Clinical Application of CRRT for Infants and Children

Geoffrey Fleming
Daryl Ingram
Jordan Symons

22nd International Conference on Advances in Critical Care Nephrology
San Diego 2017
Introduction

• Pediatric CRRT is no longer a “novel” therapy
  – Many years of experience
  – Literature to support our approach
• Each patient presents unique challenges
  – Adapting standards to clinical situations
  – Adjusting approach to address complications
• Each program faces its own issues
  – Technology, support, staffing, acuity, etc.
Format for the Session

• Present a clinical case or question
• Discuss as a group
• Review our perspective
  – Case resolution
  – Points illustrated
  – Data/literature review where available
• Summarize at the end
Case #1

CRRT AND ECMO
Case # 1– Clinical Scenario

• 14 years old, previously healthy male with h/o URI for 4-5 days, sore throat and cough.
• Transferred from outside hospital to PICU with hypoxic respiratory failure, sepsis, necrotizing pneumonia
• Cannulated for VA-ECMO
• VA-ECMO with flows currently at 3.5 Liters/Min
  – Pressures Pre-membrane 300
  – Post-membrane 310
• Weight (actual) 61.2kg
• Intubated – Vent settings R-18, 30/10,30% O2
Case # 1– Clinical Scenario (Continued)

• Urine output noted to go down
• Serum creatinine rising
  – 0.7mg/dL → 1.3mg/dL
• Worsening edema on exam
• PICU team contacts you regarding AKI and possible need for RRT
Case # 1– Discussion

• How do you address the need for RRT when a patient is on ECMO?
• What technical challenges must you anticipate?
• How do you coordinate care between teams?
CRRT and ECMO: Blood Pathway

- Blood Flow
  - ECMO Venous – Pull line, Drain line
  - ECMO Arterial – Return line, Re-infuse line
  - CRRT Arterial (Access) – Pull line
  - CRRT Venous (Return) – Re-infuse line
CRRT and ECMO: Issues with the ECMO Circuit

• Negative Pressure with Centrifugal pumps
  – CRRT circuit standard pressure mode
  – Lower pressures, likely less pressure alarms
  – Danger of **AIR** if disconnected
CRRT and ECMO: Issues with the ECMO Circuit

- Positive Pressure (roller head or centrifugal)
  - CRRT circuit positive pressure mode
  - High ECMO pressures will influence CRRT pressures, likely more pressure alarms
  - Danger of Exsanguination if disconnected
CRRT and ECMO: Ideal Connection

1. Least risk for introducing air

2. Minimize pressure alarms on CRRT
   – Connection location will determine Arterial pressure
     • Stopcocks and/or restrictors
   – Venous
     • NO restrictors
ECMO Circuit Access Centrifugal Pump

Color-coded according to color of labels

- Patient
  - Venous Sampling
  - Bladder Air Port
  - Bladder Transducer

- Arterial CDI
  - Arterial CDI Access
  - Arterial CDI Return

- Membrane
  - Post-Membrane Transducer
  - Hemofilter Access
  - CRRT Return
  - Plasmapheresis Return
  - CRRT Access
  - Plasmapheresis Access
  - Hemofilter Return

- Centrifugal Pump

- Continuous Infusions
  - Intermittent Fluids
  - Lab Sampling
  - Blood Products

- Heparin

- = Positive Pressure
- = Negative Pressure
Case # 1– Additional Discussion

- Do you perform ECMO and CRRT at your center?
- What challenges and issues have you needed to address when considering RRT for patients receiving ECMO?
Case # 1– Summary

- ECMO circuit determines CRRT pressures
- Ideal connection site: post pump/pre oxygenator
- Connections secure, frequent checks
- Standardized the process
  - Options for high pressures
Case # 2

CRRT FOR NEONATES
Case # 2— Clinical Scenario

• 3 week old term female with perinatal asphyxia (abruption) and chorioamnionitis; looks septic
• Cr has been rising (1mg/dL $\rightarrow$ 3.2mg/dL)
• Weight increased (BW 3.2kg $\rightarrow$ 4.1kg); edematous
• Increased ventilator support; urine dwindling
Case # 2– Discussion

• Does this patient require renal replacement?
• What modality would be best for support?
• What issues and complications must we watch for if we go forward with renal replacement?
Renal Support Options

• Hemodialysis, Peritoneal Dialysis, CRRT
• Each has advantages & disadvantages
• Choice is guided by
  – Patient Characteristics
    • Disease/Symptoms
    • Hemodynamic stability
  – Goals of therapy
    • Fluid removal
    • Electrolyte correction
    • Toxin removal
  – Availability, expertise, cost
CRRT for Neonates: A Series of Challenges

