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ORIGINAL ARTICLE

Hemodialysis in children weighing less than 15 kg: a single-center experience

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Abstract Despite significant technical improvements, hemodialysis in infants with end-stage renal disease (ESRD) is still associated with significant morbidity and mortality. The files of patients weighing less than 15 kg with ESRD who were treated with hemodialysis at our institute between 1995 and 2005 were reviewed for background and treatment characteristics, morbidity and outcome. The study group included 11 patients aged 7–75 months (mean 34.2 months) weighing 7.2–14.9 kg (mean 10.9 kg). Mean duration of dialysis was 11.3 months. Vascular access posed the major problem. Ten patients were dialyzed through a central venous cuffed catheter and one through an arteriovenous fistula. An average of three different vascular accesses was required per patient (range 1–9). Mechanical difficulties were the most common cause of central-line removal (56.5%), followed by infections (15.6%). Major complications causing significant morbidity were intradialytic hemodynamic instability, hyperkalemia, coagulation within the dialysis set, anemia, hypertension, inadequate fluid removal, and recurrent hospitalizations. Analysis of outcome revealed that eight patients underwent successful transplantation, one returned for hemodialysis after 4.5 years due to graft failure, and two died. Hemodialysis is a suitable option for low-weight pediatric patients with ESRD awaiting transplantation when performed in highly qualified centers.

Keywords End-stage renal failure · Infants · Vascular access · Hypertension · Anemia · Hemodynamic instability · Nutrition · Growth · Hospitalization

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Introduction

The prevalence of end-stage renal disease (ESRD) in children has steadily increased in recent years. According to the US Renal Data System (USRDS), the rate in 2004 was 84.2 per million age-adjusted population [1]. The North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) reported that 11–12.5% of all dialysis patients are younger than 2 years old at initiation of dialysis [2, 3]. During the last two decades, technological advances have helped to make long-term dialysis a feasible option in pediatric patients with ESRD [4]. Although successful kidney transplantation remains the treatment of choice, more than three fourths of children require chronic dialysis while awaiting transplantation for periods ranging from a few months to several years [2].

In infants with ESRD, peritoneal dialysis is preferred. Hemodialysis is used only when peritoneal dialysis fails or is inapplicable for social or anatomic reasons. At present, only 9–30% of dialyzed infants in North America and Europe receive hemodialysis [3, 5]. One-year survival in patients younger than 1 year at the start of treatment is 83–89% for both peritoneal dialysis and hemodialysis [2, 6, 7]. No comparable data are available for infants on hemodialysis alone owing to inadequate numbers and limited morbidity and mortality studies [8]. Furthermore, maintenance hemodialysis in infants raises serious short-term

problems, such as technical difficulties related to patient size, vascular access, and hemodynamic instability in addition to long-term problems such as poor nutrition and growth, impaired brain development, and difficult psychosocial adaptation [9].

Considering that the problems of pediatric hemodialysis are related mainly to the patients' small body size and not to their chronological age, and that the majority of children with ESRD suffer from growth retardation, we sought to describe our experience with hemodialysis in low-weight children in terms of demographic and treatment characteristics, morbidity, and outcome.

Patients and methods

We reviewed the files of all patients with ESRD weighing less than 15 kg who received maintenance hemodialysis in the Dialysis Unit of Schneider Children's Medical Center of Israel from 1995 through 2005. The following data were recorded: renal disease, age at diagnosis, age at end-stage renal failure and at the start of hemodialysis, height and weight at the start of hemodialysis and on follow-up, duration of hemodialysis, reason for discontinuing hemodialysis, complications, number and length of hospitalizations, and outcome. Dialysis was performed with Gambro AK 200 (Lund, Sweden) machines and hollow-fiber polysulfone dialyzers (Fresenius, Bad Homburg, Germany), using standard dialysate solution. Before hemodialysis was initiated, the ratio of circuit volume to patient blood volume was calculated. When the extracorporal volume was greater than 10% of the patient's blood volume, priming with normal saline was performed in order to avoid hemodynamic instability. The routine dialysis prescription was as follows: three times a week, 4-h sessions, blood flow 5 ml/kg per min, and dialysate flow 500 ml/min with target KT/V >1.3. Heparinization was performed with 10–30 U of heparin per kilogram per hour and monitored by the activated coagulation time (ACT) test with target ACT of 180–220 s.

