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 Continuous 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

Illustration of the anatomy of a hemofilter.

Blood flows through hollow fibers and the dialysis fluid is outside.

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

Illustration of Veno-Venous hemofiltration procedure.

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

Chart showing continuous venovenous hemofiltration and the role of transmembrane pressure.

CVVHDF
Continuous Veno-Venous Hemodiafiltration

Illustration of this process.

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_{EC}) is usually considered clinically significant only if its contribution to total body clearance exceeds 25 - 30%

Formula for calculating extracorporeal clearance.

- 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** **Sieving Coefficient**
- Renal replacement technique	**Convection + diffusion Cl** **Flow rates** **Blood, Dialysate, UF** **Duration of CRRT**

Sieving Coefficient (S)

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

Formula for calculating the sieving coefficient.

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

Formula

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*)

Chart illustrating this relationship.

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)

Formula for Dialystate Saturation (SD)

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

Formula

CVVHDF Clearance

Bar chart showing continuous venovenous hemofiltration – post dilution comparing urea + or-10%. with Vit B12 + or – 20% with Inulin + 20%.

Role of dialysis flows.

Extracorporeal Clearance

- **Hemofiltration clearance - formula**
  - Q_f = Ultrafiltration rate
  - S = Seiving coefficient
- **Hemodialysis clearance - formula**
  - Q_d = Dialysate flow rate
  - S_d = Dialysate saturation
- **Hemodialfiltration clearance**

Formula

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

Dosage Adjustments in CRRT

- **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**
  - **Calculate maintenance dose multiplication factor (MDMF)**

Supplemental Dose Based on Measured Plasma Level

Formula for calculating supplemental dose based on measured plasma level.

Adjusted Dose Based on Clearance Estimates

Formulation for calculating adjusted dose based on clearance estimates.

COMPARISON OF DRUG REMOVAL BY INTERMITTENT HD AND CRRT

Chart comparing drug removal by intermittent HD and CRTT.

Examples: Ceftazidime
Ceftriazone
Ciprofloxacin
Theophylline
Vancomycin

COMPARISON OF DRUG REMOVAL BY SLED AND CRRT

Chart comparing drug removal by SLED and CRRT.

Examples: Linezolid
Levofloxacin
Meropenem
Vancomycin