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PERITONEAL DIALYSIS IN CHILDREN WITH ACUTE KIDNEY INJURY: A DEVELOPING COUNTRY EXPERIENCE

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♦ ***Background:*** **Peritoneal dialysis (PD) is the preferred and convenient treatment modality for acute kidney injury (AKI) in children and hemodynamically unstable patients.**
♦ ***Methods:*** **The outcome of acute PD was studied in 57 children (39 boys) with AKI, aged 1 month to 12 years, at a tertiary care center of a teaching hospital in India.**
♦ ***Results:*** **Hemolytic uremic syndrome (36.8%) was the most common cause of AKI, followed by septicemia (24.6%) and acute tubular necrosis (19.3%). Treatment with PD was highly effective in lowering retention markers ($p < 0.001$). Overall mortality was 36.8%. The risk of mortality by multivariate analysis was higher when patients were anuric [odds ratio (OR): 8.2; 95% confidence interval (CI): 1.3 to 49; $p < 0.05$], had septicemia (OR: 3.79; 95% CI: 1.55 to 25.8; $p < 0.05$), or severe infectious complications (OR: 8.2; 95% CI: 1.5 to 42.9; $p < 001$).**
♦ ***Conclusions:*** **Because of its simplicity and feasibility, acute PD is still an appropriate treatment choice for children with AKI in resource-poor settings. Septicemia and severity of AKI are contributory factors to high mortality in pediatric acute kidney injury.**

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KEY WORDS: Acute kidney injury; outcome.

About 5% of all patients admitted to hospitals and 30% of those admitted to intensive care units develop acute kidney injury (AKI) and frequently need renal replacement therapy (1,2). In recent years, the use of continuous renal replacement therapy (CRRT) has been increasingly preferred over peritoneal dialysis (PD) for the pediatric population in most centers in the developed world (3). However, in the resource-poor settings of developing countries, PD is frequently the only dialysis modality available, and it is well accepted because it can be initiated easily, without any need for highly trained personnel or expensive equipment. In a global perspective, PD is used in a far greater number of children with AKI because of those inherent advantages (4), which are particularly relevant in patients with risks for bleeding or hemodynamic instability and posing a technical challenge with respect to vascular access (for example, neonates and young infants) (5). Some earlier reports from developing countries showed variable results (6,7). In the present study, we report a single-center experience with acute PD and analyze the factors associated with outcomes in children treated during the past 5 years.

METHODS

This retrospective analysis includes 57 children with AKI requiring acute PD who were admitted to the tertiary care center of a pediatric teaching hospital between April 2006 and March 2011. The protocol of the study was approved by the local ethics committee, and consent was obtained from parents.

Acute kidney injury was defined according to the modified pediatric RIFLE (risk, injury, failure, loss, end-stage renal disease) criteria (8). A detailed history was recorded, and a clinical examination was performed for every patient. Fluid overload was quantified by the percentage increase relative to the last recorded or estimated pre-illness weight. A complete hemogram, peripheral blood smear, blood urea, serum creatinine, electrolytes, calcium, phosphate, arterial blood gases, electrocardiogram, and chest radiograph were obtained for every patient. Blood urea and serum creatinine measurements were repeated after 20 continuous cycles of dialysis. Urinalysis and cultures were performed in the patients who passed urine. Antistreptolysin O titer, prothrombin time, activated partial thromboplastin time,

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blood culture, and renal ultrasonography were performed as clinically indicated.

Patients were managed using our standard hospital protocol for AKI (including management of fluid and electrolyte disturbances, anemia, and hypertension), and the underlying condition was appropriately addressed. In breastfed infants, breastfeeding was continued. Older infants and children were put on salt restriction and received 100% of the dietary reference intake for energy as carbohydrate and fat. Protein was administered at 1 – 1.5 g/kg daily. In unconscious patients, enteral feeding was given by nasogastric tube until consciousness was regained and spontaneous oral food intake could be resumed.

