Continuous Renal Replacement Therapy

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Definition of Terms

- SCUF - Slow Continuous Ultrafiltration
- CAVH - Continuous Arteriovenous Hemofiltration
- CAVH-D - Continuous Arteriovenous Hemofiltration with Dialysis
- CVVH - Continuous Venovenous Hemofiltration
- CVVH-D - Continuous Venovenous Hemofiltration with Dialysis
- SLED – Sustained Low-Efficiency Dialysis
Indications for Renal Replacement Therapy

- Remove excess fluid because of fluid overload
- Clinical need to administer fluid to someone who is oliguric
  - Nutrition solution
  - Antibiotics
  - Vasoactive substances
  - Blood products
  - Other parenteral medications
Advantages of Continuous Renal Replacement Therapy

- Hemodynamic stability
  - Avoid hypotension complicating hemodialysis
  - Avoid swings in intravascular volume
- Easy to regulate fluid volume
  - Volume removal is continuous
  - Adjust fluid removal rate on an hourly basis
- Customize replacement solutions
- Lack of need of specialized support staff
Advantages of SLED

- Hemodynamic stability
  - Avoid hypotension complicating hemodialysis
  - Avoid swings in intravascular volume
- High solute clearance
- Flexible scheduling
- Lack of need for expensive CRRT machines
- Lack of need for custom replacement solutions
- Lack of need of specialized support staff
Disadvantages of Continuous Renal Replacement Therapy

- Lack of rapid fluid and solute removal
  - GFR equivalent of 5 - 20 ml/min
  - Limited role in overdose setting
    - SLED – Developing role
- Filter clotting
  - Take down the entire system
Basic Principles

• Blood passes down one side of a highly permeable membrane
• Water and solute pass across the membrane
  – Solutes up to 20,000 daltons
    • Drugs & electrolytes
• Infuse replacement solution with physiologic concentrations of electrolytes
Anatomy of a Hemofilter

Outside the Fiber (effluent)
Inside the Fiber (blood)
Basic Principles

• Hemofiltration
  – Convection based on a pressure gradient
  – ‘Transmembrane pressure gradient’
    • Difference between plasma oncotic pressure and hydrostatic pressure

• Dialysis
  – Diffusion based on a concentration gradient
CVVH
Continuous Veno-Venous Hemofiltration

Blood In
(from patient)

Blood Out
(to patient)

Repl. Solution

LOW PRESS ← HIGH PRESS (Convection)
to waste
CVVH
Continuous VV Hemofiltration

• Primary therapeutic goal:
  – Convective solute removal
  – Management of intravascular volume
• Blood Flow rate = 10 - 180 ml/min
• UF rate ranges 6 - 50 L/24 h (> 500 ml/h)
• Requires replacement solution to drive convection
• No dialysate
CVVH Performance

Continuous venovenous hemofiltration
“In vitro” ultrafiltration with blood (post-dilution)
(values ± 15%) (Bovine blood at 37° C, Hct 32%, Cp 60g/l)
CVVHDF
Continuous Veno-Venous Hemodiafiltration

Blood In
(from patient)

Blood Out
(to patient)

LOW PRESS  ⇐  HIGH PRESS  
LOW CONC  ⇐  HIGH CONC

(Convection)
(Diffusion)

Dialysate Solution

to waste

Repl. Solution
CVVHDF
Continuous VV Hemodiafiltration

- Primary therapeutic goal:
  - Solute removal by diffusion and convection
  - Management of intravascular volume
- Blood Flow rate = 10 - 180ml/min
- Combines CVVH and CVVHD therapies
- UF rate ranges 12 - 24 L/24h (> 500 ml/h)
- Dialysate Flow rate = 15 - 45 ml/min (~1 - 3 L/h)
- Uses both dialysate (1 L/h) and replacement fluid (500 ml/h)
SLED
Sustained Low-Efficiency Dialysis

- Primary therapeutic goal:
  - Solute removal by diffusion
  - Management of intravascular volume
- Blood Flow rate = 100-300 ml/min
- Dialysate Flow rate = 100-300 ml/min
Pharmacokinetics of Continuous Renal Replacement Therapy
Basic Principles

• Extracorporeal clearance (Cl\textsubscript{EC}) is usually considered clinically significant only if its contribution to total body clearance exceeds 25 - 30%.

\[
Fr_{EC} = \frac{Cl_{EC}}{Cl_{EC} + Cl_{R} + Cl_{NR}}
\]

• Not relevant for drugs with high non-renal clearance.
• Only drug not bound to plasma proteins can be removed by extracorporeal procedures.
Determinants of Drug Removal by CRRT