• Small patient with small blood volume
• Equipment designed for bigger people
• No specific protocols
• Complications may be magnified
• No clear guidelines
• Limited outcome data
Prescribing CRRT: Special Neonatal Considerations

- Vascular access
- Blood Prime
- Blood flow rates
- Fluids/Modality (CVVH vs. CVVHD vs. CVVHDF)
- Ultrafiltration goals
- Anticoagulation
- Filter/membrane
Neonatal CRRT Access

• Access size is key to success
  – Frequent clotting and circuit down time is time without therapy

• Vessel size
  – French ~3x diameter of vessel in mm
  – Bedside ultrasound nearly universally available
  – SVC is bigger than femoral vein

• Low resistance
  – Resistance ~8lη/2r^4
  – So, the biggest and shortest catheter should be best
Access Considerations

• Internal Jugular
  – Very accessible
  – Large caliber (SVC)
  – Great flows
  – Low recirculation rate
  – Risk for pneumothorax
  – Cardiac monitoring may take precedence

• Femoral
  – Usually accessible
  – Smaller than SVC
  – Flows may be diminished by:
    • Abdominal pressures
    • Patient movement
  – Risk for retroperitoneal hemorrhage
  – Higher recirculation rate

• Subclavian: Many feel current double lumen vas cath are too stiff to make the turn into the SVC and I don’t personally use them. Although they are used in some centers. Better for bigger kids likely.
Successful continuous renal replacement therapy using two single-lumen catheters in neonates and infants with cardiac disease

Kamal El Masri • Kimberly Jackson • Santiago Borasino • Mark Law • David Askenazi • Jeffrey Alten


• In patients with cardiac lesions
  • concerns re upper vessels needed for future heart transplant
  • Femoral vessels may not be big enough for an 8F DLC
    – Risk for clots
    – Risk for future inability to perform catheterizations

• Reported on 6 babies
  – PD failed
  – All had 2 single lumen catheters
    • Most ran for over 60 hours....
    • Average circuit life 55.2 hr (double circuit life for infants < 5 kg in ppCRRT registry)
Blood Prime for Pediatric CRRT

- Smaller patients (e.g. <10-15kg) require blood priming to prevent hypotension/hemodilution
  - Circuit volume > 10-15% patient blood volume

- Example
  - 5 kg infant: Blood Volume (BV) 400ml (80ml/kg)
  - Extracorporeal circuit volume 100 ml (25% of BV)
  - Technique: prime first with saline, then blood/albumin mix to Hct of ~35
Blood Prime Increases Risks

- Blood product exposure – possibly repeated
- Biochemical imbalances
  - HYPOCALCEMIA
    - Citrate anticoagulant in PRBCs
  - HYPERKALEMIA
    - K+ release from RBCs – more over time (older unit)
  - ACIDEMIA
- Increases risk for bradykinin release syndrome
Bradykinin Release Syndrome

- Mucosal congestion, bronchospasm, hypotension at start of CRRT
- Resolves with discontinuation of CRRT
- Thought to be related to bradykinin release when patient’s blood contacts hemofilter
- Exquisitely pH sensitive
- Associated with AN-69 membrane
Bypass System to Prevent Bradykinin Release Syndrome

Recirculation System to Prevent Bradykinin Release Syndrome

Recirculation Plan:
- Qb 200ml/min
- Qd ~40ml/min
- Time 7.5 min

Normalize pH
Normalize $K^+$

Waste

Neonatal Double CRRT Restart

- “Cross prime” from active circuit to new circuit
- No new units of blood from blood bank
- Blood in system already equilibrated to patient
- Need several more hands
- Only good for restarts when current circuit still functioning
Neonatal Double CRRT Restart
Simple Systems to Limit Likelihood of Bradykinin Release Syndrome

Don’t prime on with blood
Don’t use the AN-69 membrane
Device Limitations for Infant CRRT
Infant-Specific/Adapted Devices

Cardio Renal Pediatric Dialysis Emergency Machine (CARPEDIEEM)

Newcastle Infant Dialysis and Ultrafiltration System (NIDUS)

Aquadex FlexFlow
Case # 2– Additional Discussion

• Do you provide CRRT for infants at your center?
• What challenges and issues have you encountered with infant CRRT?
• Do you prefer other modalities for infants? How do you choose?
Case #2– Summary

• CRRT can be an effective therapy for even the smallest patients
• Multiple challenges remain on several fronts
• The possibility of a better devices for neonates may open further options
Case #3

CRRT FOR HYPERAMMONEMIA
Case #3 – Clinical Scenario

- 4 day old infant male, initially well
- Presents with poor feeding, decreased muscle tone, obtundation
- Admitted to local hospital for evaluation
  - 2.6kg
  - Ammonia 1600 micromol/L
  - Presumed inborn error of metabolism
  - Did not respond to medical management
- Transferred to our center for further care
Case #3 – Discussion

