CRRT in the ICU : Initiating and Optimizing Therapy

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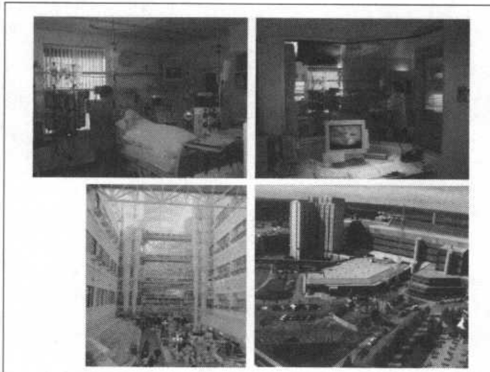
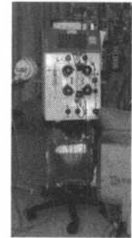


Seminar overview

- Part 1
  - Treatment selection, access and dose
  - Case study
- Part 2
  - Fluid balance and electrolyte management
  - Case study
- Part 3
  - Monitoring and modification of anticoagulation
  - Case study
- Discussion



Purpura Fulminans

- 12:05 hrs 18 y/o male presented to UAH ER.
- Called on phone for help. Found collapsed on floor in apartment. Incontinent of diarrhoea. Rousable but confused. HR 130, BP 85 systolic. ? Petechial rash. IV commenced and NS started.
- Previously healthy
- Member of college drama group
- On arrival in ER HR 140, BP 90/40, T 39 C, neck supple, evolving generalized purpuric rash.

- Rapid deterioration in hemodynamic, respiratory and acid base status.
- WBC 2.3 with 55% band forms, Plts 78, INR 2.1, PTT 67
- Urea 13 mmol/l, Creatinine 142μmol/l
- Cefotaxime 2 gms IV q 8H
- PA catheter inserted
  - PCWP 10
  - CI 3.5,
  - SVRI 900
- Aggressive fluid resuscitation guided by PA cath
- Progressive hypoxemia and fatigue
- 19:00 hrs: Intubated and placed on mechanical ventilation

- Noradrenaline infusion for BP support but required addition of adrenaline due to progressive decrease in CI to 2.4
- Vasopressin infusion 0.03 u/min
- Hydrocortisone 100 mg IV and 50 mg IV q 8H
- Progressive increase in noradrenalineine infusion dose to maintain SBP>90
- Progressive increase in serum lactate to 10 nmol/l
- Progressive peripheral digital cyanosis

- Progressive coagulopathy, INR 1.9, PTT 95, Plts 41
- Progressive hypoxaemia (P/F ratio 110) and development of pulm infiltrates
- Ventilated with lung protective strategy
  - PEEP 15 cm H2O, Vt 420 mls (6 mls/kg),
- 24:00 hrs: FiO2 0.8, pH 7.18, Noradrenaline 20 mcg/min, Adrenaline 25 mcg/min, CI 3.1, SVRI 825
- Issues?
- Strategies?

Problems

- Meningococcemia
- Septic shock
- Purpura fulminans
- Coagulopathy
- Metabolic acidosis
  - Anion gap
  - Lactic acidosis
- ARDS
- Acute renal failure
- Peripheral digital ischemia

Acute renal failure

- RRT?

Acute renal failure

- RRT?
  - Yes
    - Anuria
    - Metabolic acidosis
    - Fluid management

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- IHD or CRRT?

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- IHD or CRRT?
  - CRRT
    - Hemodynamic instability
    - Vasopressor dependency

Acute renal failure

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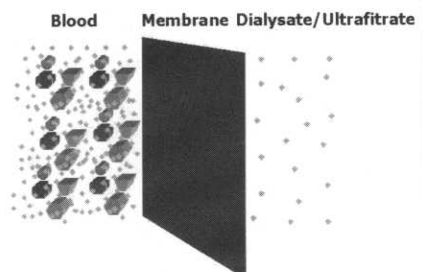
- Mode?

