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RENAL REPLACEMENT THERAPIES FOR CRITICALLY ILL PEDIATRIC PATIENTS*

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SUMMARY: Sakarcan A, Karaböcüoğlu M. (Department of Pediatrics, University of Texas Southwestern Medical Center, Dallas, Texas). Renal replacement therapies for critically ill pediatric patients. Turk J Pediatr 1995; 37: 7-13.

It could be a a great challenge for a nephrologist to prescribe a renal replacement therapy for a critically ill, hemodynamically unstable pediatric patient. Intermittent hemodialysis and peritoneal dialysis frequently fall short of being an optimal renal replacement therapy for such a patient. Continuous hemofiltration is offering new alternatives that can deliver sufficient clearance to meet the needs of a critically ill child. High fluid intake required for total parenteral nutrition and medications can easily be fulfilled by these modalities without compromising the cardivascular system. Of these techniques, continuous veno-venous hemofiltration is superior to continuous arterio-venous hemofiltration because it delivers a consistent ultrafiltration rate dependent on pump-driven blood flow and does not require the insertion of a large-bore catheter into an artery. Thus, various modalities of hemofiltration can offer an alternative to the critically ill child with acute renal failure. *Key words: critically ill pediatric patient, hemofiltration, end-stage renal disease, renal replacement therapies.*

The mortality rate associated with acute renal failure (ARF) complicating catastrophic medical illness in pediatric patients is reported to be between 83 and 100 percent[1-3]. Surgical acute tubular necrosis treated with hemodialysis also has a mortality rate as high as 70 percent[4]. On the other hand, ARF requiring hemodialysis for a primary nephrologic disorder results in a 90 percent survival rate[1]. The aggressive application of peritoneal dialysis (PD) or hemodialysis (HD) has had little impact on these mortality figures, perhaps because of the severity of the underlying medical or surgical condition. PD and intermittent HD are technically feasible procedures for infants and children, but with some major problems. Since acute intermittent HD tends to cause rapid osmolar shifts and hemodynamic instability, it is not well tolerated, particularly by children[5,6]. PD is contraindicated in patients with abdominal trauma or surgery and may also worsen respiratory function in a critically ill patient[5,7]. It may be complicated by access difficulties, peritonitis and metabolic derangements[8,9]. Newer techniques that combine dialysis and filtration on a continuous basis now offer excellent control of azotemia, solute and water removal, and hemodynamic instability[10-15].

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The purpose of this article is to discuss these new modalities in renal replacement therapy (RRT) for critically ill pediatric patients with brief case presentations.

Case 1

The patient was an eight-year-old white male admitted to the pediatric intensive care unit with high fever and seizure activity. Intravenous antibiotic and antiepileptic therapy was initiated. On the second day of hospitalization, the patient developed anuria. The laboratory results showed an increase in BUN from nine to 30 mg/dl, and in creatinine from 0.8 to 2.5 mg/dl. The patient suffered cardiorespiratory arrest due to hyperkalemia (K: 9.0 mEq/L), which necessitated HD. Meanwhile, his muscle enzyme level was found to be very high, leading to the diagnosis of rhabdomyolysis (creatine phosphokinase 6450 IU/L). On the third day of hospitalization, the patient's weight increased from 30 kg to 33 kg. He frequently developed hypotension during HD sessions due to aggressive fluid removal. Due to the limitations of his fluid intake, his calorie intake was only 11 kcal/kg/day, with a protein intake of 0.3 g/kg/day. He was placed on continuous arterio-venous hemofiltration (CAVH) using diafilter 20 cartridge (Amicon, Danvers, MA) with a blood flow of 150 ml/min at an ultrafiltration of 1000 ml/hr. He was treated with this modality for six days. Because of the unlimited allowance of fluid intake, his calorie and protein intake increased to 43 kcal/kg/day and 1.4 g/kg/day, respectively. He was transferred from the intensive care unit to the ward with normal kidney function.

