BEAUMONT HOSPITAL

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RCSI

Guidance for continuous renal replacement therapy (CRRT) in the Intensive Care management of patients during the SARS-2-Covid-19 pandemic in the Republic of Ireland

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Introduction

- Patients with COVID-19 are at increased risk of acute kidney injury (AKI).
- The need to provide renal replacement therapy (RRT) to an increasing number of critically ill patients during the COVID-19 pandemic is likely to exceed resource capacity, as has been experienced in other countries.
- Baxter is currently the sole supplier of CRRT kits in the Republic of Ireland. Due to the increased international demand for CRRT **it is anticipated that there will be a shortage of CRRT consumables for the foreseeable future.**
- Strategies to maximise our capacity to deliver RRT in critical care units with limited resources are required. These include:

    1. Tailored management of AKI in COVID to reduce risk of AKI
    2. CRRT delay or avoidance by maximising medical therapy
    3. Maximising efficiency of CRRT
    4. Use of alternate RRT modalities, including intermittent haemodialysis (IHD) and acute peritoneal dialysis (PD)

Tailored management of AKI in COVID to reduce risk of AKI

- Patients with COVID-19 have additional risk factors for AKI, including:
    - Patients often volume depleted at presentation due to prolonged fevers, hyperventilation and poor intake.
    - Increased insensible losses due to fever, non-invasive ventilation, high-flow O_2. May be several litres per day.
    - Volume depletion compounded by diuretic therapy and fluid restriction in setting of ongoing high insensible losses.
    - Renal microthrombi, thrombotic microangiopathy noted in some COVID-19 patients.
    - Evidence for direct renal infection by SARS-Cov2 virus.

- Fluid management in the setting of AKI and COVID-19:
    - The goal of fluid management is to maintain euvolemia.
    - Hypovolaemia should be avoided, as it impairs gas exchange and increases risk of AKI.
    - Avoid strict 'zero balance' fluid targets in patients with hyperpyrexia, focus instead on avoidance of large positive balance.
    - Assessment of volume status should take account of respiratory status as well as renal function. Perform a daily volume assessment.
    - Methods of volume assessment in the mechanically ventilated patient include passive leg raise, pulse pressure variation, echocardiographic assessment of inferior vena cava diameter and oesophageal doppler monitoring. Central venous pressure (CVP) measurements are not considered a reliable indicator of intravascular fluid status or fluid responsiveness in the setting of high levels of PEEP and ARDS.
    - Where respiratory function permits, and when clinical assessment is consistent with volume depletion, administer a fluid challenge of an isotonic crystalloid solution to determine if AKI is volume responsive.

- The use of crystalloids is recommended over colloids in covid-19 patients with shock. Hydroxyethyl starches should not be given to these patients[1].
- Do not administer IV fluids without a fluid assessment.

CRRT delay or avoidance by maximising medical therapy

- Delay of initiation of CRRT in critically ill patients is not associated with an increased mortality rate[2].
- Standard indications for renal replacement therapy include refractory fluid overload, life-threatening hyperkalaemia and severe metabolic acidosis.
- Maximising medical management of these entities may defer or avoid need for RRT.
- **Metabolic acidosis**
  - Sodium bicarbonate is a temporizing intervention to avert RRT in the setting of AKI[3] .
  - IV sodium bicarbonate infusion to maintain arterial pH >7.30.
  - Higher concentration (e.g. 4.2%) preferred to minimise volume (125–250 mL over 30 min, max of 1L over 24 hours). To make a 4.2% infusion add equal volumes of sodium bicarbonate 8.4% solution to 5% dextrose.
- **Hyperkalaemia**
  - Multi-modal approach including the use of a background insulin infusion and regular β-2 agonist inhaled/nebulised therapy.
  - For acute life-threatening hyperkalaemia:
    - Calcium – Ca gluconate 10% 10ml (contains 2.2mmol Ca) or Ca chloride 10% 10ml (contains 6.8mmol Ca)
    - Insulin - 10-15 units of actrapid in 50ml 50% dextrose given over 20 minutes
    - Sodium bicarbonate – 50ml 8% $NaHCO_3$
  - In addition to above, the novel potassium binder sodium zirconium may be used to treat acute hyperkalaemia, to delay or prevent the need for RRT in circumstances where RRT is not available.
  - Sodium zirconium 10g PO will reduce serum potassium over 1-4 hours. Requires a functioning gastrointestinal tract. If unavailable sodium patiromer 8.4g PO is an alternative potassium binder.
- **Refractory fluid overload**
  - Attempts at achieving a negative daily fluid balance should be guided by the current haemodynamic status of the patient.
  - High dose intravenous diuretics in combination may delay need for RRT.
  - Escalating doses up to furosemide 240mg TDS IV *plus* Metolazone 5mg BD PO may be used.
  - Escalating infusion of furosemide 80mg bolus + 30mg/hr *plus* Metolazone 5mg BD PO may also be used.
  - Diuretics are not nephrotoxic but can cause AKI due to hypovolaemia.

