Renal Replacement Therapies (RRT) for the Non-Nephrologist

Kevin Harned, MD
University of Kentucky Medical Center
Division of Nephrology, Bone & Mineral Metabolism
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Objectives:
• Review the concepts of different modalities of RRT
• Examine the necessary components involved in RRT
• Examine the indications for RRT
• Review particular caveats to specific treatment modalities

3 physiologic principles of RRT:
• Diffusion
• Convection
• Adsorption

Physiology:
• Diffusion: Process of movement of molecules across an area due to differences in concentration gradients
  – Moves from high-to-low concentration until the concentrations for both areas are equal
  – Adequate for clearing small molecules (<1kDa)
  – Na, K, Ca, Creatinine, Urea, Gentamicin

Physiology:
• Convection: Using suction to physically pull water across a membrane, and with the fluid shift anything else that can “fit” through the membrane’s pores as it rides with the water (aka “Solvent drag”)
  – Think of the white-water rafter being “pulled” downstream by the river
  – Better for clearance of middle molecular weight molecules (up to 60kDa)
  – Vancomycin, cytokines (IL-1, IL-8, etc)

Physiology:
• Adsorption: Binding of substances to the surface of the filter/membrane
  – More a factor of electrical charge of the substance, organic vs inorganic (as in removal by charcoal filters)
**Physiology:**

- **Adsorption:**
  - Binding of substances to the surface of the filter/membrane
  - More a factor of electrical charge of the substance, organic vs inorganic (as in removal by charcoal filters).

**Terminology:**

- Peritoneal dialysis (PD)
- Intermittent Hemodialysis (IHD)
- Continuous Renal Replacement Therapies (CRRT)
  - Continuous veno-venous hemofiltration (CVVH)
  - Continuous veno-venous hemodialysis (CVVHD)
  - Continuous veno-venous hemodiafiltration (CVVHDF)
  - Sustained, low-efficiency daily hemodialysis (SLEDD)
  - High-volume hemofiltration (HVHF)
- Slow continuous ultrafiltration (SCUF)
- “Liver Dialysis”
  - Molecular Adsorption Recirculating System (MARS)
  - “Prometheus” (Not in the United States)

**PD:**

- Can be performed via manual exchanges or automated cycler machine at night
- 3 Glucose concentrations:
  - 1.5%
  - 2.5%
  - 4.25%
  - The higher the Glucose concentration, the more water will be removed from the pt d/t higher osmolality of the PD fluid compared to the plasma

**Typical PD Rx (manual):**

- Volume = 2.5L
- Time = Dwell x 3hrs
- # of exchanges = 3
  - Need 9-12hrs of RRT to be sufficient
- Fluid = 1.5% Dianeal

**Typical PD Rx (cycler):**

- Volume = 2.5L
- Time = 1hr 40min fill/dwell; 20min drain
- Length of tx = 7PM – 7AM
- Fluid = 1.5% Dianeal
PD:
• D/t logistics of placing PD catheter, as well as its efficiency limitation, PD is not ideal for the Acute Kidney Injury (AKI) pt requiring RRT
• Better if slowly progressed to ESRD
• Good candidates if:
  • High-fxn'ing pt (allows them to keep their independence)
  • Still has residual kidney fxn
  • Pt's w/ CHF (fluid shifts are more gentle)

PD:
• Not good candidates if:
  • Morbidly obese (insufficient dose)
  • Multiple abdominal surgeries (scarring of peritoneum)
  • Pt is blind (can't care for catheter = infxn)
  • Pt has ascites (regardless of etiology)

IHD:
• Diffusion >>> Convection
• Ingredients
  • Vascular Access
  • Blood circuit
  • Filter w/ semipermeable membrane
  • Dialysate fluid circuit
    • Diffusive component
  • Ultrafiltrate circuit = fluid removed
  • Convective component
  • Anticoagulation

IHD: Vascular Access
• Temporary dialysis catheter (Uldall, Quinton, Vascath)
• Tunneled dialysis catheter (Cannon, Palindrome, Decathalon)
• Native arterio-venous fistulas (AVF’s)
• Synthetic and native arterio-venous grafts (AVG’s)