Peritoneal dialysis was performed in the pediatric intensive care unit by placing a commercially available disposable pediatric-size semi-rigid PD catheter. Maintaining strict aseptic conditions, the catheter was placed percutaneously with the help of a trocar under local anesthesia and connected to the PD set with bags containing PD fluid. We used 5 – 10 mL/kg of PD fluid for the initial 1 – 2 cycles to check for smooth filling and drainage of fluid without leakage. Thereafter, the fill volume was increased to 25 – 30 mL/kg in younger children and 30 – 40 mL/kg in older children. A deep subcutaneous purse-string suture was usually applied around the PD catheter at the site of entry into the peritoneal cavity to minimize the risk of fluid leakage. Leaking catheters were exchanged immediately. Total duration of each cycle was about 45 – 60 minutes (24 cycles daily). A total of 40 – 60 cycles were performed manually by a resident physician, after which a break of 12 – 24 hours was used to observe for the recovery of renal function. Dialysis was resumed if oliguria or anuria and azotemia persisted. The commercial PD solution used contained dextrose 1.7%, Na^+ 130 mmol/L, Ca^{++} 1.5 mmol/L, Mg^{++} 0.75 mmol/L, Cl^- 100 mmol/L, and HCO_3^- 35 mmol/L.

In patients presenting with features of fluid overload (assessed by tachypnea, raised jugular venous pressure, hepatomegaly, basal crepitations, and cardiomegaly in chest radiographs), PD fluid containing 2.5% dextrose was used initially for several exchanges and then switched over to 1.7% once euvolemia was attained. Potassium (4 mmol/L) was added to the PD fluid after the 4th cycle, and serum potassium was monitored. Clinical monitoring during PD included heart rate, blood pressure, oxygen saturation, and continuous electrocardiography on a dynamic monitor. Urine output and biochemical parameters (blood urea, serum creatinine, electrolytes, and arterial blood gases, among others) were monitored. After 40 – 60 continuous cycles, dialysis was electively discontinued in the survivors, and patients were observed without dialysis for further recovery of urine output even if biochemical retention levels were still elevated. This procedure was chosen to minimize treatment cost. At the end of the session, the catheter was removed, the reservoir was emptied, and the peritoneal fluid was sent for culture. Biochemical monitoring continued until normalization, and then patients were discharged.

Standard diagnostic criteria were used to categorize the causes of AKI according to the predominant pathophysiologic mechanism:

- Acute tubular necrosis
- Hemolytic uremic syndrome
- Acute glomerulonephritis
- Obstructive uropathy
- Septicemia

In 1 patient, renal failure was drug-induced (vancomycin intoxication).

Peritonitis was diagnosed based on the presence of abdominal pain, diffuse tenderness, defense, cloudy appearance of effluent, and increased effluent cell count (polymorphonuclear leucocytes > 100 cells/mm^3) with or without culture positivity.

STATISTICAL ANALYSIS

The Z and chi-square tests were used for analysis of proportions, and the Student t-test and Mann–Whitney U-test were used for quantitative variables. Multivariate regression analysis was used to identify the independent risk factors for mortality on dialysis. A *p* value of less than 0.05 was considered significant. The data were analyzed using the SPSS software application (version 16.0: SPSS, Chicago, IL, USA).

RESULTS

The cohort of 57 patients (mean age: 51.3 months; age range: 1 month – 12 years; 39 boys) included 14 patients less than 1 year of age, 23 patients 1 – 5 years of age, and 20 patients more than 5 years of age. Per the RIFLE criteria, 5 patients were formally classified at the Risk stage; 13, at the Injury stage; and 39, at the Failure stage at the time of the decision to start PD. Table 1 presents the clinical and laboratory characteristics of the patients. Table 2 lists the distribution of underlying diseases.

Hemorrhagic dialysate was noted in 5 patients because of trauma to the anterior abdominal wall vessels; it disappeared after few cycles with addition of heparin (250 IU/L) to the PD fluid. Abdominal pain was observed in some patients at the time of catheter insertion and abdomen filling, but it gradually disappeared. Leaking

catheters were immediately exchanged, but the precise number of catheter exchanges was not recorded.