Solute clearance



Mechanisms of Solute Removal

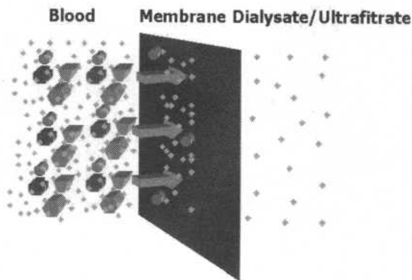
- Diffusion
- Ultrafiltration
- Diffusion + Ultrafiltration
- Adsorbtion

Principles of Haemodialysis

- Solute clearance by diffusion
- Suitable for removal of small molecules, and most middle molecules

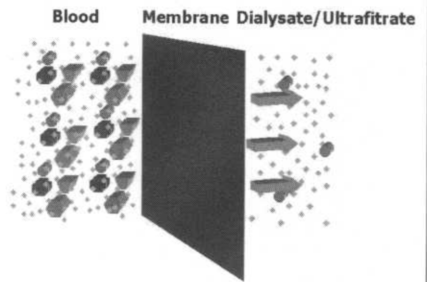
Diffusive solute clearance

Blood Membrane Dialysate/Ultrafitrate



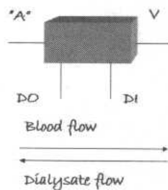
Diffusive solute clearance

Blood Membrane Dialysate/Ultrafitrate



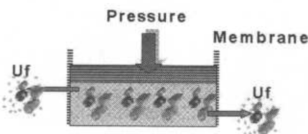
CVVHD

- Fluid removal
- Solute removal (small molecules)
- Counter-current dialysis flow
- Diffusion
- Back filtration



Principles of Haemofiltration

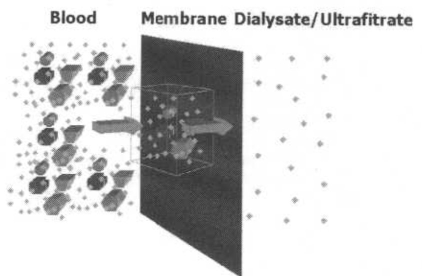
Ultrafiltration



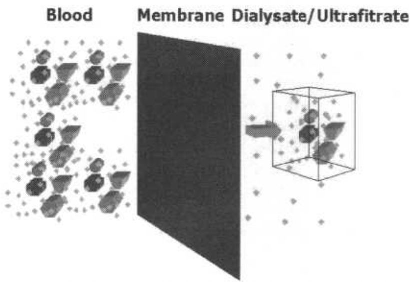
The transfer of solute in a stream of solvent, across a semipermeable membrane, mediated by a hydrostatic force

Convective solute clearance

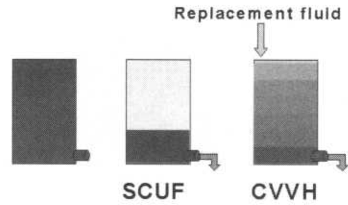
Blood Membrane Dialysate/Ultrafitrate



Convective solute clearance



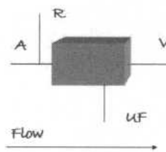
Convective solute removal



Coffee maker analogy of haemofiltration
Removal of large volumes of solute and fluid via convection and replacement of excess UF with sterile replacement fluid

CVVH

- Fluid removal
- Fluid replacement
- Solute clearance
- Convection
- Minor degree diffusion

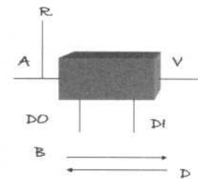


CVVHDF

- Fluid removal
- Solute removal (small and larger solutes)
- Diffusion

+

- Convection



Acute renal failure

- RRT?
  - Yes
    - Anuria
    - Metabolic acidosis
    - Fluid management
- IHD or CRRT?
  - CRRT
    - Hemodynamic instability
    - Vasopressor dependency
- Mode?
  - CVVH

Acute renal failure

- RRT?
  - Yes
    - Anuria
    - Metabolic acidosis
    - Fluid management
- IHD or CRRT?
  - CRRT
    - Hemodynamic instability
    - Vasopressor dependency
- Mode?
  - CVVH
- Dose?

ARTICLES

Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomised trial

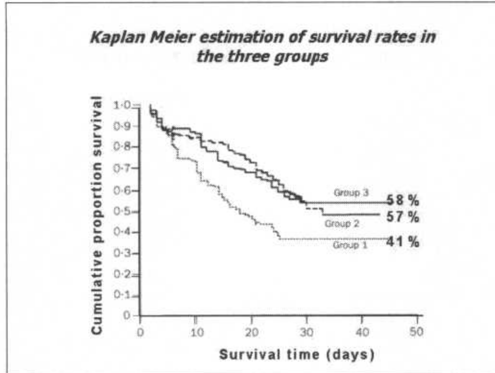
Lancet 2000;356:26-30

Claudio Ronco, Rinaldo Bellomo, Peter Homel, Alessandra Brendolan, Maurizio Dan, Pasquale Piccinni, Giuseppe La Greca

Impact of different haemofiltration doses on outcomes

- 425 patients with ARF
- Randomly assigned ultrafiltration at
  - 20 ml/kg/h
  - 35 ml/kg/h
  - 45 ml/kg/h
- Primary endpoint survival at 15 days after stopping haemofiltration
- Secondary endpoints were recovery of renal function, frequency of complications
- Intention to treat analysis

Ronco et al. Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomised trial. *Lancet* 2000;356:26-30.