Statistical analysis

Only descriptive statistics [mean, range, and standard deviation (SD)] were calculated because of the small number of patients.

Results

During the 10-year period of the study, 63 pediatric patients received maintenance hemodialysis in our institute, of whom 11 (17.4%) (seven boys, four girls) weighed less than 15 kg. The characteristics of the study group are shown in Table 1. Mean weight at start of dialysis was 10.9±2.1 kg (range 7.2 –14.9 kg, SD range −0.6 to −4). Mean age at

Table 1 Characteristics of pediatric patients on maintenance hemodialysis (HD)

Patient	Renal disease	Gender	Age at start of HD (months)	Weight at start of HD (kg)	Duration of HD (months)	No. vascular accesses	Outcome
1	Infantile nephrotic syndrome (diffuse mesangial sclerosis)	F	21	10.2	0.5	1	Successful transplantation
2	Dysplastic kidneys	M	20	7.2	12 + still on HD	9	Transplantation, graft failure, and return to HD after 4.5 yrs
3	Nephronophthisis	M	75	14.6	33	6	Successful transplantation
4	Congenital nephrotic syndrome	F	7	7.8	0.5	2	Successful transplantation
5	Infantile nephrotic syndrome (diffuse mesangial sclerosis)	F	29	9.2	25	1	Successful transplantation
6	Congenital nephrotic syndrome	M	38	11.4	10	2	Death
7	Dysplastic kidneys	M	62	14.8	20	5	Successful transplantation
8	Focal segmental glomerulosclerosis	M	49	14.9	1	1	Successful transplantation
9	Dysplastic kidneys	M	19	9.9	10.5	3	Successful transplantation
10	Familial hemolytic uremic syndrome	M	19	8.67	8	3	Death
11	Congenital nephrotic syndrome	F	37	11.3	5	1	Successful transplantation
Mean (range)			34.2 (7–75)	10.9 (7.2–14.9)	11.3 (0.5–33)	3 (1–9)	

start of dialysis was 34.2 months (range 7–75 months); five patients (45.4%) were less than 2 years old. The causes of renal failure were renal dysplasia with or without urologic malformation in three patients, congenital nephrotic syndrome in three, infantile nephrotic syndrome in two, nephronophthisis in one, familial hemolytic uremic syndrome in one, and focal segmental glomerulosclerosis in one. Eight patients were anuric, one was oliguric, and two were nonoliguric. The main reasons for using hemodialysis rather then peritoneal dialysis were presence of peritoneal failure due to recurrent peritonitis and need for a transitory treatment modality until peritoneal dialysis was feasible.

Mean duration of hemodialysis was 11.3 months (range 0.5 to 33 months). The range of KT/V was 1.3–2.3.

Vascular access

A central venous, Quinton perm-cuffed catheter (Medcomp, Sherwood) was used for chronic vascular access in ten patients and an arteriovenous fistula/graft in one patient (two fistulas in the same patient). Acute catheters were used, when needed, only for short periods as a transitory mode to permanent access. An average of three different vascular accesses was required per patient (range 1–9). Table 2 shows catheter location. Fifty-four percent of the acute uncuffed catheters were located in the internal jugular vein in contrast to only 12.5% of the chronic cuffed catheters. Mean catheter durability (catheter life) was 21.2 days for acute catheters (SD −29.6, range 4–80), 64.2 days for cuffed catheters (SD −98.6, range 6–370), and 174 days for fistulas/grafts (SD −96, range 78–270).

The main reason (56%) for catheter removal was mechanical problems, including kinking, thrombosis, and catheter stenosis. Catheter stenosis was suspected when inadequate blood flow was observed. Before catheter removal in these cases, a trial with local infusion of tissue plasminogen activator or urokinase was made. Another 15.6% of catheters were removed because of infection, due mainly to coagulase-negative *Staphylococcus* bacteremia. The rate of catheter-related bacteremia was 1.3 infections per 1,000 patient days.

