Impact of Dialysis Type on Outcome of Acute Renal Failure in Children: A Single-Center Experience

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ABSTRACT: **Background:** Acute renal failure (ARF) is a common complication in critically ill children. It is known as an important predictor of morbidity and mortality in this population. Data on the factors affecting the choice of renal replacement therapy (RRT) modality and its impact on mortality of children with ARF are limited.

Objectives: We retrospectively studied 115 children with ARF necessitating RRT during the period 1995–2005 to evaluate the effect of several prognostic factors as well as RRT type on their immediate outcome.

Methods: The data collected from charts included demographics, primary disease, accompanying medical conditions, use of vasopressor support, indications for dialysis, RRT modality, and complications of dialysis. Categorical variables were analyzed using chi-square or Fisher's exact tests. Variables associated with mortality ($P < 0.1$) at the univariable level were studied by a multivariable logistic regression model.

Results: The most common cause of ARF was congenital heart disease (n=75). RRT modalities included peritoneal dialysis (PD) (n=81), hemodialfiltration (HDF) (n=31) and intermittent hemodialysis (IHD) (n=18). Median RRT duration was 4 days (range 1–63 days). Overall mortality was 52.2%. IHD was associated with the best survival rate ($P < 0.01$ vs. PD and HDF), while children treated with HDF had the worse outcome. Hemodynamic instability and systemic infections were associated with greater mortality, but the rate of these complications did not differ between the study groups.

Conclusions: Our results suggest that IHD when applied to the right patient in an appropriate setting may be a safe and efficient RRT modality in children with ARF. Randomized prospective trials are needed to further evaluate the impact of different RRT modalities on outcome in children with ARF.

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ARF = acute renal failure
RRT = renal replacement therapy
IHD = intermittent hemodialysis
PD = peritoneal dialysis
HDF = hemodialfiltration
IHD = renal replacement therapy

Acute renal failure is a significant contributor to morbidity and mortality among critically ill pediatric patients [1]. The extent of the need for renal replacement therapy varies considerably from 7% to more than 40% of patients according to differences in population selection [2-4]. With experience increasing in pediatric dialysis, all RRT modalities are currently available for children. These include intermittent hemodialysis, peritoneal dialysis and continuous hemodialfiltration, although peritoneal dialysis is still preferred in young children. The choice of RRT modality is influenced by the patient's age, clinical condition, indication for dialysis, as well as availability of resources and clinical expertise of the medical staff [5]. Data on the correlation between RRT modality and outcome of pediatric patients with ARF are scarce and it is not known whether one modality is superior to another. We conducted a retrospective study of pediatric patients with ARF necessitating RRT and examined the effect of RRT modality choice on their short-term outcome.

PATIENTS AND METHODS

The medical files of all patients with ARF necessitating RRT who were treated at the Schneider Children's Medical Center of Israel during a 10-year period (1995–2005) were retrospectively surveyed. Patients were hospitalized in various intensive care units (general pediatric intensive care unit, pediatric care unit for patients after cardiac surgery, and neonatal intensive care unit). Dialysis was performed by dialysis nurses with supervision of pediatric nephrologists. Peritoneal dialysis was performed with manual exchange systems using either commercially available (lactate-based) or pharmacy-made (bicarbonate-based) solutions. Choice of the dialysis buffer was based on the degree of metabolic acidosis and hepatic function of the patient.

The initial PD exchange volume was 10 ml/kg, increasing to 50 ml/kg. Glucose and sodium concentration was adjusted as needed. Hemodialysis was performed using the Gambro machine with appropriate neonatal, pediatric or adult blood tubing. Blood flow, ultrafiltration rate, and HD session duration and frequency were adjusted to the patient's needs. Hemodialfiltration was performed as continuous veno-venous HD by an adapted hemodialysis machine (Gambro AK-100,

Lakewood, CO, USA). Blood flow rate was targeted to 5 ml/kg/min. Follow-up was resumed at the end of hospitalization. Clinical data collected from the charts included age, gender, primary disease, accompanying medical conditions, use of cardiac pressor support, indications for dialysis, RRT modality (PD, IHD and/or HDF), overall duration of RRT, complications during the course of dialysis, the cause of death in deceased patients, and renal function at the end of follow-up. Hemodynamic instability was defined as a drop in blood pressure necessitating cessation of the dialysis session.

STATISTICAL ANALYSIS

Categorical variables were analyzed using a chi-square test or Fisher's exact test as appropriate. Multivariable logistic regression was performed to examine associations of various characteristics of interest and mortality. Variables that were associated ($P < 0.1$) with mortality at the univariable level were included in the multivariable model.

