Canadian Society of Nephrology/
Société canadienne de néphrologie
CSN/SCN

CAPN
Canadian Association of Paediatric Nephrologists
Association des Néphrologues Pédiatriques du Canada
ANPC

Canadian Association of Paediatric Nephrologists COVID-19 Rapid Response

Guidelines for Management of Acute Kidney Injury in children

Rapid Guidelines Process

- The leadership of CAPN,which is affiliated with the CSN, solicited a team of clinicians and researchers with expertise in paediatric AKI and acute KRT.
- The goal was to adapt the guidelines recently adopted for Canadian adult patients for paediatric-specific settings.
- These included specific COVID-19-related themes that are relevant to AKI and KRT in a Canadian setting, as determined by a group of senior renal leaders.
- The revised paediatric guidelines were reviewed by a group of clinicians with deep expertise in paediatric AKI and acute KRT.

Introduction

- Reports of children with symptomatic COVID-19 infections are growing but still remain scarce.
- At this time, there is no clear data to suggest the incidence of AKI in this population.
- The goal of the guidelines is to provide the best possible care for paediatric patients with kidney disease, considering how best to ensure the safety of the healthcare team.

COVID-19 and AKI in Children

- Pediatric Data from China :
  - Incidence ~2% of all cases <18 years of age.
  - 1.7% of positive cases required ICU in children. All 3 had pre-existing conditions.
  - The likelihood of critical disease was highest in children aged less than 1 year (~1.9%).
  - Case reports : 2 infants one with mild AKI and another required dialysis both recovered.

COVID-19 and AKI in Children

- Pediatric Data from Europe
  - Paediatric COVID-19 was identified in ~1% of all confirmed cases from Madrid.No AKI data
- Pediatric Data from North America
  - A cross-sectional study from 46 US and Canadian PICU units showed 48 cases (none in canada) . Most of these patients (83%) had pre-existing comorbidities. 1 patient did require ECMO and two patients (4%) died.
  - COVID-19-associated rhabdomyolysis reported in one patient but didn't lead to AKI

COVID-19 and AKI in Adult

- The reported incidence of AKI across available studies is quite variable and ranges from 0.5% to 39% .
- Studies that have reported rates of AKI largely involved patients hospitalized with COVID-19.
- Majority of AKI patients were on KRT.

Paediatric Multi-Inflammatory Syndrome

- Children presenting with features similar to Kawasaki Disease or toxic shock syndrome, associated with COVID-19 infection
- Originally in clusters in Western Europe, subsequently reported around the world
- Case series inconsistently report kidney function in these patients, though there have been some reports of AKI associated with MIS
- Overall, a rare entity, and the incidence of renal involvement is unclear

1. Planning for Capacity to Provide Acute KRT

- **1.1 We suggest to plan for a 25-30% increase in the acute pediatric KRT capacity even though the prevalence of pediatric COVID-19 is low as this would help provide flexibility to allocate resources to adult centers as needed based on how the pandemic evolves over time.**

Rationale

- Report of children with symptomatic COVID-19 infections are growing but still remain scarce. At this time, there are no clear data to suggest the incidence of AKI in this population. This is likely related to low incidence and severity of this disease in children.
- Unpublished CSN adult guidelines suggested a 30% increase in capacity of KRT [1]. However, COVID-19 incidence is trending down at the time of this publication. Should there be a reemergence of severe COVID-19 hospitalization rates in adults requiring increased KRT needs, consideration should be given to redeploying staff and reallocating equipment from paediatric centres to support adult patients requiring KRT, provided severe paediatric COVID-19 incidence remains unchanged.

2. Timing and Modality of KRT

- **2.4 We suggest that traditional indications for starting KRT should be used in patients with COVID-19.**
- **2.5 We suggest that, during the COVID-19 pandemic, nephrology programs should primarily continue to utilize the acute KRT modalities with which they have the most expertise.**
- **2.5 We suggest not using hemoperfusion for COVID-19 patients.**

Rationale

- A sepsis-like syndrome, characterised by profound shock, and presumably related to high-levels of circulating cytokines (referred to as 'cytokine storm'), has been reported as a frequent complication of COVID-19 [23,60] including reports of "hyperinflammatory shock" related to Multi-Inflammatory Syndrome in children [27–29,31–33,61].
- KRT modalities that include convection, such as high-volume hemofiltration, are superior at removing larger molecules, such as cytokines; however, both pro- and anti-inflammatory cytokines are removed, and clinical outcomes are not improved in data from randomized trials of septic patients without COVID-19 [62,63].
- In addition, high-volume hemofiltration involves the use of very large volumes of replacement solution, which could become scarce in the context of increased KRT use during the COVID-19 pandemic.
- Paediatric literature does not suggest a survival benefit attributable to one specific CRRT modality over another in critically ill children [64,65]. In the absence of persuasive evidence of benefit for any particular modality, programs should use the KRT modalities with which they have the greatest expertise and those for which they have adequate staff.

