Current Practice

Management of acute kidney injury in children

***Randula Ranawaka[1], Kavinda Dayasiri[2], Manoji Gamage[3], David Milford[4]**

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Introduction

Acute kidney injury (AKI) in children is associated with significant morbidity and high mortality[1]. AKI is defined as a sudden deterioration of normal renal function leading to a reduction in glomerular filtration rate (GFR) and impaired regulation of fluid, electrolyte and acid-base balance, together with accumulation of waste products[2]. AKI may adversely affect control of the blood pressure (BP), especially in children with oliguria or anuria[3]. In addition, AKI may be associated with abnormal regulation of the inflammatory process occurring in multi-organ failure[3,4].

As slight changes in serum creatinine (rise of 0.3 mg/dL) are associated with adverse short term (duration in hospital, death) and long-term [chronic kidney disease (CKD)[5]] outcomes, the new terminology 'acute kidney injury' is used instead of 'acute renal failure' emphasizing the spectrum of organ injury[6]. Therefore, clinicians should promptly recognize the early stage of AKI and intervene to minimise progression to organ failure.

Detection of AKI

Serum creatinine, traditionally relied upon to diagnose AKI, is a poor biomarker, as levels only rise significantly when 25–50% of kidney function has been lost[7]. Further, the validity of serum creatinine is limited as it correlates poorly with GFR outside of steady-state filtration (GFR alters fast during AKI)[8], variation with age, sex, and muscle mass[9].

Due to a lack of consensus in the clinical utility of serum creatinine as a marker of renal dysfunction, there have been over 30 definitions for AKI in the literature[9]. Two widely used criteria for paediatric AKI are pRIFLE (paediatric, Risk of renal injury, Injury to kidney, Failure of renal function, Loss of renal function, and End-stage renal disease) and KDIGO (Kidney Disease Improving Global Outcomes) classifications (Tables 1 and 2).

Table 1: ***pRIFLE criteria for detecting AKI in children***

	eCCl	Urine output
Risk	Decrease by 25%	<0.5 ml/kg/hour for 8 hours
Injury	Decrease by 50%	<0.5 ml/kg/hour for 16 hours
Failure	Decrease by 75% or <35 ml/min/1.73m^2	<0.3 ml/kg/hour for 24 hours or anuric for 12 hours
Loss	Persistent kidney failure for >4 weeks	Not applicable
End stage	Persistent kidney failure for >3 months	Not applicable

eCCl: estimated creatinine clearance

Table 2: ***KDIGO criteria for detecting AKI in children***

Stage	Serum creatinine	Urine output
Stage 1	Increase by 1.5-1.9 times from baseline	<0.5 ml/kg/hour for 6-12 hours
Stage 2	Increase by 2- 2.9 times from baseline	<0.5 ml/kg/hour for >12 hours
Stage 3	Increase by 3 times from baseline or serum creatinine >354µmol/L or initiation of RRT, eGFR<35 ml/min/1.73m^2	<0.3 ml/kg/hour for >24 hours or anuric for 12 hours

RRT: renal replacement therapy, eGFR: estimated glomerular filtration rate

[1]*Department of Paediatrics, Faculty of Medicine, University of Colombo, Sri Lanka,* [2]*The John Radcliffe Hospital, Oxford, United Kingdom,* [3]*Nutrition Unit, Lady Ridgeway Hospital for Children, Colombo, Sri Lanka,* [4]*Department of Nephrology, Birmingham Children's Hospital, United Kingdom*

**Correspondence:* rrandula@yahoo.com

https://orcid.org/0000-0002-4382-489X

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The pRIFLE classification was developed and validated based on changes in estimated GFR and urine output[10] and was adapted from the adult RIFLE criteria[11]. The KDIGO guidelines[2] define and stage AKI according to the change in serum creatinine level and urine output. These classifications are of limited use when there is no baseline value because a patient has not had a previously recorded creatinine. Under these circumstances it is appropriate to consider the child as having previously had a normal GFR (e.g. 120 ml/min/1.73m^2); if the child's height is known it is possible to impute the baseline estimated GFR from the Schwartz formula (eGFR= height (cm) x k /creatinine (µmol)[12].

Management

Current therapy for AKI in children includes provision of nutritional support, limitation of nephrotoxic medication, adequate kidney perfusion, and management of AKI sequelae (fluid overload, electrolyte anomalies, acidosis and uraemia). Careful history, physical examination and basic investigations are important in determining underlying aetiologies for AKI. However, the key to a successful outcome is determined by the institution of treatment following early detection and treatment of underlying aetiologies such as sepsis, hypovolaemia, renal immunological diagnoses and urinary tract obstruction. If urinary tract obstruction is suspected, an ultrasound evaluation should ideally be performed within 24 hours of hospital admission[13].