Vascular Access

- Principles
  - Vessel(s) and catheters should be large enough to permit blood flow rates > 400 mls/min
  - Venous access preferable to arterial
  - Double lumen catheters preferable
  - Polyurethane preferable to PVC
- Problems
  - Poor flow (high positive/negative pressures)
  - Bleeding
  - Clotting
  - Infection
  - Venous stenosis

Recirculation

Access recirculation may limit clearances

- Subclavian 4.1%
- Femoral 13.5 cm - 22.8%
- Femoral 19.5 cm - 12.6%
- @Blood flow 300 ml/min

More problematic in IHD or HVHF than CVVH/CVVHDF

Kelber J et al. *Am J Kidney Dis* 1993; 22: 24-29.
Leblanc M et al. *J Am Soc Nephrol* 1995; 5: 496.

- What dose CVVH for weight 80 kg?
- Catheter?
  - What type?
  - Where?
  - Why?

CRRT Treatment, dose and access

- 24:00 hrs started CVVH
- 3L/hr (37.5 ml/kg/hr)
- Qb 180 mls/hr
- Hemodialysis catheter
  - R femoral vein 11.5Fr X 19.5 cm
  - PA catheter already in RIJ vein
  - Coagulopathy
  - Preferably avoid subclavian access
    - Risk of pneumothorax in critically ill patient
    - Delayed venous stenosis

Seminar overview

- Part 1
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  - Case study
- Part 2
  - Fluid balance and electrolyte management
  - Case study

Fluid and electrolytes 24:00 hrs

- Septic shock
- Anuric
- Positive 6 liters
- ARDS
- Metabolic (lactic) acidosis
  - pH 7.18, PO2 76, PCO2 45, SaO2 94%, BXS -15
  - Lactate 10 nm/l
  - Na 138, K 5.6, Cl 102, HCO3 11
  - Urea 19 mmol/l, creatinine 190 μmol/l
- High dose infusions epinephrine and norepinephrine
- Vasopressin and steroid replacement therapy

Fluid balance during CRRT

- Issues
  - Primary diagnosis
    - Sepsis
    - Trauma
    - Cardiac dysfunction
  - Current status of intravascular fluid volume
  - Ongoing fluid losses
  - Presence of ALI/ARDS
  - Time frame of illness

Fluid balance during CRRT

- Issues
  - Primary diagnosis
    - Sepsis
      - Capillary permeability/vasodilatation
      - Vigorous fluid resuscitation
      - Positive fluid balance
    - Cardiac dysfunction
  - Current status of intravascular fluid volume
  - Ongoing fluid losses
  - Presence of ALI/ARDS
  - Time frame of illness

Fluid balance during CRRT

- Issues
  - Primary diagnosis
    - Sepsis
    - Cardiac dysfunction
      - Poor cardiac contractility
      - Cardiogenic pulmonary oedema
      - Negative/even fluid balance
  - Current status of intravascular fluid volume
  - Ongoing fluid losses
  - Presence of ALI/ARDS
  - Time frame of illness

Fluid balance during CRRT

- Issues
  - Primary diagnosis
    - Sepsis
    - Cardiac dysfunction
  - Current status of intravascular fluid volume
    - If unsure - even or positive fluid balance
    - Hemodynamic monitoring
      - PA catheter
      - PICCO
      - Echocardiography

Fluid balance during CRRT

- Issues
  - Primary diagnosis
    - Sepsis
    - Cardiac dysfunction
  - Current status of intravascular fluid volume
  - Ongoing fluid losses
    - Capillary permeability
    - Burns
    - Bleeding
    - GI losses
  - Presence of ALI/ARDS
  - Time frame of illness

Fluid balance during CRRT

- Issues
  - Primary diagnosis
    - Sepsis
    - Cardiac dysfunction
  - Current status of intravascular fluid volume
  - Ongoing fluid losses
  - Presence of ALI/ARDS
    - Improved survival when fluid overload avoided
  - Time frame of illness

