysis.[24] Umbilical catheters do not have favorable flow qualities for hemodialysis, although larger sizes (e.g., at least 5 Fr for each lumen) sometimes can be used successfully. Catheter options for hemodialysis in infants are summarized in Box 206.2; availability of catheters may vary by country. Small double-lumen hemodialysis catheters (7 Fr) can provide acceptable blood flow between 25 and 50 mL/min, sufficient to deliver adequate hemodialysis in a newborn. Placement of even these small catheters can be challenging in the tiniest

BOX 206.2

Catheter Options for Infant Hemodialysis and Continuous Renal Replacement Therapy

- Single-lumen 5 Fr (small neonates)
- Double-lumen 7 Fr (3–6 kg)
- Triple-lumen 7 Fr (provides option for infusion)
- Umbilical catheters (single lumen)
  - 5 Fr umbilical artery for source
  - 5 Fr or larger umbilical vein for return

babies, and use of two separate single-lumen catheters (e.g., 5 Fr) may be preferable. If the available dialysis machine offers a single-needle option, this approach also can be successful in a small neonate and can limit the need for additional or more complex vascular access. In view of the difficulties in achieving vascular access in a small infant, this should be attempted by the most skilled practitioner available to reduce the likelihood of complications and increase chances for success.

Most patients receiving IHD require heparin for anticoagulation. In the neonate, heparin requirements for dialysis must be balanced with the risks of systemic anticoagulation. Neonatology and nephrology personnel should discuss the anticoagulation plan and consider the best option for the individual patient. Some patients may tolerate dialysis successfully with little or no heparin as a result of poor clotting status related to their systemic disease, but the risk of circuit clotting is increased with heparin-free dialysis. In the smallest patients smaller dialyzers are used to limit extracorporeal blood volume and to reduce the risk of dialyzer clotting with slower blood flow rates. These small dialyzers have a lower theoretical clearance than a dialyzer with a larger surface area. However, because of the low blood flow used for infant dialysis, mass transfer through small and through large dialyzers becomes roughly equivalent. Neonatal-specific tubing sets are available for hemodialysis machines. Even using low-volume tubing and a small dialyzer, the extracorporeal circuit still can represent 30% or more of the infant's intravascular volume. In view of the relatively large extracorporeal volume in a hemodialysis circuit, infants usually require priming of the hemodialysis circuit with reconstituted whole blood. This can be accomplished with a blend of packed red blood cells and 5% albumin. As a result of the nonphysiologic properties of banked blood used for blood priming (low pH, high potassium content, low calcium content, citrate load), infants can be at risk for metabolic instability at dialysis initiation. These factors must be considered when a blood prime is to be used. The development of dialysis machines with volumetric ultrafiltration control has allowed for accurate and safe hemodialysis in neonates and infants, for whom small inaccuracies in ultrafiltration volumes potentially could lead to severe fluid imbalances.

Disadvantages and Complications

The principal disadvantage of IHD is the requirement for vascular access. As noted previously, difficulties with vascular access are magnified in the smallest patients. Complications related to the access can include infection, bleeding, and thrombosis. Relatively large catheters placed in vessels of small infants can occlude venous flow.

Infants undergoing hemodialysis are at increased risk for hemodynamic instability. This can occur at the time of hemodialysis initiation with exposure to the blood prime as noted earlier or may be due to rapid expansion of the blood volume and dilution of vasoactive medications, or to rapid ultrafiltration related to the relatively short hemodialysis sessions used with intermittent therapy. The care provider must give thoughtful consideration to these potential problems and be prepared to intervene with blood pressure support or early discontinuation of the hemodialysis session.