RESULTS

The study population consisted of 115 patients (62 boys and 53 girls) with a median age of 9 months (range 0–198 months). The patients' primary illnesses are presented in Table 1.

The most common cause of ARF was congenital heart disease and cardiac surgery (75 patients, 65%). Seventy-four patients (64%) required cardiac pressor support prior to initiation of RRT. The most common indications for RRT were fluid overload due to oliguria/anuria and hyperkalemia. The most prevalent modality was PD (81 patients, 70.4%); in 18 patients (15.6%) IHD was used and in 31 patients (26.9%) HDF was applied. Sixteen patients were treated with more than one modality. The choice of RRT modality depended on the clinical condition of the patient, the age (younger children were treated more frequently with PD and HDF), and the indication for dialysis. The most common reasons for switching to another modality were peritonitis and access failure in PD patients. In 42 patients PD was performed by short-term catheter and in 41 by a surgically placed cuffed Tenckhoff catheter. In two patients the temporary catheter was replaced by a Tenckhoff catheter due to exit-site leak. Intermittent HD and HDF were carried out by short-term double-lumen central venous catheters placed in the internal jugular, the subclavian or the femoral veins.

The median duration of RRT was 4 days (range 1–63). Complications during the course of dialysis included access failure (8 patients, 7%), exit-site leak (6 patients, 5.2%), peritonitis (5 patients, 4%), systemic infection (8 patients, 7%), thrombosis of access (2 patients, 1.7%), hemodynamic instability (9 patients, 7.8%), and excessive bleeding (3 patients, 2.6%).

Overall mortality was 52.2% (60 patients). Most of the patients (90%) died due to complications of their primary disease. The vast majority of survivors had complete recovery of renal function. Only two patients (3.6%) had persistent renal failure necessitating RRT at the end of follow-up.

The association between specific RRT modality and survival was studied in the 99 patients who were treated by a single RRT modality. A statistically significant association was found between RRT modality and mortality rate [Figure 1]. Intermittent hemodialysis was associated with improved survival rate (8.3%), while hemodialfiltration was related to the worst prognosis with a mortality rate of 83.3%. Peritoneal dialysis was associated with an intermediate mortality rate of 52.2% ($P < 0.001$). Hemodynamic instability and systemic infection in the course of RRT were associated with increased mortality ($P < 0.01$ and $P = 0.038$, respectively); however, the prevalence of these complications did not differ among the RRT modality groups.

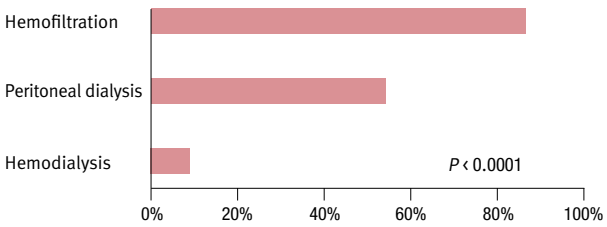
To study the associations of various parameters and mortality, a multivariable logistic regression analysis was constructed using the following parameters: age, gender, primary disease, use of vasopressor support, and RRT modality. IHD

Table 1. Primary illnesses in the study population*

Diseases	No. of patients (%)
Hemato-oncological	12 (10.4)
Congenital heart disease	75 (65.2)
Sepsis	29 (25.2)
Liver disease	5 (4.4)
Trauma	2 (1.7)
Asphyxia due to preterm birth	5 (4.4)
Hemolytic uremic syndrome	7 (6.1)
Post-infectious glomerulonephritis	2 (1.7)
Acute glomerulonephritis, other than post-infectious	1 (0.9)
Obstructive uropathy	1 (0.9)
Vasculitis	1 (0.9)
Central nervous system disease	4 (3.5)
Others	2 (1.7)

*Several patients suffered from more than one illness

Figure 1. Mortality rate according to RRT type



was associated with a significantly lower mortality rate (odds ratio 0.076, 95% confidence interval 0.006–0.888), while HDF was significantly associated with higher mortality (OR 8.0, CI 1.20–53.16). Male gender was also associated with greater mortality (OR 2.82, CI 1.07–7.46). Age, primary illness type and use of cardiac pressor support did not affect mortality.

DISCUSSION

Data on the effect of RRT modality on survival of pediatric patients with ARF are limited. A retrospective analysis of 118 pediatric patients treated either by PD (n=82) or HDF (n=36) demonstrated better fluid control with HDF, which was the modality of choice for ARF associated with sepsis, but there was no difference in mortality rates between the modalities [6]. Another retrospective study compared HDF (n=21) and PD (n=21) in 42 children following repair of congenital heart defects [7]. Hemodialfiltration was superior to PD for ultrafiltration, solute clearance and nutritional provision, but no survival benefit was demonstrated between the modalities. Our patients did better on PD than on HDF.