2.1 Anticoagulation for KRT

- **2.14 We suggest, for programs with experience using regional citrate anticoagulation (RCA) for CKRT, consider using it based on the clinical status of each patient with COVID-19.**
- **2.16 We suggest that programs that do not have experience using regional citrate anticoagulation protocols for CKRT not implement them immediately.**
- **2.17 We suggest that low molecular weight heparin may be considered with caution for CKRT anticoagulation in children with COVID-19 if providers already have experience using it.**

Rationale

- In similar circumstances, low-molecular weight-heparin is already in widespread use for out-patient intermittent hemodialysis and nocturnal dialysis in adults and there have been reports of successful use in chronic hemodialysis in children as well [76,77].
- With this experience, there is consideration that LMWH could be used for CKRT or for acute intermittent HD or SLED. This requires close collaboration with other disciplines to develop or adapt dosing protocols, recognition by the whole team that the anticoagulation effect may be prolonged beyond the end of dialysis, and recognition that quantification of its effect, if needed (e.g., if bleeding occurs) is by anti Xa level rather than by PTT.
- There are no studies of LMWH use in CKRT in children, and caution and close monitoring should be exercised if it is to be used. It is recommended that only centres with experience using LMWH in CKRT consider its use during the COVID-19 pandemic.

3. Delaying the need for KRT

- **3.1 We suggest that pre-emptive KRT (i.e. before an acute indication is present) should not be used.**
- **3.2 We suggest that, in the context of an overall shortage of KRT resources, clinicians consider using high dose diuretics (including serial nephron blockade, the use of a loop and a thiazide-type diuretic together) and off-label use of potassium-binding resins to delay the need for KRT, depending on the clinical context and resource availability (46)**
- **3.3 We suggest, in the context of a shortage of CKRT machines, using intermittent hemodialysis (IHD) in patients in whom intradialytic hypotension is likely to be manageable with increased vasopressor dosing.**
- **3.4 We suggest, in the context of a shortage of CKRT machines, using IHD machines for prolonged HD section or SLED for hemodynamically unstable patients.**
- **3.5 We suggest, in the context of a shortage of CKRT machines at centres that use both CKRT or prolonged IHD (or SLED) for hemodynamically unstable patients.**
- **3.6 We suggest, in the context of a shortage of CKRT machines, consider using CKRT machines to provide shorter sessions of CKRT for 2 patients in 24 hours.**

Rationale

- In outpatients, an increased risk of intestinal ischaemia, thrombosis for users of sodium-polystyrene-sulphonate (SPS, Kayexalate), compared with non-users, has been noted in observational research: the increased risk was 5.6 events per thousand patient-years in stable outpatients, but the hazard ratio was 4.9 (95% confidence intervals 1.1- 22.3) [83].
- The team should be alerted to the possibility that this incremental risk may be higher in patients with COVID-19 because of the higher baseline risk of thrombosis; they should also be aware that because of this tendency, the occurrence of intestinal thrombosis in a patient treated with potassium binders should not necessarily be attributed to the use of the binder.

3.1 Shortage of IHD/SLED Machines

- **3.12 We suggest, in the context of a shortage of capacity for intermittent HD or SLED, that centres consider redeploying resources by decreasing the frequency of dialysis for selected stable out-patients treated with maintenance HD patients, as outlined in the CSN COVID- 19 Rapid Response Team recommendations for outpatient HD** [88]
- **3.13 We suggest, in the context of a shortage of capacity for intermittent HD or SLED machines, that centres review and consider using outdated, but still operable, dialysis machines and portable RO units.**
- **3.14 We suggest, in the context of a shortage of staff for intermittent HD or SLED dialysis-trained staff be redeployed from other areas to provide necessary support.**
- **3.15 We suggest, in the context of a shortage of machines for intermittent HD or SLED, that centres consider using any available home HD machine stockpile.**
- **3.16 We suggest, in the context of a shortage of machines for intermittent HD or SLED, that centres consider whether home hemodialysis patients who use their machines on alternate days would be willing to share a machine, allowing the return of a machine to the program for acute KRT.**

Rationale

- There are potential barriers to this approach including the near- inevitability of a breach in patient confidentiality and the potential for COVID-19 transmission between patients who have agreed to share machines.
- As above, staff training on the unfamiliar machine will also likely be necessary. These machines may also be considered for allocation to adult patients if needed.