Case 2

A four-month-old male, a neonatal intensive care unit graduate, was admitted to the pediatric intensive care unit with candida meningitis. He was placed on Amphotericin B. On the third day of hospitalization, he developed hemodynamic instability and acute respiratory distress syndrome that required mechanical ventilation. On the fourth day of hospitalization, his blood culture grew Pseudomonas auregenosa, and the patient was placed on gram negative antibiotic coverage. Subsequently, he developed anuria that did not respond to aggressive diuretic therapy. Laboratory results yielded an increase in BUN from 22 to 40 mg/dl and creatinine from 1.3 to 2.5 mg/dl. His weight increased from 4 kg to 5.5 kg with a concomitant increase in ventilatory support. Inotropic support was also initiated due to persistent hypotension. The patient was placed on continuous veno-venous hemofiltration (CVVH) with bm 11 Blood Monitor Pump (Baxter, Illinois) using a diafilter 20 cartridge (Amicon, Danvers, MA) with a blood flow of 140 ml/min and an ultrafiltration rate of 800 ml/hr. Five filters were changed due to clotting. On CVVH his calorie intake increased from 60 kcal/kg/day to 100 kcal/kg/day, and the protein intake was up to 2.9 g/kg/day

from 2.2 g/kg/day. The patient developed hypothermia, which was ameliorated by mounting a blood warmer to the circuit. After seven days of CVVH, the patient no longer required any RRT. On the 20th day of hospitalization, he was discharged with normal kidney function.

Discussion

There are at least five basic configurations to the clinical application of continuous hemofiltration: continuous arterio-venous hemofiltration (CAVH), slow continuous ultrafiltration (SCUF), continuous arterio-venous hemodiafiltration (CAVHD), continuous veno-venous hemofiltration (CVVH) and continuous veno-venous hemodiafiltration (CVVHD) (Table I).

Table I: Renal Replacement Therapies For Critically Ill Patients

Modality	Goals	Solute Transport	Uremia Control	Tolerance by Unstable Patient
HD	Complete RRT	Diffusion and convection	Excellent	Poor
PD	Complete RRT and convection	Diffusion	Good	Fair to good
SCUF	Continuous removal of plasma water and solutes without replacement	Convection	Poor	Excellent
CAVH	Continuous removal of uremic plasma water replaced with balanced electrolyte solution	Convection	Good only when large volumes replaced	Excellent
CAVHD	Combines CAVH and HD without blood pumps	Convection and diffusion	Good to excellent	Excellent
CVVH	Continuous removal of uremic plasma water replaced with balanced electrolyte solution	Convection	Good	Excellent
CVVHD	Combines CAVH and HD with blood pumps	Convection and diffusion	Excellent	Excellent

HD : hemodialysis.
PD : peritoneal dialysis.
SCUF : slow continuous ultrafiltration.
CAVH : continuous arteriovenous hemofiltration.
CAVHD : continuous arteriovenous hemodiafiltration.
CVVH : continuous venovenous hemofiltration.
CVVHD : continuous venovenous hemodiafiltration.
RRT : renal replacement therapy.

Continuous RRT was first described as CAVH in 1977[15]. The simplicity of the CAVH system is striking; a small filter, which is highly permeable to water and small solutes (500 to 30.000 daltons) but impermeable to plasma proteins and the formed elements of the blood, is placed in a low-resistance extracorporeal circuit connecting a large artery and vein. The patient's arterial-to-venous pressure gradient provides sufficient perfusion pressure to drive the system. The ultrafiltrate is concurrently replaced using a fluid with an electrolyte composition that is, either similar to that of normal plasma or specifically designed to correct abnormalities present in the individual patient[7].

SCUF is a variation of CAVH, where fluid is removed from the patient without specific replacement on an ongoing basis[7]. In CAVH, which is driven by the patient's blood pressure gradient, fluid removal with ultrafiltration could be efficient, but urea clearance is low because it depends only on convection. The convection occurs when a solute molecule is swept through the membrane by a moving stream of solvent (solvent drag). In order to increase the solute removal, the process that allows dialysate to flow through the ultrafiltrate compartment of the filter, so creating diffusive transport which depends upon the solute concentration gradients that exist between blood and the dialysate, can be added to create CAVHD[7]. Since hemofiltration besides SCUF can give an ultrafiltration of 1 L/hr with simultaneous administration of replacement fluid, it is possible to achieve normovolemia and metabolic homeostasis without exposing the patient to sudden fluid and metabolic shifts. Case 1 above is a good example of how CAVH can effectively provide RRT when the patient suffers from complications of HD. Since HD is not well tolerated by young infants[5], this RRT modality has already found an application int his patient population[5].

Despite all these advantages, CAVH or CAVHD has some self-limiting features. When the mean arterial blood pressure falls, the driving force for ultrafiltration diminishes and slow blood flow results in filter clotting. These two factors can lead to inefficient ultrafiltration and frequently to its complete cessation. Systemic heparinization is generally required to prevent clot formation in the filter and is utilized as the anticoagulation modality in the two index cases.

