Continuous renal replacement therapy for critically ill infants and children

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ABSTRACT

INTRODUCTION: Continuous renal replacement therapy (CRRT) is an important treatment in critically ill children with acute kidney injury (AKI). Over the past decade, CRRT has been the preferred method of renal replacement therapy. We compared children with CRRT-treated adults with AKI in terms of return of kidney function (renal recovery (RR)) and mortality. Furthermore, we compared RR and mortality in children above and below 10 kg.

MATERIAL AND METHODS: The present study was a prospective cohort study of all paediatric patients treated with CRRT over a period of 13 years at the paediatric intensive care unit (PICU), Odense. We obtained data on gender, age, weight, diagnosis, indication for CRRT, need for vasoactive drugs, days using CRRT, days in the PICU, mortality and RR.

RESULTS: A total of 36 critically ill children were recorded. The overall mortality was 39%. The primary diagnosis was sepsis with multiple organ failure. 80% started CRRT due to a combination of anuria/oliguria, high azotemia and fluid overload. Among the 22 surviving patients, eight had continuing renal impairment at discharge from the PICU.

CONCLUSION: CRRT is an effective treatment for the haemodynamically unstable child with AKI. There was no difference in mortality between the group of children above and below 10 kg. In this study, mortality was lower in children than in adults with CRRT-treated AKI. In comparison with adults, fewer children regained kidney function.

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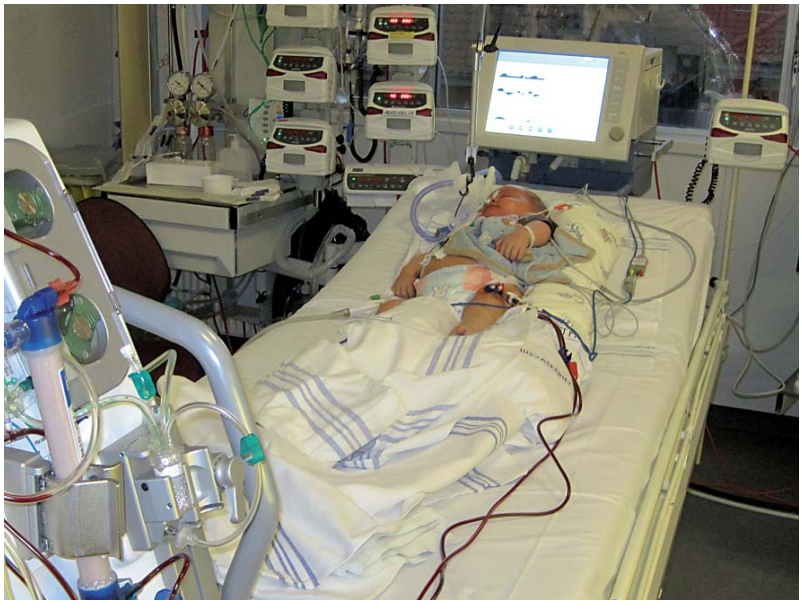
Acute kidney injury (AKI) in critically ill children occurs with increasing frequency as a result of advances in treatment of acute and chronic diseases [1, 2]. AKI is often a serious complication of severe diseases such as sepsis with multiple organ failure (MOF), haemolytic uremic syndrome (HUS), surgery for congenital heart disease or following bone marrow transplantation; but is rarely the result of primary renal disease [3]. The incidence of AKI among critically ill children in a Danish paediatric intensive care unit (PICU) has not previously been described. In foreign studies, the incidence varies between 2.5% and 4.5%, and the associated mortality ranges from 8% to 89% depending on aetiology, treatment modality used and definition of AKI [3, 4]. An accepted definition is the paediatric-modified RIFLE criteria (pRIFLE), which stratifies AKI from mild (RIFLE, R, risk) to severe (RIFLE, F, failure) based on changes in serum creatinine and urine output [5]. Previously, the majority of PICUs used peritoneal dialysis in the treatment of these children. In the past decade, continuous renal replacement therapy (CRRT) has become increasingly used [6]. During CRRT, blood purification is achieved by a combination of ultrafiltration and haemodialysis. An ongoing development of techniques and equipment has resulted in improved haemodynamic tolerance, even in critically ill children weighing less than 3 kg. In the early days of CRRT, blood was passed through the extracorporeal tubing and filter driven by the patient's perfusion pressure via an arterio-venous circuit. Modern extracorporeal circuits are veno-venous, consisting of low-volume tubing and filters intended for children, and controlled by dialysis machines with volume control and accurate pumps.

