CRRT in combination with ECMO, TPE and MARS

David Askenazi MD MS
Associate Professor of Pediatrics
CRRT 2015
Potential Conflicts of Interest

- Speaker for AKI Foundation
ECMO
Therapeutic Plasma Exchange
CRRT  <->  MARS
ECMO

CRRT

Therapeutic Plasma Exchange
ECMO

CRRT

MARS

Therapeutic Plasma Exchange
Why Me?

- ECMO has historically been primarily a neonatal / pediatric therapy
- Vessel preservation is critical in our patients!
- Priming a circuit in an adult is usually no big deal...it can be very dangerous in babies...
“Necessity is the Mother of (our) Invention”
Hellooooo, there’s a baby under all these machines!!

4 kg baby – blood volume = 320 cc

ECMO circuit ECV = 350 ml

CRRT circuit ECV = 100 ml

TPE circuit ECV = 200 ml

ECV = 600 ml
60 kg adult–blood volume = 5 Liters

CRRT circuit ECV = 1500 ml

ECMO circuit ECV = 5 liters

TPE circuit ECV = 3 liters

ECV = 9.5 liters
Why may this be important to you?

- Increasing use of ECMO in adult ICU’s
- Increasing use of TPE for Thrombocytopenia-associated Multi-organ Failure
- Increasing use of MARS
- Vessel preservation
- Decreased blood product exposure
- Maximize therapy time and minimize personnel times
Extracorporeal Membrane Oxygenation (ECMO)

- ECMO is a potentially life-saving procedure used in the most critically ill patients.

Indications for ECMO:
- Severe acute heart or lung failure
- Expected mortality risk ≥ 80% despite optimal conventional therapy

ELSO Registry General Guidelines. April 2009
Epidemiology of AKI in ECMO patients
How often does AKI happen in ECMO patients?

- Neonates w/congenital diaphragmatic = 71%
  - Gadepalli et. al. Pediatric Surgery 2010
- Children with Cardiac indications = 72%
  - Smith et. al. ASAIO 2009
- Adults with respiratory indications = 78%
  - Lin et.al NDT 2006
- Adults with cardiac indications = 81%
  - Yan X. et al.; Eur J Cardthorac Surg 2010
Askenazi et al. Pediatric Critical Care Medicine 2011

Survival in AKI/ RRT subjects

- Neonates
- Children
- Adults
AKI and Fluid Overload during pediatric ECMO
AKI and Fluid Overload during pediatric ECMO

- AKI occurs in about 60% of ECMO patients
- AKI portend poor outcomes
- higher % FO at ECMO initiation portends poor outcomes
Access

Veno-veno (VV) ECMO

double lumen cannula

return to patient

to ECMO circuit

right atrium
ECMO with RRT device

- Patient return cannula
- Flow probe
- Membrane oxygenator
- ECMO roller pump
- ECMO bladder
- Patient venous drain cannula
ECMO with RRT device
CRRT machines with ECMO

- Access Pressure on CRRT may be positive
  - Some Dialysis Machines can allow for alarms to be adjusted during ECMO
  - Clamps can be used to avoid these alarms
    - Increases Hemolysis
- Circuit prime
  - Careful with heparin rinse
CRRT on ECMO using “Homemade” In-Line system

- IV “volume regulators” are not engineered to maintain accuracy at higher pressures
  - Up to 12.5 % inaccuracies in some studies
  - less error in Dialysis mode
    - (Askenazi et. al. data not published).
## Differences between RRT methods

<table>
<thead>
<tr>
<th></th>
<th>In Line Hemofilter</th>
<th>CRRT machine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ultrafiltration control</strong></td>
<td>IV pump controlled</td>
<td>CRRT machine controlled</td>
</tr>
<tr>
<td><strong>Metabolic Control</strong></td>
<td>NOT if only using SCUF</td>
<td>YES</td>
</tr>
<tr>
<td><strong>ECMO Flow</strong></td>
<td>Blood Shunt</td>
<td>NO systemic changes</td>
</tr>
<tr>
<td></td>
<td>- decrease ECMO flow</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- decreased PaO2</td>
<td></td>
</tr>
<tr>
<td><strong>Complexity</strong></td>
<td>Less People</td>
<td>More People</td>
</tr>
</tbody>
</table>
Therapeutic Apheresis:
a.k.a. “Evil Humor Dialysis”
Examples of “Evil Humors”

- Waste bag plasma exchange
- Leukoreduction for blast crisis
- Platelet reduction
Apheresis