IHD: Blood circuit
• BFR = Blood Flow Rate
  – Target = 300 – 500ml/min
• PA = Arterial port pressure
  – This is a negative # measured inside the lines of the RRT circuit that represents the amount of suction required to physically pull the blood from the patient
  – Goal -75 to -250mmHg
• PV = Venous port pressure
  – This is a positive # measured inside the lines of the RRT circuit that represents the amount of pressure required to PUSH the blood back to the patient
  – Goal 100 to 250mmHg
IHD: Blood circuit

- PA alarms ONLY when it is too low (<-250)
  - ALWAYS represents an ACCESS problem
- Improper needle placement (AVF/AVG)
- Insufficient arterial inflow of blood into the access (AVF/AVG)
- Kink in dialysis catheter
- Catheter sucking against interior wall of vein
- Clot at tip of catheter acting as a one-way valve

- PV alarms typically when it is too high (>250)
  - ACCESS problem
  - Improper needle placement (AVF/AVG)
  - Outflow stenosis (AVG >> AVF)
    - Venous anastomosis (AVG)
    - Draining vein (needle stick sites, proximal swing segment of transposed brachial-basilic AVFs, Cephalic Arch, central venous stenosis)
    - Kink in dialysis catheter
    - Clot inside lumen of tip of catheter obstructing outflow
      - Thrombosis of Venous Drip chamber

IHD: Dialysate circuit

- DFR = Dialysate Flow Rate
  - Target = 500-750ml/min
  - Provides the DIFFUSION component for solute clearance
  - NO EFFECT ON VOLUME STATUS OF PT

- Solutes we can control:
  - Metabolic acidosis
  - K+
  - Ca²⁺
  - Uremia
  - Na (somewhat)
  - Phos (somewhat)
IHD: Ultrafiltrate circuit

- **UF** = Actual volume removal
  - Requires **CONVECTION** to physically pull the fluid from the pt's blood across the membrane
  - Nothing selectively removes just water!
  - Small amount of clearance simply d/t solvent drag
  - Amount of UF entirely dependent on intravascular volume status of pt and his/her blood pressure
  - The volume of fluid removed is what leads to hypotension, not the actual BFR

IHD: Anticoagulation

- Heparin = #1 type used worldwide
  - Bolus only
  - Bolus + infusion
  - Infusion only
  - “Tight” Heparin

  - No anticoagulation

  - If already anticoagulated for another reason, nothing additional is given.

Continuous Renal Replacement Therapies (CRRT)

- Continuous veno-venous hemofiltration (CVVH)
- Continuous veno-venous hemodialysis (CVVHD)
- Continuous veno-venous hemodiafiltration (CVVHDF)
- High-volume hemofiltration (HVHF)
- Sustained, low-efficiency daily hemodialysis (SLEDD)

CVVH:

- **All CONVECTION**
- Blood flow rates 150-400ml/min
- Uses a higher fluid removal rate than required to restore “euvolemia”
  - Pull 2-6 **LITERS** from the patient/hr
- Requires use of **replacement fluid** to prevent patient from becoming hypotensive
  - Most machines BOTH REMOVE AND REPLACE this volume, so the net fluid loss is ZERO

  - Net fluid loss = (RF_OUT + UF) − RF_IN

CVVH:

- Replacement Fluid Rate/Substitution Fluid Rate
  - Clearance of solutes by solute drag
  - Machine PULLS this volume and gives this volume back
  - No fluid balance is lost/gained
  - Target = 35ml/kg/hr

- **UF**
  - Extra fluid that is NOT replaced, leading to actual water-loss
CRRT: Continuous Hemofiltration

- Blood flow rates 150-400 ml/min
- Uses a higher fluid removal rate than required to restore "euvolemia"
- Pull 2-6 liters/hr
- Requires use of replacement fluid to prevent patient from becoming hypotensive

Net fluid loss = Total UF rate \times Replacement fluid rate

Palevsky, PM; "Continuous Renal Replacement Therapies." ASN Board Review Course—August 2001. HDCN online symposium.