Despite more than 20 years of experience using CRRT in children, the area is sparsely investigated and it is characterized by studies with small populations. In children, there are no generally accepted treatment indications. In adults, there is a paucity of available evidence about the timing of CRRT treatment.



Child treated with continuous renal replacement therapy.

ORIGINAL ARTICLE

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The PICU at Odense University Hospital (BRITA), Denmark, has been using CRRT in children since 1998. The purpose of this paper was to present the use of CRRT in children and to evaluate the efficacy of such treatment. We compared children with CRRT-treated adults with AKI with respect to return of kidney function (renal recovery (RR)) and mortality. Furthermore, we compared RR and mortality in children above and below 10 kg.

MATERIAL AND METHODS

By means of a central venous catheter – a dialysis catheter – blood was drained from the venous circulation through a filter with a semipermeable membrane and returned to the venous circulation. In children, the size of the dialysis catheter is crucial to a successful implementation of CRRT treatment. Cannulation of the dialysis catheter was performed surgically or percutaneously depending on the child's age and weight to ensure that a properly sized catheter was employed. The catheter was placed preferentially in the subclavian vein or the internal jugular vein. We used size 7 French for infants below 3 kg, 8 French for children 3-15 kg and 11.5 French for children 20-50 kg. In the beginning, the CRRT modus was continuous veno-venous haemodiafiltration (CVVHDF), which later changed in favour of continuous veno-venous haemofiltration (CVVH). As the principles of CRRT have previously been described in Ugeskrift for Læger [7], these are not detailed further.

Since the introduction in April 1998, we have registered the use of CRRT in paediatric patients. This study consisted of a journal review of the registered children below 16 years treated with CRRT in the PICU until 1 April 2011. The following clinical data were recorded: gender, age, premorbid weight, diagnosis, indication for CRRT, the number of vasoactive drugs to support circulation, number of days with CRRT, number of days in the PICU and outcome (discharge from the PICU ± RR).

The following indications for CRRT were used in our department:

- Severe sepsis with anuria/oliguria and rising azotemia
- Fluid overload > 10% and oliguria/anuria
- Organ failure triggered by uraemia
- Hyperkalaemia > 7 mmol/l which did not respond immediately to conventional therapy
- Metabolic disorders (e.g. with hyperammonaemia)
- Refractory hyper- or hyponatraemia
- Tumour lysis syndrome combined with renal failure
- Acute liver failure until the regeneration of the liver, and while waiting for liver transplantation.

Trial registration: not relevant.

RESULTS

In all 36 children with a total of 41 CRRT treatments were included in the study, **Table 1**. The children ranged in age from one day to 14 years on admission, with an average age of six years and eight months and they weighed 3.1 kg to 60 kg. Seven children (20%) weighed less than 5 kg. The overall mortality was 39% (14 patients). The primary diagnosis and mortality of the children grouped by weight above or below 10 kg are shown in **Table 2**. All patients were critically ill at admission, and 53% were in shock (shock defined as persistent hypotension despite fluid resuscitation) and were treated with vasoactive medications in the form of either noradrenaline, adrenaline, dopamine, dobutamine or milrinone, or a combination hereof for circulatory support. Among the survivors, 36% received vasoactive medications, while this was true for 79% of the non-survivors. The majority of patients (80%) started CRRT treatment due to anuria/oliguria/high azotemia/fluid overload. Of these patients, 38% (11 patients) died. Indications for CRRT as well as the number of survivors and RR in the group above and below 10 kg are shown in **Table 3**. Eight patients had renal impairment at discharge from the PICU. One was briefly in haemodialysis before regaining renal function, two died, while five had chronic renal failure (CRF) and were later kidney transplanted. Among the patients who received transplants, none had sepsis as the underlying cause of their AKI.