Fluid balance during CRRT

- Issues
  - Primary diagnosis
    - Sepsis
    - Cardiac dysfunction
  - Current status of intravascular fluid volume
  - Ongoing fluid losses
  - Presence of ALI/ARDS
  - Time frame of illness
    - Acute illness – fluid load aggressively
    - Plateau – even balance
    - Recovery- negative fluid balance

Electrolyte management

- Issues
  - Na
  - K
  - HCO_3
  - Mg
  - PO_4

Electrolyte management

- Issues
  - Na
    - Generally CRRT fluid - 140 mmol/l
    - Usually limited to available solutions
  - K
  - HCO_3
  - Mg
  - PO_4

Electrolyte management

- Issues
  - Na
  - K
    - Depends on serum level
    - Generally 3-5 mmol/l
    - Aim to keep serum K level 4-4.5 mmol/l
  - HCO_3
  - Mg
  - PO_4

Electrolyte management

- Issues
  - Na
  - K
  - HCO_3
    - Usually fixed 32-35 mmol/l
    - May add extra to CRRT fluid
    - If severe acidosis increase dose ± use IV HCO_3 infusion
  - Mg
  - PO_4

Electrolyte management

- Issues
  - Na
  - K
  - HCO_3
  - Mg
    - Aim to keep 0.8-1.2 mmol/l, (>1.0 if arrhythmias)
    - Usually fixed 0.5-0.7 mmol/l
    - May require extra $MgSO_4$ IV 2-4 gms IV over 1-2 hours or continuous infusion
  - PO_4

Electrolyte management

- Issues
  - Na
  - K
  - HCO_3
  - Mg
  - PO_4
    - Aim to keep 0.8-1.0 mmol/l
    - Hypophosphataemia relatively common over time with CRRT
    - No phosphate in CRRT fluids
    - May add potassium phosphate or sodium phosphate to calcium free CRRT fluid
    - May supplement PO4 IV or by NGT as needed

Fluid and electrolytes 24:00 hrs

- Septic shock
- Anuric
- Positive 6 litres
- ARDS
- Metabolic (lactic) acidosis
  - pH 7.18, PO2 76, PCO2 45, SaO2 94%, BXS -15
  - Lactate 10 nm/l
  - Na 138, K 5.6, Cl 102, HCO3 11
  - Urea 19 mmol/l, creatinine 190 μmol/l
- High dose infusions adrenaline and noradrenaline
- Vasopressin and steroid replacement therapy

So, what are your CRRT orders, Doctor?.....

- Fluid management?
  - Positive balance 250 mls/hr
- Electrolyte management
  - CRRT fluid composition
    - Na 140 mmol/l
    - K 4 mmol/l
    - HCO3 32 mmol/l
    - Mg 0.5 mmol/l
- Management of acidosis
  - $NaHCO_3$ infusion 10 mmol/hr IV
  - ABGs with whole blood electrolytes q4h

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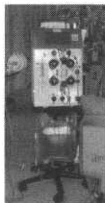
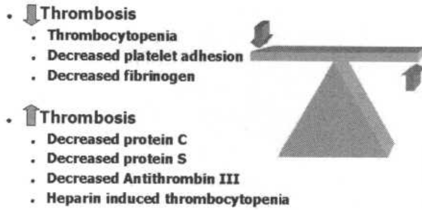


Patient coagulation profile 24:00 hrs

- Platelets 41
- PTT 95
- INR 1.9
- About to start on Activated Protein C infusion

Coagulation profile in critically ill



- ⇩Thrombosis
  - Thrombocytopenia
  - Decreased platelet adhesion
  - Decreased fibrinogen
- ⇧Thrombosis
  - Decreased protein C
  - Decreased protein S
  - Decreased Antithrombin III
  - Heparin induced thrombocytopenia

Impact of filter clotting

- Decrease in dialysis dose
- Wasted nursing time
- Increase in cost

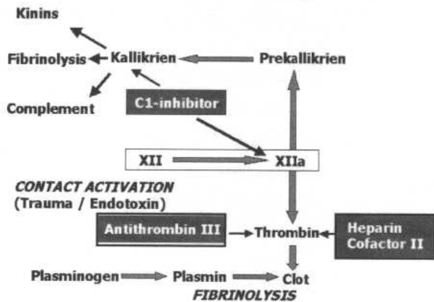
Anticoagulation options

- No anticoagulation
- Unfractionated heparin
- LMW Heparin
- Citrate
- Prostaglandins - PGI_2, PGE_1
- Heparinoid
- r-Hirudin
- Argatroban