- **Drug**: Same as hemodialysis but increased MW range
- **Membrane**: Permeability, Size
  - Sieving Coefficient
- **Renal replacement technique**: Convection + diffusion
  - CI
  - Flow rates
  - Blood, Dialysate, UF
  - Duration
Sieving Coefficient (S)

- The capacity of a drug to pass through the hemofilter membrane

\[ S = \frac{C_{uf}}{C_p} \]

- \( C_{uf} \) = drug concentration in the ultrafiltrate
- \( C_p \) = drug concentration in the plasma
- \( S = 1 \)  Solute freely passes through the filter
- \( S = 0 \)  Solute does not pass through the filter

\[ CL_{HF} = Q_f \times S \]
Determinants of Sieving Coefficient

• Protein binding
  – Only unbound drug passes through the filter
    • Protein binding changes in critical illness

• Drug membrane interactions
  – Not clinically relevant

• Adsorption of proteins and blood products onto filter
  – Related to filter age
  – Decreased efficiency of filter
Relationship Between Free Fraction ($fu$) and Sieving Coefficient ($SC$)
Dialysate Saturation ($S_d$)

- Countercurrent dialysate flow (10 - 30 ml/min) is always less than blood flow (100 - 200 ml/min)
- Allows complete equilibrium between blood serum and dialysate
- Dialysate leaving filter will be 100% saturated with easily diffusible solutes
- Diffusive clearance will equal dialysate flow
Dialysate Saturation ($S_d$)

$$S_d = \frac{C_d}{C_p}$$

- $C_d = $ drug concentration in the dialysate
- $C_p = $ drug concentration in the plasma

- **Decreasing dialysate saturation**
  - Increasing molecular weight
    - Decreases speed of diffusion
  - Increasing dialysate flow rate
    - Decreases time available for diffusion

$$Cl_{HD} = Q_d \times S_d$$
CVVHDF Clearance

Continuous venovenous hemofiltration - post dilution

QB = 150 ml/min - QD = 2000 ml/h (in vitro saline)
Extracorporeal Clearance

- Hemofiltration clearance ($Cl_{HF} = Q_f \times S$)
  - $Q_f$ = Ultrafiltration rate
  - $S$ = Seiving coefficient

- Hemodialysis clearance ($Cl_{HD} = Q_d \times S_d$)
  - $Q_d$ = Dialysate flow rate
  - $S_d$ = Dialysate saturation

- Hemodialfiltration clearance
  $$Cl_{HDF} = (Q_f \times S) + (Q_d \times S_d)$$
Case History

- AP 36yo HM s/p BMT for aplastic anemia
- Admitted to ICU for management of acute renal failure
- CVVH-D initiated for management of uremia
- ICU course complicated by pulmonary failure requiring mechanical ventilation, liver failure secondary to GVHD and VOD, and sepsis
Case History
Antibiotic Management on CRRT

- Gentamicin 180 mg IV q24h
- Vancomycin 1 g IV q24h
- Dialysis rate 1000 ml/hour
  - 12 hour post gentamicin levels: 3 - 4 mg/L
  - 12 hour post vancomycin levels: 20 - 23 mg/L
- Dialysis rate increased to 1200 ml/hour
  - 12 hour post gentamicin levels: < 0.4 mg/L
  - 12 hour post vancomycin levels: < 4 mg/L
Dosage Adjustments in CRRT/SLED

• Will the drug be removed?
  – Pharmacokinetic parameters
    • Protein binding < 70 - 80%
      – Normal values may not apply to critically ill patients
    • Volume of distribution < 1 L/kg
    • Renal clearance > 35%

• How often do I dose the drug?
  – Hemofiltration: ‘GFR’ 10 - 20 ml/min
  – Hemofiltration with dialysis: ‘GFR’ 20 - 50 ml/min
  – SLED: ‘GFR” 10 – 50 ml/min
Dosage Adjustments in CRRT/SLED

• Loading doses
  – Do not need to be adjusted
  – Loading dose depends solely on volume of distribution

• Maintenance doses
  – Standard reference tables
  – Base on measured loses or blood levels
  – Calculate maintenance dose multiplication factor (MDMF)
Supplemental Dose Based on Measured Plasma Level

\[ Dose_{\text{Suppl}} = (C_{\text{target}} - C_{\text{measured}}) V_d \]
Adjusted Dose Based on Clearance Estimates

$$MDMF = \frac{CL_{EC} + CL_{R} + CL_{NR}}{CL_{R} + CL_{NR}}$$
## COMPARISON OF DRUG REMOVAL BY INTERMITTENT HD AND CRRT

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<th>$CL_R + CL_{NR}$ (mL/min)</th>
<th>$MDMF$</th>
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## COMPARISON OF DRUG REMOVAL BY SLED AND CRRT

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