• Would you have accepted this patient?
• How would you approach overall care?
• What are your goals for ammonia removal?
• How would you organize and implement treatment for this patient?
Hyperammonemia and Inborn Errors of Metabolism

• Diagnoses include:
  – Urea Cycle Defects
  – Organic Acidemias

• Duration of hyperammonemia associated with neurodevelopmental outcome

• Goal is rapid detoxification
  – Ammonia level below 200 micromol/L
Toxin (NH$_3$) Removal Procedures

• Current recommendations:
  – Bring down ammonia as quickly as possible
  – Keep it there until you get metabolic control

• Extracorporeal therapy options include:
  – Peritoneal dialysis (slow)
  – Hemodialysis (efficient)
  – CRRT (can be as efficient as HD for the neonate)
CRRT vs IHD for Inborn Errors

- IHD had been the standard
- Rapid detoxification due to high Qb and Qd
  - Hemodynamic stability
  - Small infant
  - Rebound after cessation
- CRRT has gained popularity
  - Detoxification can be as rapid if Rx adjusted to increase clearance
Dialysis in neonates with inborn errors of metabolism

Franz Schaefer, Emine Straube, Jun Oh, Otto Mehls and Ertan Mayatepek

Results. Plasma ammonia or leucine levels were reduced by 50% within $7.1 \pm 4.1$ h by CVVHD and within $17.9 \pm 12.4$ h by PD ($P < 0.05$). Also, total dialysis time was shorter with CVVHD ($25 \pm 21$ h) than with PD ($73 \pm 35$ h, $P < 0.02$). A comparison of the CVVHD results with published literature confirmed superior metabolite removal compared to PD, and
Nonrenal indications for continuous renal replacement therapy: A report from the Prospective Pediatric Continuous Renal Replacement Therapy Registry Group

Geoffrey M. Fleming, MD; Scott Walters, MD; Stuart L. Goldstein, MD; Steven R. Alexander, MD; Michelle A. Baum, MD; Douglas L. Blowey, MD; Timothy E. Bunchman, MD; Annabelle N. Chua, MD; Sarah A. Fletcher, MS; Francisco X. Flores, MD; James D. Fortenberry, MD; Richard Hackbarth, MD; Kevin McBryde, MD; Michael J. G. Somers, MD; Jordan M. Symons, MD; Patrick D. Brophy, MD

Table 2. Patient- and therapy-specific variables by subgroup and outcome

<table>
<thead>
<tr>
<th>Variable</th>
<th>Inborn Errors of Metabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Survivors</td>
</tr>
<tr>
<td>Survival</td>
<td>62% (n = 13)</td>
</tr>
<tr>
<td>Dose delivered [IQR]</td>
<td>3140a</td>
</tr>
<tr>
<td>CRRT modality</td>
<td>8%a</td>
</tr>
<tr>
<td>Continuous venovenous hemofiltration</td>
<td>54%a</td>
</tr>
<tr>
<td>Continuous venovenous hemodialysis</td>
<td>38%a</td>
</tr>
<tr>
<td>Prior intermittent hemodialysis</td>
<td>No</td>
</tr>
<tr>
<td>Fluid overload at initiation</td>
<td>Yes</td>
</tr>
<tr>
<td>&lt;10%</td>
<td>54%</td>
</tr>
<tr>
<td>≥10%</td>
<td>46%</td>
</tr>
</tbody>
</table>

- 21 infants with IEM
- Clearance was all > 2000 ml/1.73m2/min
- Prior IHD did not affect outcome
- 100% of the non-survivors were > 10% FO

Pediatr Crit Care Med 2012 Vol. 13, No. 5
High-dose continuous renal replacement therapy for neonatal hyperammonemia

Joann M. Spinale · Benjamin L. Laskin · Neal Sondheimer · Sarah J. Swartz · Stuart L. Goldstein

<table>
<thead>
<tr>
<th>Time (hours)</th>
<th>Ammonia level (µmol/L)</th>
<th>Time (hours)</th>
<th>Ammonia level (µmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1454</td>
<td>0</td>
<td>1000</td>
</tr>
<tr>
<td>2</td>
<td>367</td>
<td>1</td>
<td>814</td>
</tr>
<tr>
<td>4</td>
<td>227</td>
<td>3</td>
<td>398</td>
</tr>
<tr>
<td>6</td>
<td>178</td>
<td>6</td>
<td>183</td>
</tr>
<tr>
<td>8</td>
<td>118</td>
<td>8</td>
<td>91</td>
</tr>
<tr>
<td>10</td>
<td>92</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Case 1

Case 2

(8,650 mL/h/1.73 m²).

Case 2*

(7,700 mL/h/1.73 m²).
Case #3 – Additional Discussion

• How do you address medical management of inborn errors while providing extracorporeal therapy?

