

Advances in Pediatric Renal Replacement Therapy

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Advances in the understanding and clinical application of hemodialysis, peritoneal dialysis, and continuous renal replacement therapy have resulted in strategies designed to further improve their safety and efficacy. These advances have been particularly important to children, in whom a variety of clinical and technical issues must be taken into consideration for optimum dialysis across a broad spectrum of patient size and need. This manuscript reviews recent data pertaining to the use of renal replacement therapy, with an emphasis on those aspects of dialysis management that are especially pertinent to pediatric ESRD and acute kidney injury care.

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In North America, children and adolescents aged <20 years account for <2% of the total ESRD patient population.¹ Data from the USRDS reveal that the incidence of ESRD in pediatric patients (<20 years) is 15.1 patients per million population, ranging from 10.8 for patients aged 0 to 4 years to 28.3 for those aged 15 to 19 years. In terms of dialysis alone, the number of incident pediatric patients in 2007 was 1096 (1% of total incident dialysis patients), with a mean age of 12.6 years. Of the 2200 prevalent patients, 1263 (57%) were receiving hemodialysis (HD). Low pediatric dialysis patient counts are due to both the relatively low incidence of ESRD in children and the extensive use of transplantation as the preferred therapeutic option. As has been characterized in the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) dialysis registry, the youngest children (0-1 years) are preferentially (92%) placed on peritoneal dialysis (PD) as a result of the challenges of vascular access, with a progressive increase in the use of HD with age (>13 years; PD: 51%, HD: 49%).²

Unlike in adults, in whom hypertension, diabetic nephropathy, and chronic glomerulonephritis account for the greatest percentage of patients with ESRD, focal segmental glomerulosclerosis, aplastic/hypoplastic/dysplastic kidneys, and obstructive uropathy (eg, posterior urethral valves) account for 14.4%, 14%, and 12.9%, respectively, of cases of ESRD in the pediatric dialysis population; for all other causes, each accounts for <5% of patients. Data derived from both the USRDS and the NAPRTCS provide age-related patient survival data and confirm the significantly compromised life expectancy of the youngest children on dialysis.^{1,2} In the 2009 report, the USRDS revealed 1-year survival probabilities of 82.3%, 93.8%, 93%, and 97.1% for patients in the age

groups of 0 to 4 years, 5 to 9 years, 10 to 14 years, and 15 to 19 years, respectively. In the 2011 NAPRTCS report, the 12-month survival rate was only 88.9% for children aged <1 year, which decreased substantially to 75.1%, 36 months after the initiation of dialysis. The best survival rate for children, seen in those aged >12 years (98.2% at 12 months after dialysis initiation), still shows a modest decrease after 3 years of dialysis (95.4%). Overall, the survival rate for all children receiving chronic dialysis has increased only slightly over the past 15 years. The main causes of death are cardiopulmonary disease (21%), infection (20.5%), cancer/malignancy (6.5%), and dialysis-related complications (3.4%) (Table 1).² At 21 deaths per 1000 patient-years in 2000 to 2006, the rate of cardiovascular mortality during the initial month of dialysis for patients aged 0 to 19 years is 4.4 times greater than in the previous decade secondary to a variety of conventional and uremia-related risk factors.^{1,3-6}

Choice of Dialysis Modality in Children

Although the vast majority of all dialysis patients in the United States receive HD, nearly 50% of children receive chronic PD. It is of interest that pediatric centers more frequently use PD (65%) than do those adult centers that provide dialysis to children (45%).⁷ The advantages of HD include the minimal technical assistance required of the patient and family when the procedure is conducted in a dialysis center, along with the decreased treatment time relative to PD. In contrast, the use of PD is associated with less dependence on the dialysis center; increased flexibility for performance of treatments, which permits greater school attendance; decreased dietary restrictions; and fewer venipunctures. Most recently, a limited number of children have received HD at home.⁸

Chronic Pediatric HD

The capacity to provide chronic HD to a pediatric population mandates the availability of equipment and personnel that can meet the particular needs of infants, children, and adolescents with ESRD. Although the use of HD increases in frequency with age in pediatric patients, even young infants can receive HD in an effective

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manner when provided in a center with multidisciplinary (eg, pediatric nephrologist, nurse, social worker, dietitian, child life therapist, psychologist) expertise.⁹⁻¹¹