There was no overall difference in mortality between the group of children above and below 10 kg. There was no difference in the number of days of

TABLE 1

Patient characteristics.

	Total	≤ 10 kg	> 10 kg
Patients, n	36	16	20
Male, n (%)	22 (61)	10 (63)	12 (60)
Age, median (range), months	18.3 (1 d-170)	4.1 (1 d-12)	67 (12-170)
Admission weight, median (range), kg	11.8 (3.1-60)	5.4 (3.1-9.5)	18 (10.9-60)
Vasoactive medicine, n (%)	19 (53)	8 (50)	11 (55)
Adrenaline	9 (25)	2 (13)	7 (35)
Noradrenaline	9 (25)	4 (25)	5 (25)
Dopamine	13 (36)	7 (44)	6 (30)
Dobutamine	12 (33)	5 (31)	7 (35)
Milrinone	5 (14)	2 (13)	3 (15)
Creatinine,[a] median (range), mikromol/l	179 (60-1,033)	174 (63-472)	179 (60-1,033)
BUN,[a] median (range), mmol/l /l	22 (4.9-39.2)	20.7 (4.9-35.4)	24.2 (8-39.2)
Mechanical ventilation, n (%)	29 (81)	16 (100)	13 (65)
Length of CRRT treatment, median (range), days	3 (0.13-47)	4 (0.5-17)	3 (0.13-47)
LOS PICU, median (range), days	6.5 (1-70)	8 (1-60)	6 (1-70)

BUN = blood urea nitrogen; CRRT = continuous renal replacement therapy; d = days; LOS = length of stay; PICU = the paediatric intensive care unit.
a) Missing data for two children below 10 kg, and six children above 10 kg.

CRRT treatment between survivors and non-survivors (six days).

The severity score expressed in terms of Pediatric Index of Mortality score (PIM2) was available for the last 17 patients. The median score was 7% (range 0-93%).

DISCUSSION

CRRT is the most widely used technique today for purifying the blood in critically ill children with AKI. Compared to peritoneal dialysis and intermittent haemodialysis, the treatment allows controlled correction of body fluid and electrolyte balance. This makes it an ideal modality for the haemodynamically unstable child [8] in contrast to intermittent haemodialysis. In addition, the use of CRRT eliminates the risk of peritonitis associated with peritoneal dialysis. Our results show an overall mortality of 39% which correlates well with the studies of Lopez-Herce et al [9] and Pichler et al [10] who observed mortality rates of 36% and 39%, respectively. However, the studies of Goldstein et al [11] and Hayes et al [12] described a mortality of 48% and 45%, respectively. This higher mortality may be attributed to the greater proportion of patients with MOF, post-operative congenital heart cases and bone marrow transplant cases. The survival of the two latter patient groups is inferior to that of the population described herein. Accounting for 11 patients (30%), sepsis with MOF was the most frequent diagnosis in our study. Mortality within this group was 64% (seven patients), Table 2. This is comparable to the mortality in adults with MOF and AKI treated with CRRT [13].In the group of children under 10 kg, we found a mortality of 38%. In the study by Symons et al [14] with 85 patients under 10 kg, mortality was 62%. The discrepancy in the population of small children (< 3 kg) and children with congenital heart disease between Symons' study and ours must be considered when interpreting these results.

Like adults, children with AKI requiring CRRT treatment have a significantly higher mortality than sick children who do not develop severe AKI requiring treatment [4, 15].The overall mortality in children with AKI treated with CRRT is lower than in critically ill adults with CRRT demanding AKI [7, 13]. This can be explained by the high frequency of causes other than sepsis for AKI, such as HUS and malignant diseases.