Patients with infection were given a trial of parenteral antibiotics; in cases of treatment failure, the catheter was removed. In the event of recurrent line sepsis or *S. aureus* bacteremia, we added an antibiotic lock solution consisting of vancomycin 2.5 mg/ml and heparin 2,500 U/ml. Routine exit-site care consisted of hydrogen peroxide cleansing and sterile gauze dressing performed at each hemodialysis session. If exit-site erythema, granulation tissue, or purulent discharge was observed, swab culture was performed, and Mupirocin ointment was applied after routine care. Surveillance for *S. aureus* nasal carriage was conducted and intranasal mupirocin was administered when carriage was detected.

Table 2 Data on central venous catheters

Location	Temporary catheter	Cuffed venous catheters
Subclavian vein	3 (23%)	12 (75%)
Internal jugular vein	7 (54%)	2 (12.5%)
Femoral vein	1 (7.7%)	0
No data	2 (15.3%)	2 (12.5)
Total	13 (100%)	16 (100%)

Growth and nutrition

Patient mean and SD weight at the beginning of hemodialysis were 10.9 kg and −2.1, respectively (weight range 7.2–14.9 kg, SD range −0.6 to −4). Mean SD for weight at cessation of dialysis was −2.38 (range −1 to −3.2). Average height deficit was −2.9 SD (range −1.3 to −6.4) at the beginning of dialysis and −2.9 SD (−1.5 to −6.4) at the end. All patients were on an age- and weight-adjusted diet and under careful follow-up by a renal dietitian. Target caloric intake was 150 Kcal/kg per day. Four children were fed a special caloric-enriched (1–1.2 Kcal/cc, meaning 130–140 cc/kg per day) renal-adapted formula (low potassium, phosphate, and sodium). Three children were fed via gastrostomy in order to achieve adequate food intake; only one of them showed a weight gain at the end of the dialysis period. The rest of the patients were fed orally. Enteral feeding was usually provided one half hour after the start of the dialysis session and generally was well tolerated. Three patients were treated with recombinant growth hormone during the period of hemodialysis; two showed improvement in growth velocity. Considering the fact that there was no significant change in weight gain or growth velocity during the dialysis period despite the wide range of KT/V, it may be concluded that KT/V had no influence on growth parameters in our patients.

Hospitalization

Seven patients were hospitalized at least once during the period of hemodialysis. The mean number of hospitalizations per hemodialysis period was eight (range 2–17), meaning 0.7 hospitalizations per patient month (range 0.1–2). The length of hospitalization ranged from 2 to 7 days. The main reasons for hospitalization were vascular access complications and fever.

Hypertension

Eight patients had stage 2 hypertension, defined as blood pressure >5 mmHg above the 99th percentile for age,

height, and gender. We used the following hypertensive approach: estimation of dry weight and assessment of volume-overload-induced hypertension; in positive cases, increased ultrafiltration was implemented. If blood pressure control was still not achieved, antihypertensive medications were introduced, including combination of angiotensin-converting enzyme (ACE) inhibitors, calcium-channel blockers, and beta blockers. When these were unsuccessful, direct vasodilators, central alpha-2 agonists, or peripheral alpha-1 antagonists were added. In all patients, we routinely performed echocardiography every 6 months, including estimation of left ventricular mass index. Left ventricular hypertrophy (mass index >51 $g/m^{2.7}$) was found in five patients during hemodialysis. One patient had two episodes of hypertensive encephalopathy.

Anemia

Ten patients had anemia, treated in all cases with intravenous recombinant erythropoietin. The average dose attained was 510 U/kg per week (330–800 U/kg per week). Eight patients needed at least one transfusion of packed cells (mean 1.5/patient). Treatment was given in order to achieve a target hemoglobin concentration of 11 g/dL to 13 g/dL (hematocrit 33–36%), according to the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines for management of anemia in pediatric dialysis patients. Iron stores were assessed routinely every month. When transferin saturation was below 20%, intravenous iron sucrose (Venofer) in a dose of 1–4 mg/kg per dose was added at least once a week and usually two to three times a week (at each hemodialysis session).