Infants undergoing IHD for ongoing RRT in the ICU require special attention to fluid and electrolyte balance. Potassium and phosphorus delivery should be limited because the intermittent nature of the treatment makes it difficult to ensure appropriate balance and prevent accumulation in the interdialytic period. Similarly, total daily fluids also may have to be limited because ultrafiltration only occurs intermittently. Fluid and electrolyte balance is of particular concern in the critically ill infant, who will receive high volumes of fluid to deliver daily medications and nutrition and to simply maintain patent vascular access. Medication doses and schedule may require adjustment owing to poor excretion with renal failure and subsequent rapid removal on dialysis.

CONTINUOUS RENAL REPLACEMENT THERAPY

First applied to infants as described in an early series by Ronco et al.[25] using the nonpumped arteriovenous technique, use of continuous RRT (CRRT) in critically ill children continues to expand. Technologic improvements in catheters, blood pumps, ultrafiltration control mechanisms, and venovenous technique permit the application of CRRT to even the smallest infants.[26,27] New devices, specifically designed for infants, are now becoming available for use[28,29]; these infant-specific CRRT machines hold promise for safer and more accurate therapy.

Indications

As a result of the slow, continuous removal of fluid, CRRT is particularly well suited to the treatment of volume overload in neonates and infants, for whom rapid removal of fluid may be poorly tolerated. CRRT is useful to maintain metabolic balance through ongoing removal of unwanted particles. CRRT can be used as a secondary method to maintain metabolic balance after rapid correction with hemodialysis, as may be necessary in hyperammonemia of the newborn with ammonia rebound.[23] The most recent CRRT machines can deliver dialysate and replacement fluids at much higher rates than those of earlier generations; this permits the use of CRRT at high clearances as the sole dialytic therapy to address neonatal hyperammonemia,[4] rather than using hemodialysis and CRRT sequentially. CRRT can serve as a method for renal support for infants with diminished renal function, permitting administration of the daily load of fluids required to deliver medication and nutrition. This can be useful in the infant for whom PD is unsuitable.

Technique

As with hemodialysis, successful CRRT requires adequate vascular access (see Box 206.2). The same difficulties apply in the CRRT setting, with the added issue of continuous use of the vascular access and associated risk for inadequate function, infection, and hemorrhage. If the extracorporeal volume is large, priming of the CRRT circuit with reconstituted whole blood (e.g., blood-albumin mix) may be required. Blood flow rates for an infant on CRRT would be similar to those seen for IHD (i.e., 25 to 50 mL/min), limited by the flow through the vascular access, the CRRT device, and the clinical status of the patient.

Systemic heparinization has been the traditional form of anticoagulation used in CRRT. Infants may be at increased risk for hemorrhage with continuous systemic anticoagulation. Neonates may suffer intracranial hemorrhage as part of their overall critical illness, and the likelihood rises with systemic heparinization. Careful coordination between neonatology and nephrology services is warranted. Regional citrate anticoagulation is a well-established alternative, and several protocols exist for regional citrate anticoagulation in CRRT, including use in pediatric patients.[30] Citrate anticoagulation can be used successfully in the infant on CRRT; careful attention must be paid to electrolyte and acid-base balance.

Many brands of hemofilter are available for CRRT. Some CRRT devices require the use of a proprietary hemofilter, whereas others employ open systems that permit the use of a hemofilter from any manufacturer. Hemofilter size and material must be considered when performing CRRT in infants. In particular, hypotensive events related to the use of the AN69 membrane have been reported.[31,32] This reaction is thought to be related to the release of bradykinin in response to the low pH of blood used to prime the CRRT circuit. Infants may be at highest risk for this reaction, termed the *bradykinin release syndrome,* because blood priming frequently is used in these patients. Maneuvers to adjust pH within the circuit, with the aim of limiting this reaction, have been described.[32,33] Some institutions avoid the use of the AN69 membrane in infants, choosing to use a larger hemofilter, if necessary, made from a different material. The application of a biocompatible polymer layer to the AN69 membrane partially neutralizes the electronegative surface and is reported to reduce the incidence of the membrane reaction; this membrane (AN69ST) is available outside of the United States.