- RBC exchange
  - Sickle cell crisis
- Stem Cell Collection
- Leukopheresis
- LDL Apheresis
- Platelet depletion
- Therapeutic Plasma Exchange (TPE)
- “Psychopheresis” is not an indication!
TPE ≠ Dialysis

- Dialysis
  - Cannot clear large particles
  - Cannot remove protein bound particles
Therapeutic Plasma Exchange (TPE)

- TPE rapidly and massively decreases pathogenic (and useful) substances present in the plasma
  - TPE does not stop underlying problem!
- Known pathogenic substance in the plasma
  - Autoantibodies
  - Complement components
  - Cytokines
Guidelines on the Use of Therapeutic Apheresis in Clinical Practice—Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Sixth Special Issue

Joseph Schwartz,1 Jeffrey L. Winters,2 Anand Padmanabhan,3 Rasheed A. Balogun,4 Meghan Delaney,5 Michael L. Linenberger,6 Zbigniew M. Szczepiorkowski,7 Mark E. Williams,8 Yanyun Wu,9 and Beth H. Shaz10,11*
Centrifugal TPE

- Separate each blood component based on density
- Remove a certain part of the blood
Membrane TPE (Prismaflex)

- Permeable blood filters
  - Separation is according to molecular size.
  - Plasma filter membrane pores are up to 0.2 µm in diameter
    - 30 times the diameter of pores in conventional high-flux hemofilter membranes
  - removal of substances up to a molecular weight of $3 \times 10^6$ Da,
    - immunoglobulins, immune complexes, complement factors, lipoproteins, and endotoxin.
## Sieving coefficient with Membrane TPE

<table>
<thead>
<tr>
<th>Protein</th>
<th>Sieving coefficient</th>
<th>Size MW (daltons)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>0.97</td>
<td>68,000</td>
</tr>
<tr>
<td>IgG</td>
<td>1</td>
<td>150,000</td>
</tr>
<tr>
<td>Apolipoprotein B</td>
<td>0.95</td>
<td>512,000</td>
</tr>
<tr>
<td>IgM</td>
<td>0.92</td>
<td>950,000</td>
</tr>
</tbody>
</table>
Apheresis Complications

Anti-coagulation-related

- Bleeding
  - Loss of platelets
  - Heparin
  - TPE REMOVES COAG FACTORS
    - Low Fibrinogen
      - Especially with multiple treatments
      - We check level before we start
      - Protocols to provide FFP if Fibrinogen low
Apheresis Complications

Procedure Related

- Citrate toxicity:
  - Hypocalcemia
  - Metabolic Alkalosis
  - REMEMBER
    - FFP contains $\approx 7$ mmol citrate/unit
    - RBC contain $\approx 2-3$ mmol citrate/unit
Apheresis Complications
Procedure Related

What happens to other drugs?
- Removed at what rate? How do we replace them?

PHARMACOTHERAPY Volume 27, Number 11, 2007

Drug Removal by Plasmapheresis:
An Evidence-Based Review

Rami B. Ibrahim, M.Sc., Pharm.D., Chin Liu, M.S., Pharm.D., Simon M. Cronin, M.S., Pharm.D., Bridgette C. Murphy, Pharm.D., Raymond Cha, Pharm.D., Paul Swerdlow, M.D., and David J. Edwards, Pharm.D.
Tandem TPE and CRRT

Choices...
- Treat them as completely individual treatments using the same access
- Establish double access and run both at the same time.
- “Cross Prime” circuits
- Run them in parallel with one another
Cross Priming Circuits
Cross Priming Circuits
Cross prime circuits

Advantages
- No new blood exposure
- Blood already equilibrated to patient

Disadvantage
- Need several more hands
- Recirculating CRRT can clot
TPE and CRRT in parallel
First CRRT / TPE tandem

Concurrent centrifugation plasmapheresis and continuous venovenous hemodiafiltration
CRRT/Apheresis

After Apheresis is completed, you MUST turn the stopcocks OFF to both the pull line and return line used for Apheresis.
MARS/CRRT Tandem
MARS® Adsorber Cartridges

- **Activated charcoal column**
  (diaMARS® AC250)
  Removes low molecular weight, non-polar compounds (i.e., fatty acids)

- **Anion-exchanger resin column**
  (diaMARS® IE 250)
  Removes anionic molecules (i.e., bilirubin)
MARS

Blood Circuit  Albumin Circuit  Dialysate Circuit
Indications for MARS®

- In USA
  - Drug overdose
  - Poisoning
  - Hepatic encephalopathy
TPE and CRRT and ECMO

Picture provided by Jim Fortenberry MD with permission
Thank you

Questions / Comments