• Does your approach to hyperammonemia or metabolic intoxication differ for an older/larger child?
  – 5 year old with MSUD crisis?
  – 15 year old with hyperammonemia in liver failure?
Case #3 – Summary

• Inborn errors of metabolism are life-threatening disorders in which rapid reduction of ammonia is imperative
• CRRT can effectively reduce and stabilize ammonia in small children with inborn errors of metabolism
• Larger children may require a different or combined approach to achieve NH$_3$ clearance
Case #4

CRRT IN PEDIATRIC LIVER FAILURE
Case #4 – Clinical Scenario

• 12 year old girl (previously healthy); weight 35kg
• Admitted to PICU with fulminant hepatic failure
  – INR 9, NH₃ 814, lactate 11, AST >20,000, ALT >3,500
  – T 40C, altered mental status, seizures, hypotension
• Resuscitated, intubated, massive blood product requirement
  – 10% FO within first 24 hours of admission
  – BUN 45mg/dL, Creatinine 1.8mg/dL
  – Urine output 100ml last 12 hours
Case #4 – Clinical Scenario (Continued)

• Clinical problems at this time include
  – Liver failure
  – AKI
  – Fluid overload
  – Large volume requirements
  – Elevated ammonia levels
  – Increased bleeding risk

• Nephrology consulted; CRRT initiated
Case #4 – Discussion

• What prescription/clearance challenges are posed by this patient?
• What are the priming considerations?
• What are our options for anticoagulation?
Case #4 – Prescription and Clearance

• Can use fairly standard Rx
  – May want to run blood flow rate higher to reduce clotting

• Clearance
  – In a smaller patient with large volume needs, UF alone will lend a tremendous amount of clearance
  – Citrate 100mL/hr
  – Ca 50mL/hr
  – Average 2.6L/day 110mL/hr
  – Total 260mL/hr → 10kg pt → 26mL/kg/hr
Clearance: Goals and Delivery

• UF: may give target CRRT clearance (20-25mL/kg/hr)
• Minimum Qd (50mL/hr) and Qr (50-100mL/hr) settings on some devices add another 10-15mL/kg/hr
• High rates of clearance may have their own risks for complications (metabolic imbalance, etc.)

Intensity of Continuous Renal-Replacement Therapy in Critically Ill Patients
The RENAL Replacement Therapy Study Investigators
Case #4 – Prescription and Clearance

• Recognizing caveats – should we treated like a hyperammonemic neonate?
  – 8000mL/1.73m²/hr
  – Our patient is 1.1m²
  – Target a Qd+Qr of 5000mL/hr

• Advantages: rapid metabolic correction, clearance of NH₃, mediator clearance (theoretical)

• Disadvantages: negative impact on electrolytes, medication dosing, nutrition, calcium balance
Anticoagulation

- Anticoagulation options: Heparin, citrate, others(?)
- No anticoagulation: circuit loss (bad)
- Citrate and heparin have equal circuit survival
- More bleeding with heparin
- Accumulation risk with citrate

Case #4 – Clinical Case (Continued)

• 24 hours later:
  – Total calcium 19.7mg/dL
  – Patient pH 7.09 (HCO3 12meq/L)
  – Pt iCal 1.15mmol/L, circuit iCal 0.38mmol/L
  – Qb 100mL/min
  – Citrate infusion 150mL/hr
  – Calcium chloride infusion 450mg/hr

• Suspected citrate accumulation
  – Elevated total calcium = Ca-citrate
  – Although *alkalosis* is more common, unmetabolized citrate can cause *acidosis*
Citrate Accumulation: Management

• Techniques to mitigate citrate accumulation
  – Increase clearance
  – Reset citrate/calcium
  – Increase circuit iCal target/reduce citrate delivery
  – Reduce Qb (less citrate required)
  – Heparin (wholesale switch or low dose infusion into arterial lumen with higher circuit iCal range)
  – Look the other way and hope for transplant 😊
Case #4 – Additional Discussion

- How do you determine clearance goals (“dose”) for your patients?
- What is your approach to anticoagulation?
- In special clinical circumstances (e.g. liver failure) does your approach differ from a “standard” patient with AKI?
Case #4 – Summary

• Clearance maintains metabolic balance but data on best goals for dose are lacking
• Anticoagulation is necessary, and sometimes it can be tricky
• Highly complex patients are more challenging to manage
Clinical Application of CRRT for Infants and Children: Summary

• Pediatric CRRT can present many challenges:
  – Prescription
  – Coordination with other therapies/interventions
  – Complications

• We have touched upon some common problems and some unique issues

• CRRT is a team effort:
  – Between colleagues at the bedside
  – Among colleagues around the world
Any Other Comments or Questions?
Thanks for Your Participation!