To the best of our knowledge only one study retrospectively reviewed survival outcome in pediatric patients receiving PD, IHD and HDF. Bunchman et al. [8] retrospectively reviewed survival outcome in 226 pediatric patients with ARF receiving various forms of RRT, namely PD (n=59), IHD (n=61) and HDF (n=106). Factors that influenced patient survival included low blood pressure at the initiation of dialysis, vasopressor use, primary disease (improved outcome in those with primary renal disease), and RRT modality (40% survival with HDF, 49% survival with PD and 81% survival with IHD, $P < 0.01$ IHD vs. PD or HDF). Despite the obvious superiority of IHD over the other modalities in that study, the authors concluded that hemodynamic instability imparted a greater prediction of mortality than RRT modality.

Our patients did significantly better on IHD than PD or HDF ($P < 0.01$ vs. HDF and PD). Several explanations may be proposed for our findings. Since the study was retrospective and randomization according to standardized disease severity score was not used, in more severely ill patients PD or HDF might have been preferred with consequently increased mortality. The need for vasopressor support prior to initiation of RRT was used in our study as an indicator of hemodynamic instability. Indeed, vasopressor support prior to initiation of RRT was more prevalent in patients treated with PD and HDF than in those treated with IHD. Vasopressor support was not found to correlate with mortality in our multivariate analysis; therefore, it cannot entirely explain the differences in survival rates between our study groups. Yet, since other criteria for disease severity were not used, the choice of RRT modality could be influenced by the gravity of the patient's condition. Hemodynamic instability during the course of dialysis was more common in the HDF group, but it did not affect survival. Another possible explanation for the superiority of IHD over the other modalities could be the selection of younger patients for PD and HDF. Young age was shown previously to be a poor prognostic factor for outcome in children with ARF [9]. However, in our study no association was found between age and mortality. This finding may be biased by preference for PD or HDF in younger patients. Finally, the difference in group size (the PD group being significantly larger than the IHD and HDF groups) might have caused bias in interpretation of the results.

OR = odds ratio
CI = confidence interval

Table 2. Clinical parameter according to renal replacement modality

		PD	IHD	HDF	*P* value
Median age (mos)		2	51	57	< 0.001
Male: female ratio		1.38	0.33	2.0	0.06
Primary disease	Cardiac (%)	82.6	8.3	27.8	< 0.001
	Sepsis (%)	23.2	8.3	33.3	NS
	Hemato-oncological (%)	1.5	16.7	44.4	< 0.001
Vasopressor use (%)		81.2	16.7	38.9	< 0.001
Complications of dialysis (%)	Hemodynamic instability	2.9	8.3	22.2	< 0.02
	Systemic infection	7.3	8.3	0	NS
	Access failure	8.7	0	0	NS
	Peritonitis	4.3	0	0	NS
	Bleeding	0	0	5.6	NS

PD = peritoneal dialysis, IHD = intermittent hemodialysis, HDF = hemodialfiltration

Nonetheless, along with its limitations, our study has several advantages: namely, a large study group and the availability of all types of RRT modalities in our institution. Intermittent hemodialysis for pediatric patients is usually available in secondary and tertiary care centers and is considered by many to be less favorable for severely ill and very young children, thus there are limited data on this modality. Along with its disadvantages, including rapid fluid and electrolyte shifts, IHD has the advantage of greater efficacy of fluid and metabolic control, lower doses of anticoagulation compared to HDF, and shorter treatment time (patients do not have to be hospitalized in an intensive care unit). Only 3 of 18 (16.6%) of our patients treated with IHD had hemodynamic instability, and this complication was not more frequent in this modality group. The use of appropriate equipment (dialysis tubes containing small blood volumes), volume priming at the start of dialysis, intensive hemodynamic monitoring, blood flow and ultrafiltration rate adjustment as well as vasopressor support may make IHD more tolerable for hemodynamically unstable and very young children. Frequent (daily) hemodialysis sessions with low blood flow and ultrafiltration rates may achieve better fluid control and allow more adequate nutrition.

Keeping in mind the limitations of this study, our findings suggest that when applied to the right patient in an appropri-

ate setting IHD may be a safe and efficient RRT modality in children with ARF. Randomized prospective trials using a uniform illness severity score and standardized criteria for initiation of dialysis are needed to further evaluate the impact of different RRT modalities on outcome in children with ARF.

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