Dry-weight management, intradialytic hypotension, and other complications

Dry weight was estimated initially by ultrasound measurement of the inferior vena cava diameter (normal=8–11.5 mm/m^2, collapse index=40–75%) and more recently by continuous measurement of hematocrit variations using noninvasive methods during the hemodialysis session (Crit-Line, Salt Lake City, UT, USA). Nevertheless, six patients had at least one episode of hemodynamic instability and intradialytic hypotension per hemodialysis course (mean 5.5 episodes per patient, range 3–12). Two patients needed four to five hemodialysis sessions per week for adequate fluid removal, and four patients needed a dose of Kayexalate on day-off dialysis because of hyperkalemia. Blood coagulation in the dialysis circuit was a major problem despite adequate heparinization, and in one case, it resulted in significant blood loss and a need for packed-cell transfusion. One patient had recurrent episodes of hypoglycemia during the dialysis sessions, warranting intravenous glucose supplementation in addition to a glucose-containing dialysis solution.

Outcome

Eight patients (72.7%) underwent successful transplantation (three from a living-related/unrelated donor). One 7.5-year-old boy with end-stage renal failure due to dysplastic kidneys had been treated with peritoneal dialysis from the age of 6 months and transferred to hemodialysis at the age of 18 months. He underwent transplantation at age 2.5 years, but graft failure occurred 4.5 years later, and hemodialysis was restarted. Two patients (18.2%) died: a 2.5-year-old boy with familial hemolytic uremic syndrome died of pulmonary edema after 8 months on hemodialysis, and a 4-year-old boy with congenital nephrotic syndrome died of hyperkalemia after 1 year on hemodialysis (Table 1).

Discussion

In our institute, 11 patients weighing less than 15 kg (five less than 2 years old) were treated with hemodialysis over a period of 10 years. To the best of our knowledge, this is one of the largest series in the literature dealing with hemodialysis in low-weight pediatric patients. For comparison, Al-Hermi et al. [8] described ten infants on hemodialysis over a period of 14 years, and Shroff et al. [9] described 18 children under 2 years of age on chronic hemodialysis over a period of 16 years. Recently, Shroff et al. [10] reported the long-term outcome of 12 of these patients younger than 5 years old who had received chronic hemodialysis over a period of 14 years.

The most common diseases leading to end-stage renal failure in our patients were renal dysplasia with or without urologic malformation and congenital nephrotic syndrome. The main obstacle in providing hemodialysis to infants is adequate vascular access. This is crucial, because children with ESRD have a relatively longer lifespan than affected adults, so clinicians need to meet their immediate needs without compromising future access sites. Although primary arteriovenous fistulas are associated with the lowest rate of secondary failure and complications [11], many pediatric centers, because of technical difficulties, limit them to patients weighing more than 25 kg [11, 12]. In lower-weight infants, cuffed catheters are the most common form of chronic hemodialysis access. According to the NAPRTCS [2], 79% of children have central-line access at the initiation of hemodialysis. In our institute, 88.8% of patients were dialyzed via a central venous cuffed catheter.

The Adult Dialysis Outcome Quality Initiative (K/DOQI) guidelines stipulate that the right internal jugular vein is

the preferred site for central venous catheterization and that the subclavian vein should be avoided because of the risk of stenosis [13]. Nevertheless, studies have shown that 82% of external percutaneous catheters are placed in the subclavian vein, only 14% in the jugular vein, and 6% in the femoral vein [2]. Our data were similar: 75% of the cuffed catheters were located in the subclavian vein and only 12.5% in the internal jugular vein. The decision regarding the site of the central catheter was made by our surgeons on the basis of their experience and personal preference. However, prompted by the K/DOQI recommendations, we are working toward changing this approach.

The term of vascular access durability was 3 weeks for acute temporary catheters, 16 weeks for cuffed catheters, and 43.5 weeks for the arteriovenous fistula/graft. Goldstein and colleagues [14] reported a 1- and 2-month actuarial survival of 69% and 48%, respectively, for uncuffed catheters, and Lumsden et al. [15] reported a mean survival of 8.1 weeks for cuffed catheters. As in the study of Goldstein et al. [14], the major cause of catheter removal in our series was mechanical problems, such as kinking and thrombosis.