Vascular Access in Children

Permanent vascular access in the form of an arteriovenous fistula (AVF) is preferred for children with ESRD on maintenance HD, as it is in adults, because of superior performance, longevity, and decreased risk of complications when compared with central venous catheters (CVCs). In younger children, in whom it is difficult to create an AVF, an arteriovenous graft (AVG) is an additional option. Preservation of vessels before AVF/AVG placement is important and mandates educating the patient with advanced CKD, as well as his/her family and health care team, about the importance of avoiding venipuncture/intravenous line placement in vessels that are candidates for creation of the access. A single-center pediatric study has revealed AVF and AVG survival rates of 90%, 60%, and 40% at 1, 3, and 5 years, respectively.¹²

The KDOQI Pediatric Vascular Access Work Group does recommend that a cuffed venous catheter be placed if there is lack of surgical expertise available to place an AVF/AVG in small children; if the patient is too small (<20 kg) to create an AVF/AVG; or if HD is not to be the final mode of renal replacement therapy, either because the patient will be placed on PD or the patient is expected to receive HD for <1 year because of transplantation.¹³ Nevertheless, catheters remain the most common access for children receiving chronic HD, even in good candidates for an AVF/AVG who receive dialysis for a prolonged period.¹⁴ In 2011, NAPRTCS revealed that 78.7% of 3363 chronic HD accesses were external percutaneous catheters, located in the subclavian (51.1%) and jugular (43.7%) veins.² Similarly, the USRDS reported that 74% of pediatric patients initiated HD with a catheter and that there has been little increase in the use of fistulas among new HD patients when comparing the experience of 2001 to 2003 (19.6%) with 2004 to 2006 (22.3%).¹ Several different catheters exist for children, with catheter survival rates of 58.5% and 46% at 1 year with the Ash and Tesio catheters (MedComp Inc., Harleysville, PA), respectively, when cared for using strict aseptic technique.^{15,16} However, infection remains a significant complication of catheter usage when compared with the experience with AVFs/AVGs. One study documented a hospitalization rate of 3.7 d/100 HD treatments for

pediatric patients with a CVC versus 0.2 d/100 HD treatments for AVF/AVG patients.¹⁷ Although Eisenstein and colleagues recently reported a remarkable CVC infection rate of 0.52/1000 catheter days in a single center with use of a meticulous catheter management protocol, event rates for infection and sepsis among new pediatric HD patients with a catheter rose to 66% and 133%, respectively, between 2001 to 2003 and 2004 to 2006 in the United States, emphasizing the overall lack of effective preventative measures.^{1,18} Interestingly, catheter-related bacteremia can be successfully treated on occasion without the need for catheter exchange with the use of combined antibiotic lock solutions and systemic antibiotic therapy.¹⁹ Of 3363 catheters recorded in NAPRTCS, 80.2% have required revision for a variety of reasons, including reaccess (25.3%), malfunction (25.6%), clot (22.7%), and infection (14.5%).²

Technical Aspects of HD

A wide variety of lines and dialyzers are available from various manufacturers to meet the requirements of most

patients, irrespective of age/size (Table 2).²⁰ Pediatric dialyzers have a small volume, in addition to a safe ultrafiltration coefficient, a low-resistance blood circuit, a high degree of biocompatibility, and a predictable relationship between clearance and blood flow rates. Newer generation dialysis membranes made from polysulfone and polymethylmethacrylate also cause less proinflammatory

cytokine activation compared with cellulose membranes. Nevertheless, data reveal that children dialyzed with biocompatible membranes still exhibit a proinflammatory response with HD with subsequent increases in tumor necrosis factor- α and interleukin-1 β levels.²¹

As one initiates HD in children, it is important to recognize that although small solute clearance is equivalent to the blood flow rate when the blood flow rate is low, there is a maximum clearance that will be achieved for each dialyzer at a certain blood flow rate, with no further increase possible; further increases in clearance mandate use of a larger dialyzer. The small infant must be monitored particularly closely, as current HD machines have an ultrafiltration accuracy of approximately 50 to 100 mL, a value that may contribute to hemodynamic instability if ignored. Finally, rapid osmolar changes experienced by patients during their initial few HD sessions can be associated with cerebral edema, disequilibrium syndrome, and the development of seizures. Children are also known to have a relatively low seizure threshold; therefore, limiting the

CLINICAL SUMMARY

- Children receiving frequent hemodialysis have been found to exhibit normal growth without the use of growth hormone therapy, decreased BP load, better phosphate control, and a markedly improved nutritional state.
- Catheters configured with 2 cuffs, a swan-neck tunnel, and a downward pointed exit-site are associated with a significantly longer time to initial peritonitis episode.
- Patients with $\geq 20\%$ fluid overload at initiation of CRRT have an adjusted mortality odds ratio of 8.5, when compared to patients with <20% fluid overload.

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