Overall mortality was 36.8%. Deaths occurred 2 – 7 days after hospitalization. Mortality was significantly higher in patients whose AKI was attributable to septicemia than in patients whose AKI had other causes ($p = 0.001$, Table 2).

Table 3 summarizes the univariate analysis of further potential risk factors for a fatal outcome. Age, sex, anemia, hypertension, encephalopathy, and disseminated intravascular coagulation at the initiation of dialysis did not differ significantly between surviving and non-surviving patients, but volume overload ($p = 0.002$) and anuria ($p = 0.009$) were significantly more common in non-survivors. Of 23 patients with significant fluid overload at the start of dialysis, 2 of 7 with less than 10% overload, 9 of 13 with 10% – 20% overload, and 3 of 3 with more than 20% overload did not survive. Compared with the survivor group, the non-survivors also had a significantly higher ($p = 0.001$) proportion of severe complications of infection (septic shock in 10 vs 4, and peritonitis in 6 vs 5). Septic shock was present in all patients who had infection at the time of hospitalization.

Of 11 patients with peritonitis, the peritonitis was present at time of admission in 8 and developed during dialysis in 3. Peritoneal fluid culture revealed *Staphylococcus aureus* in 2 patients, and *Escherichia coli* in 1; cultures were sterile in 8 patients. The isolated organisms were sensitive to ceftriaxone. The likely cause of the low culture yield was administration of antibiotics in most patients before admission to our hospital. All cases of sepsis with shock and peritonitis received intravenous cloxacillin 100 – 150 mg/kg daily and ceftriaxone 50 – 100 mg/kg daily.

Blood urea decreased by 40% and serum creatinine by 34% during the course of dialysis therapy (both trends significant at $p < 0.001$). Mean serum creatinine at both pre- and mid-dialysis (after 20 cycles) was significantly higher in the non-survivors than in the survivors (7.5 mg/dL vs 5.7 mg/dL, $p < 0.05$, and 6.3 mg/dL vs 4.4 mg/dL, $p < 0.005$, respectively). The mean serum phosphorus level was also higher in non-survivors (6.1 mg/dL vs 5.1 mg/dL, $p < 0.05$). Other parameters such as weight, hemoglobin, blood urea, sodium, potassium, calcium, and number of PD cycles did not differ significantly between the groups.

On multivariate regression analysis of factors affecting outcome, the risk of death was increased independently

TABLE 1
Patient and Treatment Characteristics

Variable	Value	
	Mean	Range
Age (months)	51.3±44.3	1.0–144.0
Weight (kg)	13.3±7.4	2.0–32.0
Hemoglobin (g/dL)	8.5±2.5	2.5–15.0
Serum sodium (mmol/L)	129±13	97.0–156.0
Serum potassium (mmol/L)	5.1±1.5	2.2–7.8
Serum calcium (mg/dL)	7.7±1.3	4.4–10.9
Serum phosphate (mg/dL)	5.5±1.6	1.9–12.0
PD cycles (*n*)	55±27	30.0–115.0
Blood urea (mg/dL)		
Pre-dialysis	198±76[a]	60–372
After 20 cycles of PD	146±58[a]	51–310
After last PD cycle	116±53[a]	40–290
Fall from pre-dialytic value (%)	40.3±16.2	6.7–73.4
Serum creatinine (mg/dL)		
Pre-dialysis	5.4[b]	4.5–7.1[b]
After 20 cycles of PD	4.6[a,b]	3.4–6.1[b]
After last PD cycle	3.6[a,b]	2.4–5.3[b]
Fall from pre-dialytic value (%)	34.3±25.9	66.7–84.4

PD = peritoneal dialysis.
[a] Paired Student *t*-test and Mann–Whitney U-test $p < 0.001$ for intergroup comparisons.
[b] Median and interquartile range.