Infection is a common and serious complication of hemodialysis catheters. Marr et al. [16] estimated that the rate of catheter-related bacteremia in long-term tunneled cuffed catheters is one episode per 252 catheter days. The most common organism isolated in their patients was *S. aureus*, followed by coagulase-negative *Staphylococcus*. In our series, the rate of catheter-related bacteremia was 1.3 infections per 1,000 patient days; 75% were due to coagulase-negative *Staphylococcus*.

Data on morbidity in infants receiving hemodialysis are limited. In our patients, the major problems included impaired growth despite adequate nutrition and recombinant growth hormone therapy, recurrent hospitalizations (up to 17 per patient), and hypertension (72%), with a high incidence of complications. As in our patients, Shroff et al. [9] found no significant change in median weight and height SD scores in their series.

The correct estimation of dry weight is challenging in pediatric patients. Although hemodynamic instability was a major problem in the present series, since the introduction of the Crit-Line in our unit, we have been able to estimate dry weight more precisely and thereby decrease the incidence of intradialytic hypotension.

Anemia and the need for large doses of recombinant human erythropoietin (rHuEPO) (average dose 510 U/kg per week) and blood transfusions (in 8/11 patients, 1.5 transfusions per patient) was another major problem. The need for a high rHuEPO dose in small children has been previously reported and is thought to be due to the larger relative volume of distribution and more rapid clearance compared with adults [17]. In the series of Shroff et al. [9], 15 of 18 patients required blood transfusion (total 46 transfusions, maximum eight per patient). They suggested that besides end-stage renal failure, anemia was also attributable to ongoing blood loss in hemodialysis lines, the need for frequent venipuncture, and the operative procedure.

Another relatively frequent event in our patients was blood coagulation in the dialysis circuit despite adequate heparinization. This is probably explained by hemoconcentration caused by excessive ultrafiltration relative to the dialyzer surface area. Additional complications included hypoglycemia and hyperkalemia. The dependence of infants on fluids for nutrition, combined with the high fluid intake and intradialytic hemodynamic instability, made it very difficult for thrice-weekly hemodialysis to provide adequate fluid removal. Indeed, two of our patients required four to five hemodialysis sessions per week. Although short daily dialysis seems to be a good option in small children owing to its benefits for nutrition, neurodevelopment, management of dry weight, and blood pressure, it is not always feasible for patients who live a long distance from the hospital.

Management of the children's well-being during the dialysis sessions was a major concern. Several different means were used, such as entertainment, artwork, medical clowns, teaching, psychological support, parental holding, and even breast feeding during dialysis in one case. For optimal results, a multidisciplinary team is needed to organize these activities.

According to NAPRTCS reports, mortality rates for pediatric patients on dialysis varies with age from 13.6 to 8.2, and 6.1 deaths per 100 patient years for those aged <1 year, 1–2, and 2–5 years, respectively. The survival rates were 95% at 1 year, 90.1% at 2 years, and 85.7% at 3 years. The highest mortality rate was found in children younger than 1 year at the start of dialysis; in this group, survival rates were 84.5% at 1 year, 74.4% at 2 years, and 68.2% at 3 years. Nevertheless, 61% of all initial terminations of dialysis were due to transplantation [2, 3, 18]. These findings are consistent with our data: eight patients (72.7%) currently have functioning renal transplants, one (9.1%) is still on dialysis, and two (18.2%) deceased.

Together, our findings indicate that although hemodialysis is not the treatment of choice for low-weight pediatric patients awaiting a renal transplant, it may well provide an option when peritoneal dialysis is not feasible. However, given the specific problems, including technical difficulties, hemodynamic instability, and environmental adaptation, this form of renal replacement therapy should be performed only in highly specialized centers with an experienced multidisciplinary team. Our study is limited by its retrospective design and small number of patients. Yet, considering the sparse data on hemodialysis treatment in

low-weight children, we believe our study provides additional important information relevant to this challenging patient group.

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