Anticoagulation either with heparin or prostacyclin and even as regional heparinization may lead to external bleeding or internal hemorrhage[5,16-18]. Clotting requires changing the hemofilter, which could be associated with air bubbles, heparinization, rupture of capillaries and infection.

One of the most important disadvantages of CAVH or CAVHD is the requirement for arterial cannulation, which can expose the patient to complications such as hematoma, fistula formation and significant bleeding on catheter dislodgement[17,19]. This type of procedure is much more difficult in a neonate

and can also compromise the blood flow to a limb[6] or lead to a theoretical risk of limb shortening.

CVVH technique is similar to CAVH, However, instead of depending on the patient's mean arterial blood pressure as the driving force, a blood pump is used to ensure adequate blood flow through the hemofilter to maintain the required ultrafiltration rate. The blood pump rate is set between 80 and 200 ml/min to achieve an ultrafiltration rate between 500 and 1000 ml/min. Case 1, whose body weight was 30 kg, had a blood flow of 150 ml/min and an ultrafiltration rate of 1000 ml/hr on CAVH, whereas Case 2, despite being a 4 kg patient, had a comparable blood flow of 140 ml/min and ultrafiltration rate of 800 ml/min on CVVH. In our institution, ultrafiltration of 1 L/hr can be achieved with diafilter 20 cartridge (Amicon, Danvers, MA) regardless of the patient's weight (4 kg to 50 kg) without causing any hemodynamic instability (unpublished data). CVVH requires only a single double-lumen venous access[5]. Using a double-lumen catheter could be technically difficult in small infants. This problem can be overcome by using two single-lumen catheters and placing the suction catheter into the upper part of the right atrium[5]. In comparison to CAVH, blood flow rates and urea clearance were significantly higher during CVVH, probably due to its dependence on the pump[5].

CVVH has also found an application in the treatment of intractable hyperphosphatemia due to tumor lysis syndrome in a six-year-old patient with ALL[20]. In our institution, CVVHD has been found to be very effective in delivering the required higher calorie and protein to critically ill patients with hypercatabolism (unpublished data). CVVH could also remove both TNF-α (tumor necrosis factor) and Interleukin-1β from the circulation of septic, critically ill patient[21]. This cytokine extraction may prove to be of benefit in attenuating the progression of multiple organ dysfunction in patients with sepsis-associated renal failure who are receiving CVVH with dialysis.

As seen in the above-cited cases, continuous hemofiltration, especially CVVH, can ensure optimum nutrition. In a series of 11 patients treated in our institution, CVVH increased calories from 33.3 ± 8.9 calories/kg/day to 54.6 ± 9.2 calories/kg/day and protein intake from 0.73 ± 0.2 g/kg/day to 1.45 ± 0.23 g/kg/day ($p < 0.05$) (unpublished data). The enhanced recovery from ARF associated with total parenteral nutrition has been previously emphasized in the literature[22,23]. Although CAVHD has been complicated by hyperglycemia[18], metabolic alkalosis[24] and metabolic acidosis[25,26], CVVH has not been reported in association with these complications in our experience.

One theoretical risk associated with all hemofiltration modalities is infection. Although in our institution this complication is carefully monitored with daily blood

cultures, we did not notice an increased risk, as was also not reported in the literature.

Cost is an important factor to be considered when comparing RRT's for a critically ill child with ARF. According to the only adult study reported in the literature[27], seven-day CAVHD costs 809 dollars, whereas the expense for five treatments of four-hour HD done in one week is only 251 dollars, excluding nursing expenses. The actual difference in cost is reduced somewhat by factoring in the amortized costs of a water purity system and dialysis machine.

The pediatric literature reports a mortality rate of up to 83 percent in patients with ARF complicating medical or surgical illness, whereas ARF due to primary renal disease had only a 10 percent mortality rate[2]. The positive impact of continuous hemofiltration on mortality in critically ill children with ARF has been addressed by Zobel et al[5]. The survival rates in CAVH and CVVH patients were 60 percent and 35 percent, respectively. In our institution, six of 11 CVVH patients survived (unpublished data).

In conclusion, CAVH and CVVH are effective methods of renal support in critically ill pediatric patients. CVVH may have advantages that make it the preferred continuous RRT. Although it is unlikely that hemofiltration will replace acute PD and HD in pediatrics, it should be the RRT for hypotensive, critically ill, highly catabolic, volume-overloaded pediatric patients. As our experience with hemofiltration grows, the applications for these modalities will surely expand.

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