TABLE 2
Causes of Acute Kidney Injury and Patient Survival

Cause	Patients [*n* (%)]		
	Overall (*n*=57)	Survivors (*n*=36)	Non-survivors (*n*=21)
Hemolytic uremic syndrome	21 (36.8)	16 (44.4)	5 (23.8)
Septicemia	14 (24.6)	4 (11.1)	10 (47.6)[a]
Acute tubular necrosis	11 (19.3)	8 (22.2)	3 (14.3)
Acute glomerulonephritis	5 (8.8)	4 (11.1)	1 (4.8)
Obstructive uropathy	5 (8.8)	3 (8.3)	2 (9.5)
Drug-induced (vancomycin)	1 (1.7)	1 (2.8)	0 (0.0)

[a] Significantly different from other categories, $p < 0.001$.

TABLE 3
Comparison of Clinical Parameters Between Survivors and Non-survivors

Parameter	Subgroup	Survivors (*n*=36)	Non-survivors (*n*=21)	Chi-square *p* value
Age group (months)	<12	10 (27.7)	4 (19.0)	0.077
	12–60	15 (41.6)	8 (38.1)	
	>60	11 (30.5)	9 (42.9)	
Sex	Boys	26 (72.2)	13 (61.9)	0.167
	Girls	10 (27.8)	8 (38.1)	
Hypertension	Present	10 (27.8)	6 (28.6)	0.238
	Absent	26 (72.2)	15 (71.4)	
Fluid overload	Present	9 (25.0)	14 (66.7)	0.002
	Absent	27 (75.0)	7 (33.3)	
Anuria	Present	7 (19.4)	11 (52.4)	0.009
	Absent	29 (80.6)	10 (47.6)	
Anemia	Present	23 (63.9)	18 (85.7)	0.053
	Absent	13 (36.1)	3 (14.3)	
Encephalopathy	Present	14 (38.9)	13 (61.9)	0.055
	Absent	22 (61.1)	8 (38.1)	
DIC	Present	6 (16.7)	7 (33.3)	0.093
	Absent	30 (83.3)	14 (66.7)	
Infectious complications	Present	9 (25.0)	16 (76.2)	0.001
	Absent	27 (75.0)	5 (23.8)	

DIC = disseminated intravascular coagulation.

by anuria [odds ratio (OR): 8.2; 95% confidence interval (CI): 1.3 to 49; $p < 0.05$], septicemia at PD start (OR: 3.79; 95% CI: 1.55 to 25.8; $p < 0.05$), and severe infectious complications (septic shock, peritonitis—OR: 8.2; 95% CI: 1.5 to 42.9; $p < 0.01$) at PD start or during the course of the illness.

DISCUSSION

The predominant causes of pediatric AKI vary in different regions of the world (9). We found that hemolytic uremic syndrome, septicemia, and acute tubular necrosis were the predominant causes in our series from a single-center developing-country setting. The common occurrence of gastroenteritis leading to severe dehydration and subsequent acute tubular necrosis and enterohemorrhagic *E. coli* enterocolitis leading to hemolytic uremic syndrome were the main factors for AKI in our rural setting. Although multicenter or even population-based epidemiologic pediatric AKI data do not exist, early single-center studies reported a similar distribution of causes. By contrast, other diagnoses such as post–cardiac surgery AKI, chemotherapy, and organ and bone marrow transplant have become more prevalent in tertiary care units in developed countries in recent years (10–12).

Depending on the facilities and expertise available, PD, intermittent hemodialysis, and CRRT are all currently used for pediatric AKI (13). The CRRT and hemodialysis technologies require vascular access, equipment, technical expertise, and financial resources, all of which largely preclude their use because of non-availability at most centers in developing countries, including ours. Hence, because of its simplicity and affordability, especially where extracorporeal techniques are not available, PD is clearly invaluable in reducing the mortality attributable to AKI in developing countries. The usefulness of PD in the treatment of AKI has also been emphasized in the past by Mohandas and Chellapandian (14), who recommended that it should be instituted as early as possible, thus avoiding the delay caused by referring critically ill patients to nephrologists.