CRRT machines up to this point have been developed for use with adult patients, requiring adaptation by pediatric specialists for use in children. Application to infants represented the greatest challenge because the mechanical requirements for CRRT in the smallest patients (low flow rates, high levels of accuracy at reduced levels of ultrafiltration) fell at the technical limits of the CRRT device's capabilities. Recently, miniaturized devices have been developed[28,29] with operational parameters designed specifically for CRRT in the infant. Comparison of the technical specifications for a typical CRRT machine designed for an adult with those of the recently developed Cardio-Renal Pediatric Dialysis Emergency Machine (CARPEDIEM) device illustrate the potential advantages of infant-specific therapy (Table 206.1). These miniaturized devices can function with smaller vascular access, addressing another significant challenge seen when applying CRRT to the care of critically ill infants.

TABLE 206.1

Comparison of Standard Versus Infant-Specific Continuous Renal Replacement Therapy Machine Characteristics

	STANDARD CRRT MACHINE	INFANT-SPECIFIC CRRT MACHINE (CARPEDIEM)
Extracorporeal volume	60 mL–186 mL	27 mL–41 mL
Filter surface area	0.2 m^2–1.4 m^2	0.075 m^2; 0.15 m^2; 0.25 m^2
Blood pump range	10 mL/min–450 mL/min	5 mL/min–50 mL/min
Infuse fluid flow range	0–8000 mL/hr	0–60 mL/min
Maximum ultrafiltration	2000 mL/hr	150 mL/hr–300 mL/hr
Ultrafiltration accuracy	±300 mL/24 hr	±1 mL/hr

CRRT, Continuous renal replacement therapy.

Disadvantages and Complications

As with IHD, a significant obstacle to successful CRRT in infants is the requirement for vascular access; similar caveats apply. Continuous extracorporeal perfusion and anticoagulation carries increased risks of bleeding and infection. Hemodynamic instability can develop despite the slow, continuous method of ultrafiltration. Continuous exposure to heparin runs the risk of hemorrhage or heparin-induced thrombocytopenia. Citrate anticoagulation may cause acid-base disturbance or hypocalcemia. Citrate accumulation can cause low patient ionized calcium with normal or high total calcium levels. In our experience infants are particularly susceptible to electrolyte complications during CRRT, related to citrate anticoagulation and excess loss of electrolytes through the hemofilter. This susceptibility may be due to smaller body mass relative to citrate delivery and clearance capabilities. Careful monitoring and adjustment to CRRT prescription, intravenous fluids, and nutritional support are warranted. Attention must be paid to appropriate replacement of electrolytes lost through CRRT. Similarly, nitrogen losses on CRRT can be high,[34] and infants will require thorough nutritional evaluation with increased delivery of protein and calories. Coordination between ICU and nephrology personnel is essential to establish appropriate goals for fluid removal and metabolic control.

CONCLUSION

The requirement for infant RRT represents a special challenge in clinical management. Any modality available for older children and adults may be used for the infant; choice of modality may depend on clinical status of the patient and local expertise. Careful attention to fluid and electrolyte balance, appropriate nutritional support, and close interaction between critical care and nephrology personnel will yield the best outcomes. New infant-specific devices hold promise for safer, more accurate CRRT and additional options to aid the smallest patients who require RRT.

Key Points

1. Peritoneal dialysis (PD) remains an excellent form of acute renal replacement therapy for infants and is often the preferred method.
2. Hemodialysis is the preferred modality for rapid correction of metabolic imbalance and may be the required modality if PD is not a viable option.
3. Continuous renal replacement therapy can be an effective treatment for infants who need renal replacement therapy. Newer infant-specific devices may increase opportunities for this modality.
4. Infants receiving renal replacement therapy require careful monitoring of fluid and electrolyte balance and nutritional needs.
5. Coordination between critical care and nephrology personnel is essential to successful care of infants requiring renal replacement therapy.

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