Maximising efficiency of CRRT

- A conservative approach to RRT should be adopted to conserve stocks of replacement fluids and kits. **All staff involved in the delivery of CRRT – ICU nurses, dialysis nurses, medical staff – need to be informed of expected critical shortage of CRRT consumables** and should have a focus on preserving filter life.
- Discuss RRT modality options with covering nephrologist. Are alternatives to CRRT appropriate?
- **Do not electively change filters at 3 days**. Allow run until filter circuit clots or patient no longer requires RRT.
- It should become standard protocol in all ICUs nationally that if the filter circuit clots prematurely that the ICU team should be asked before re-starting CRRT with a new kit.
- **Stopping CRRT to allow for transfer to scan etc should only be done if absolutely indicated.**
- Review daily the indications and type of RRT.
- Prompt response to filter alarms is associated with prolonged filter life.
- Close collaboration with renal team and identification of patients who are suitable to switch to IHD, medical management or step down to renal ward.
- A centralised distribution of CRRT consumables is planned which will allow for improved distribution based on current requirement. The ICU Bed Information System (BIS) will facilitate this and all ICUs are requested to input data on a daily basis.

- *CRRT Modalities*
    - CRRT fluid use should be minimised – there will likely be a shortage of solutions.
    - CVVH – pure convection. Most efficient in terms of substitution fluid use.
    - CVVHD – predominantly diffusion.
    - CVVH(D)F – combination of diffusion and convection to increase solute management. Highest solution requirement.

- *Prescription*
    - Adjust depending on local supplies. CVVH, CVVHD and CVVHDF all acceptable modalities and are largely equivalent. In terms of prolonging filter lifespan it is likely that CVVH and CVVHDF when used with regional citrate anticoagulation are equivalent.
    - Most efficient modality in terms of fluid use is CVVH with regional citrate anticoagulation. However this is not in use in most centres.
    - Protocol for CVVH with regional citrate anticoagulation is available to share with centres that wish to adopt in the case that there is a critical shortage of CRRT solutions.
- *Dose*
    - Higher doses of RRT do not improve outcomes in AKI[4].
    - Recommended starting dose: – CRRT: 25mL/kg/hr of effluent rate, then adjusted daily.
    - Adjust dose daily – typically aim for urea 20–25mmol/L and serum creatinine 200–300µmol/L.
    - Note: urea < 10 mmol/L, creat <150 µmol/L or frequent necessity to replace phosphate or other electrolytes suggest dose is too high.

- Consider an interruption in CRRT if patient urine output > 400ml/day with good small solute and fluid control, particularly after several days of continuous treatment.

- *Vascular access*
  - Optimal vascular access is essential to prevent premature filter clotting – for jugular catheters the tip should be in the lower SVC*, just above the right atrium.*
  - The vascath should be checked for good flow through both ports prior to suturing the line.
  - Site
    - first choice: right internal jugular
    - second choice if proning likely: left internal jugular vein
    - second choice if proning unlikely: femoral vein.
  - Choice of catheter
    - femoral vein: 25-cm catheter
    - right internal jugular vein: 15-cm catheter
    - left internal jugular vein: 20-cm catheter (25cm in larger patients).
  - If prismaflex machine is alarming "access extremely negative" or "return pressure extremely positive" then it is most likely an issue with the line. Review line position on CXR. Check for kinking on the line or withdraw the line 1-2cm in case it is against vessel wall. If no issue with the line is identified then consider a fluid bolus if hypovolaemia is suspected or potentially decreasing the blood flow rate temporarily.

- *Anticoagulation*
  - COVID-19 infection may induce a hypercoagulable state, with frequent clotting of CRRT circuits observed.
  - Regional citrate anticoagulation is associated with prolonged filter half-life as compared to systemic heparin[5]. Can be combined with full systemic anticoagulation, if separately indicated.
  - Mild-moderate liver dysfunction is NOT an automatic contraindication to citrate based CRRT[6]. Close attention must be paid to acid-base balance and electrolytes in this circumstance.
  - In cases of frequent clotting:
    - optimise vascular access
    - consider combination anticoagulation: citrate and heparin (systemic or via circuit); argatroban
    - increase pre-/post-filter replacement ratio (CVVH).
  - There is emerging evidence to suggest that there is increased factor VIII activity in covid-19 infections[7]. In this case **aPTT measurements may not be an accurate reflection of in vivo heparin activity** i.e. the aPTT may underestimate the effect of heparin. Anti-Xa levels will more accurately reflect heparin effect however this test is only available in a limited number of hospitals nationally. If it appears that the patient has "heparin resistance" this may need to be considered and the target aPPTR should be kept within the lower range if systemic anticoagulation is being given only for the purposes of CRRT. In the case of systemic anticoagulation for other reasons we advise discussion with a haematologist.

Alternate RRT modalities: IHD and acute PD

- *Intermittent haemodialysis*
  - Haemodynamic instability may not be a prominent feature in COVID-19 patients.
  - IHD may often be possible, even if patient is on vasopressors – discuss with nephrology.
  - Efforts should be made to maximise capacity to deliver IHD at each unit, with specific consideration given to:
    - Number of haemodialysis machines.
    - Anticoagulation, pumps and consumables.
    - Trained dialysis nurses.
    - Reverse osmosis (RO) units to provide ultrapure water.
    - High flow / pressure water access points within COVID and non-COVID areas.
  - All forms of intermittent RRT can be provided with conventional haemodialysis machines and usual CRRT machines.
  - These machines may be used for up to three patients in a 24-hour period.
  - A new set of consumables is needed each time.

- *Peritoneal dialysis*
  - May be an option in circumstances of severe stock shortages.
  - The insertion technique for the PD catheter should be percutaneous.
  - Patients must lie on their back during PD, so generally not suitable for patients that require proning
  - In extremis, two strategies may be considered in prone patients:
    -turn more frequently and deliver fluid, leaving in situ when turned back.
    -use the 8-hour window between turns to deliver rapid exchanges.

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