A potentially important indication for CRRT is severe fluid overload. This was described in a recently published observational study from the Prospective Pediatric Continuous Renal Replacement Therapy Registry [16]. The study shows that children with high levels of fluid overload (> 20%) at CRRT initiation have a significantly higher mortality than children with a degree of fluid overload below 10% (65% and 29%, respectively). The surviving children were on average 13% fluid overloaded, whereas non-survivors were 23% fluid overloaded. Similar findings are seen in other smaller studies [12, 17]. There may be an association between fluid overload and the severity of illness, and randomized studies are needed to reveal any causality.

Fluid overload > 10% as an independent indicator will result in earlier initiation of CRRT at a lesser degree of fluid overload. This must be balanced with the possible complications of treatment. In a prospective study, Santiago [18] demonstrated that CRRT-related complications in children were frequent and that they mainly consisted of hypotension at CRRT initiation, catheter-related problems, bleeding and electrolyte disturbances. Like in adult-based studies [19], the timing of initiation of CRRT is a much discussed topic in the paediatric population. Decisions about early implementation of CRRT and the question of whether degree of fluid overload should be a compelling indicator should be addressed by prospective randomized studies.

TABLE 2

Distribution of patients by diagnosis, led by numbers of survivors respectively for all patients and weight groups. The values are n (%).

	Total		≤ 10 kg		> 10 kg	
Diagnosis	**all**	**survivors**	**all**	**survivors**	**all**	**survivors**
Sepsis	11	4	5	2	6	2
HUS	6	5	2	1	4	4
Malignant disease	6	4	2	1	4	3
Polycystic kidneys	3	1	1	–	2	1
Metabolic disease	2	2	2	2	–	–
Neonatal asphyxia	2	2	2	2	–	–
Chronic kidney disease	1	1	–	–	1	1
Liver disease	1	1	1	1	–	
Congenital heart disease	1	–	–	–	1	–
Malignant hypertension	1	1	–	–	1	1
Trauma	1	–			1	
Post surgery	1	1	1	1	–	–
Total	36 (100)	22 (61)	16 (44)	10 (62)	20 (56)	12 (60)

HUS = haemolytic uraemic syndrome.

TABLE 3

Distribution of surviving patients according to indication for initiation of continuous renal replacement therapy treatment, showing renal recovery at discharge from the Paediatric intensive care unit for all patients and weight groups. The values are n (%).

	Survivors		≤ 10 kg		> 10 kg	
Indication	**all**	**RR**	**all**	**RR**	**all**	**RR**
Anuria/high azotemia/fluid overload	18	11	9	8	9	3
Hyperkalaemia	2	2	–	–	2	2
Acidosis	1	1	–	–	1	1
Liver failure	–	–	–	–	–	–
Hyperammonaemia	1	–	1	–	–	–
Total	22 (100)	14 (64)	10 (45)	8 (80)	12 (55)	6 (50)

RR = renal recovery (regaining renal function).

Development of CRF is usually due to AKI of renal aetiology [15]. Of the five patients (23% of survivors) who developed CRF, three had primary renal disease and none had AKI due to sepsis. For comparison, 8.3% of adults with AKI treated with CRRT developed CRF in the study by Bell et al [20]. An important explanation for the difference in the CRF was the relatively larger proportion of primary renal disease in children than in adults, while children who had sepsis as a triggering cause of AKI had similar or better renal recovery.

CONCLUSION

Our population of CRRT-treated children was small and highly heterogeneous. In this study, the overall survival among children with critical illness and AKI treated with CRRT was better than that observed in adults. Treatment outcome was not inferior among the smallest children < 10 kg compared with children > 10 kg. The percentage of children who regained renal function was lower than that observed in adults because of the higher proportion of children with CRF due to renal aetiology. All surviving children with AKI due to sepsis regained their renal function.

As shown in this study, CRRT treatment of AKI in critically ill children achieves results that are comparable with the best international results. The treatment should be centralized to a few centres in Denmark.

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CONFLICTS OF INTEREST: none

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