CVVH: Filter

CVVHD:
- Diffusion >>> Convection (just like IHD)
- Blood flow rate 150-400 ml/min
- Solute removal dependent on diffusion across membrane w/ dialysate
  - Dialysate is counter-current to blood flow in order to maximize concentration gradients across entire length of the filter
  - Usually on the order of 1.5-3L/hr
- UF set only at rate that pt hemodynamically can withstand, w/ goal of restoring "euvolemia" (0-150 ml/hr)

CRRT: Continuous Hemodialysis

CVVHDF:
- Diffusion > Convection
- Blood flow rate 150-400 ml/min
- Utilize dialysate for diffusion clearance of small molecules along w/ high-UF rates for convection to remove "middle molecules"
  - Like CVVH, requires the use of replacement fluid

CRRT: Continuous Hemodiafiltration

Palevsky, PM; "Continuous Renal Replacement Therapies." ASN Board Review Course—August 2001. HDCN online symposium.
HVHF:
- Simply put is CVVH, but instead of 35ml/kg/hr, target Substitution Fluid Rate is >60ml/kg/hr.

SLEDD:
- Actually is IHD, except the tx is continued for 8-20hrs instead of 3-4hrs, and fluid is pulled more gingerly
- Cheaper
  - Don’t have to buy new machine
  - Ran by Dialysis Nurse
- No evidence that SLEDD is any better OR worse than IHD or CRRT

SCUF:
- Think of it as CVVH, but w/ convection SO LOW that really there is NO SOLUTE CLEARANCE
- The HYDROSTATIC pressure of the blood going through the filter is what “pushes” the UF out, with a small amount of convection to pull a little extra fluid.
  - UF 50-300ml/hr

Molecular Adsorption Recirculating System (MARS):
- Often called “liver dialysis”
- Use hemofilter similar to RRT, but then the ultrafiltrate is then further dialyzed in a second filter, followed by contact w/ several adsorption columns, then returned to the patient

CRRT: Vascular Access
- Temporary dialysis catheter
  - Uldall, Quinton, etc
- Tunneled dialysis catheter
  - Cannon, Tessio, etc
- Native AVF or AVG
  - Rarely used since this would require needles to remain in the access constantly
    - Risk of infection and damage to the access

CRRT: Anticoagulation
- Essential to keep the circuit from thrombosing
  - Unless patient extremely coagulopathic
- 2 main areas of thrombosis
  - Venous chamber
  - Filter
Anticoagulation strategies:

- Heparin infusion
- Therapeutic on coumadin/warfarin
- Coagulopathy from various reasons
  - Sepsis
  - Liver failure
  - Xigris
- Argatroban (as in HIT)
- Citrate
  - If using Heparin or citrate, best to administer Pre-blood pump
    - "Blood-air interface" = thrombogenic (for the filter)

Heparin:

- Can try to use “just enough” to “thin” the circuit or fully anticoagulate the patient
- Important to check APTT for monitoring
- Can add-in volume of heparin to the UF so that extra volume is removed as well
- Should be placed pre-blood pump to make certain blood is anticoagulated before it reaches the filter

Citrate:

- “The Principle”
  - Ionized Ca (ie, free Calcium) is required in multiple steps of the coagulation cascade to form the final stable thrombus

Theory of citrate:

- Use an agent on the “arterial side” (coming from the patient) of the CRRT circuit to bind the majority of ionized calcium so that very little is available for the coagulation cascade
  - Citrate LOVES to complex w/ Calcium
- Note that some of the [agent+Ca] chelate will be removed via the filter
- Add back elemental Ca on the “venous side” (going to the patient) of the CRRT circuit to replenish Ca stores for normal coagulation properties inside the patient’s body, as well as for all the other biochemical reactions requiring Ca

Complications of Citrate:

- Hypocalcemia or hypercalcemia
- Metabolic alkalosis
  - 1 molecule citrate metabolized via liver, skeletal muscle and renal cortex into 3 molecules of HCO₃⁻ (less metabolism in liver impairment)
- Hypernatremia
  - Most protocols call for tri-sodium citrate, thus yielding the extra Na load
- Citrate toxicity
  - Increased total Ca, decreased Ionized Ca, widening anion gap (d/t citric acid in serum)
5 Indications:
- Volume overload not sufficiently responding to diuretics
- Hyperkalemia
- Metabolic acidosis refractory to bicarbonate replacement
- Uremia
- Intoxications (Ethylene glycol, Lithium)