Our center is a good example of the foregoing scenario. Patients are typically referred to us quite late from remote places, often presenting at admission with oliguria or anuria and life-threatening complications such as septic shock and peritonitis.

Because the most prevalent cause of AKI in our setting is severe dehydration secondary to intestinal infections, education of primary health care professionals in the early detection of prerenal AKI and swift institution of fluid resuscitation would be the most effective measure to reduce the incidence of, and death from, AKI.

As the only modality available in our setting, PD is started as soon as possible after hospitalization in

patients with volume overload or with dehydration that does not improve with fluid resuscitation. We use commercially available PD solutions and disposable catheters under aseptic conditions with standardized monitoring of vital functions and biochemical parameters. With respect to the efficacy of PD in our study, blood urea and serum creatinine values decreased significantly throughout the period of dialysis, indicating efficient purification. Mainly because of cost considerations, we limit the total duration of PD in AKI survivors to 2 – 3 days. Our experience with this "minimalistic" approach has been good, typically with complete renal recovery during follow-up.

The mortality rate in children with AKI is highly variable and considered to depend largely on the nature of the underlying disease process rather than on renal failure itself. Children with AKI caused by a renal-limited condition such as post–infectious glomerulonephritis reportedly have a very low mortality rate (<1%), while mortality is usually very high (up to 90%) in patients with AKI related to multiorgan failure (15).

The overall mortality in our study was 36.8%, not dissimilar to that in previous studies, which reported mortality rates of 22.2% – 63.9% in AKI patients treated with PD (16,17). The presence of anuria and features of volume overload at onset were associated with higher mortality. That finding accords with results from a study by Goldstein *et al.* of pediatric CRRT patients. Those authors found significantly higher mortality in patients more marked fluid overload at the time of treatment initiation (18). Both of the foregoing features not only indicate severity, but also reflect the late arrival of patients at hospital. Van Biljon (19) similarly found a higher incidence and duration of anuria in nonsurvivors with AKI. Anochie and Eke (20) found that lack of dialysis and intractable hypertension significantly increased mortality.

We also noted significantly higher pre-dialysis serum creatinine and phosphorus concentrations in the nonsurvivors. Vachvanichsanong *et al.* (21) similarly found a 1.9 times higher risk of mortality when serum creatinine exceeded 2 mg/dL in patients with AKI. Retention levels reflect the duration and severity of AKI, and hence again reflect the overall status of the patient at the time of PD initiation. By contrast, the relative decline of retention parameters did not differ between survivors and nonsurvivors in the present study, implying that the relative efficacy of PD had no independent impact on outcome.

Independent of anuria and fluid overload, the presence of septicemia conferred a greater risk of death in our study. That finding is in keeping with previous experiences of pediatric AKI in developing countries (19,21). Septicemia leads to liberation of various nephrotoxins and may cause vasodilation and relative hypovolemia, thereby aggravating renal failure. The septicemic process also affects other organs, resulting in multiorgan dysfunction, with a detrimental effect on overall prognosis. Indeed, the occurrence of infectious complications (that is, septic shock or peritonitis, either at start of dialysis or during treatment) further multiplies the risk of a fatal outcome. In our patients, peritonitis most likely reflected the septic disease process rather than a complication of PD, even in patients who developed the complication during treatment, because strict aseptic measures were taken during catheter insertion.

CONCLUSIONS

In rural regions of a developing country, PD is well suited for the treatment pediatric AKI. Late patient presentation with uncontrolled systemic or very severe local infection is the most important mortality risk factor in this setting. Hence, to improve pediatric AKI outcomes, what is required is more efficient primary health care, with better identification and earlier referral of children at high risk of AKI, rather than the implementation of costly CRRT infrastructure.

DISCLOSURES

The authors have no financial conflicts of interest to report.

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