Serum creatinine and urine output should be measured in all children who are at risk of kidney injury (hypovolaemia, sepsis, renal transplant, stem cell transplant) and changes from baseline should be acted on at an early stage[14]. Urine testing is extremely useful and the result should be recorded on admission. Early referral to a paediatric nephrologist has also been shown to be associated with improved renal survival and long-term outcome[15].

The pharmacological management of AKI in children is quite debatable. Though it is common practice to treat fluid overload with loop diuretics, routine use is not recommended given the poor outcomes in children with hypovolaemia. 'Low-dose' dopamine is in common usage in intensive care units but studies have thus far not provided proven evidence of prevention or amelioration of kidney injury[16].

Children with AKI should be referred for renal replacement therapy (RRT)[17] when they have refractory fluid overload, hyperkalaemia, hyponatraemia, uraemia or acidosis. Continuous haemofiltration /diafiltraton and/or peritoneal dialysis (PD) are indicated for haemodynamically unstable children with AKI. Intermittent haemodialysis (HD) is only suitable for haemodynamically stable patients given the risk of hypotension[18].

Medical nutrition therapy should be an integral part of the management of AKI[19]. The aim of such therapy is to preserve protein stores, prevent metabolic derangements and nutritional deficiencies. Protein of at least 1g/kg per day is indicated for children with AKI[20]. Children on RRT need higher protein intake (1.5 -2g/kg) as all forms of dialysis contribute to protein losses[21]. Patients with oliguric and anuric AKI usually require sodium and potassium restriction. Children undergoing any form of RRT should receive supplemental water soluble vitamins above the recommended dietary allowances[22].

Prevention of AKI is important and clinicians need to be vigilant for the nephrotoxic effect of medications such as aminoglycosides, non-steroidal anti-inflammatory drugs, calcineurin inhibitors, angiotensin converting enzyme inhibitors and angiotensin receptor blockers. These medications are better not used if the children are dehydrated or hypovolaemic and hence at risk of AKI. Appropriate fluid management in children with hypovolaemia and sepsis is required as both dehydration as well as fluid overload can increase morbidity and mortality.

All children with AKI need to be followed up to confirm full recovery, detect recurrences, if any, and monitor for the development of CKD. Urine analysis and BP are important monitoring parameters for early detection of CKD.

Neonatal AKI

In a healthy term neonate, the GFR increases from 10-20 ml/min/1.73 m^2 on first day of life to 30-40 ml/min/1.73 m^2 by 2 weeks, and then increases steadily over the first few months, reaching the adult GFR by 2 years of age[23]. In preterm babies, GFR at birth is lower and the increase slower compared to term infants[24].

Neonatal AKI needs a systematic approach, which commonly involves assessing pre-renal, intrinsic, and post- renal aetiologies. There are sparse data on management of neonatal AKI. In asphyxiated neonates, theophylline can prevent AKI by inhibiting the adenosine-induced vasoconstriction[25]. Studies have shown that prophylactic theophylline, given early after birth, would help to improve renal outcomes[25,26].

Many practising physicians used diuretics in neonates with AKI in attempts to maintain urine output. Even though the evidence on improved outcome is sparse, a trial of loop diuretics in oliguric newborns with AKI is warranted due to the practical difficulties of RRT[27]. More randomized multi-centre clinical trials of these drugs in newborns are really required.

In neonates with ischaemic AKI (e.g. following sepsis, asphyxia, post-cardiac surgery), maintenance of optimal mean arterial pressure with avoidance of nephrotoxic agents[28], is the single most important step in the management. At present, PD is the modality of choice for RRT in neonates[29].

Advances in novel bio-markers

It is crucial that clinicians identify AKI early in its course to prevent high mortality[30]. Due to deficiencies of serum creatinine as a sensitive and early marker of AKI, much of the current attention has been directed towards identifying early markers of renal dysfunction. Recent research has identified several promising novel AKI biomarkers including: neutrophil gelatinase-associated lipocalin[31], kidney injury molecule 1[32], liver-type fatty acid-binding protein, interleukin 18, cystatin C and neutrophil elastase-2 Studies have shown that combined use of risk stratification and new biomarkers are associated with improved outcomes in paediatric AKI[33].

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