Volume overload:
- Fluid MUST be INTRAVASCULAR
- We CANNOT quickly remove 3rd-spaced fluid:
  - Pleural effusions
  - Ascites
  - Pericardial effusions
  - Generalized Anisarca
    - Possible w/ Albumin vs other oncotic agent priming and prolonged, repeated treatments

Volume overload:
- Not responding to IV diuretics
  - Diuril 500mg IV, then Lasix 120mg IV x 1
  - Lasix vs Bumex gtt
- Increasing O₂ requirements
- Worsening CHF
- Elevated CVP/PCWP

Hyperkalemia:
- If serum K⁺ ≤ 6.5, can try medical tx alone
  - Kayexalate 30-60g PO/PT q2' until has BM's
  - EXCEPT: If possible ileus, bowel ischemia, etc as Kayexalate can promote bowel perforation
  - Insulin 10units SQ + 1amp D50
  - Albuterol neb (continuous)
  - 1 amp bicarb (only if acidodic)
  - Ca gluconate/chloride (only if EKG Δ’s)

Hyperkalemia:
- If serum K⁺ > 6.5, initiate medical tx but still call Renal for possible emergent dialysis

Metabolic acidosis:
- If serum pH < 7.2, consider IV buffering
  - D5W + 3amps NaHCO₃ @ 0.5-1.ml/kg/hr
  - Tris hydroxymethyl aminomethane (THAM)
    - mL of 0.3M THAM = wt (kg) x BD (mEq/L) x 1.1
    - EXCEPT:
      - Anuria
      - Uremia
- Lactate = ‘potential bicarb’, so correct the underlying problem (if possible)
Uremia:
• Usually do not have sx’s until BUN >100
  – MS Δ’s
  – Itching
  – Anorexia
  – N/V
  – Pericarditis w/ pericardial rub

Intoxications:
• Clearance ability is highly dependent upon:
  – Size of molecule
  – % of protein binding
  – Volume of distribution in the body
    • Water-soluble
    – Fast redistribution from peripheral compartments into the blood

Intoxications: Size of Molecules
• **Diffusion** – limited to ~ 1kDa
  – Methanol
  – Ethylene glycol
  – Lithium

• **Convection** – up to ~ 60kDa depending on properties of the filter

• **Adsorption** – up to 40 or 60kDa

Intoxications: Protein Binding
• We can only remove the free-drug
  – Must be < 80% protein bound
    • Alcohols
    • Aminoglycosides
    • Li
    – > 80% protein bound
    • Arsenic
    • CCB’s
    • Diazepam
    • Phenytoin
    • Salicylate
    • TCA’s

Intoxications: Volume of Distribution
• Vd = Apparent volume into which the drug is distributed at equilibrium
  – < 1 L/kg Vd ideal for clearance by RRT
    • Alcohols
    • Salicylates
    • Li
    • Theophylline
    • Atenolol
    • Aminoglycosides
  – > 1 L/kg include Digoxin, CCB’s, β-Blockers, TCA’s, Quinine

Intoxications: Hemoperfusion
• Uses circuit similar to RRT, but instead of a dialysis filter there is an adsorbent-containing cartridge
  – Activated charcoal OR
  – Resin
• BFR 250-400ml/min
• Clearance of the toxin totally dependent upon the affinity for the charcoal/resin for the substance
  – NO Diffusion and NO Convection
  – NOT limited to size, water-solubility or protein binding
  – Clearance continues until the cartridge is saturated
    • Approximately 6-8hrs
Intoxications: Hemoperfusion

- Charcoal HP binds substances irreversibly
- Resin HP is reversible
- HP is the preferred method when the toxin is:
  - Lipid soluble
  - Highly protein bound
- Most common use is for Theophylline

Intoxications: Hemoperfusion

- Prone to biocompatibility problems:
  - Thrombocytopenia (drop by 30%)
  - Leukopenia (drop by 10%) d/t:
    - Activation of complement
  - Reduction of fibrinogen and fibronectin d/t adsorption to charcoal
  - Hypothermia
  - Hypocalcemia (charcoal)
  - Hypoglycemia