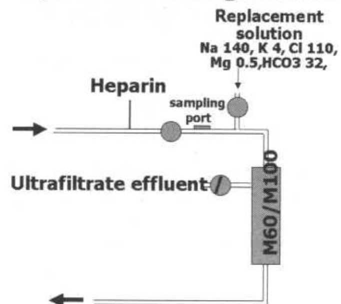
No Anticoagulation

- Short haemofilter life 6-18 hrs
- Significant system down-time in CRRT
- Wasteful of nursing time
- Expensive at $180 per M100 Prisma haemofilter
- However, useful if severe coagulopathy

Unfractionated heparin



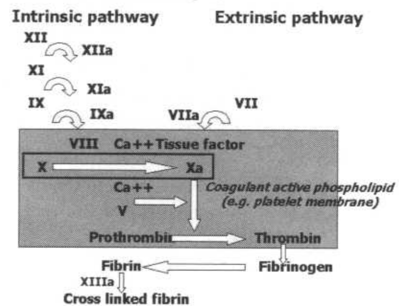
Heparin anticoagulation



Unfractionated heparin

- Aim for PTT 50-60 secs, ACT 160-180
- If bleeding risk PTT 40-50 secs, ACT 140-160
- Risk of bleeding with heparin
  - 2% per day
  - 3.5-10% of deaths
  - 25% of new hemorrhagic episodes
- If bleeding stop UF heparin
- Mean filter life 24 hrs

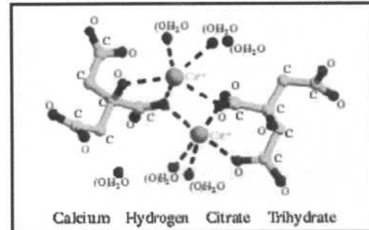
LMW Heparin



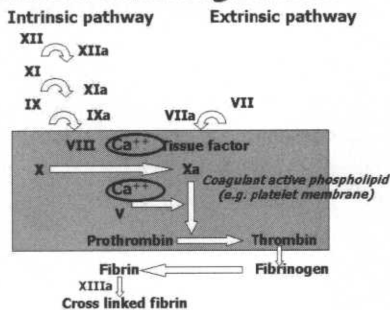
LMW Heparin

- Enoxaparin 8-30u/kg bolus
- Enoxaparin 5u/kg/hr infusion
- LMWH eliminated by kidneys
- Accumulates in renal failure
- No antagonist if bleeding occurs
- Bleeding rates similar to UF Heparin
- Monitoring
  - Free factor Xa levels

Trisodium citrate



Citrate anticoagulation



Citrate anticoagulation

- Trisodium citrate 4% or ACD-A
- Citrate chelates calcium in extracorporeal circuit
- No clotting if serum ionized Ca^{++} is < 0.25 mmol/l
- On return to patient blood has normal serum ionized calcium levels
- Citrate metabolized to HCO_3 and H_2O
- Mean filter life 48 hrs

Calcium replacement

- Progressive depletion of Cai with continuous TSC/ACD infusions
- Risk of serious hypocalcemia
- Avoid with CaCl infusion
  - Must be via CENTRAL LINE
  - Preferably NOT via CRRT circuit
  - 0.75% solution -20 mls CaCl in 250 mls 0.9% NaCl - start at 60 mls/hr
- Titrate to maintain systemic Cai 0.95-1.20

Complications of citrate anticoagulation for CRRT

- Metabolic alkalosis
- Hypernatraemia
- Ionized hypocalcaemia
  - Paraesthesia
  - Arrhythmia

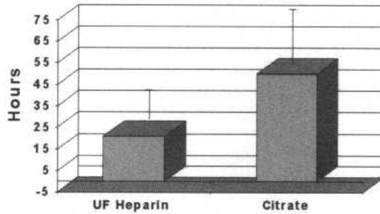
Citrate accumulation/toxicity

- Progressive ionized hypocalcemia with increasing serum total calcium
- Cardiac arrhythmias
- Avoid by
  - Keeping blood pump speed 125 mls or less
  - Keeping TSC infusion below 250 mls/min
  - Monitoring Cai/Total Ca ratio

Monitoring

- Circuit serum ionized calcium q $4\text{-}8^H$
  - keep 0.2-0.35 mmol/l
- Systemic serum ionized calcium q 8^H
  - keep 0.95-1.2 mmol/l
- Serum electrolytes, urea, creatinine q 8^H
- Arterial blood gases q 8^H
- Serum Total Ca, PO_4 and Mg q $8\text{-}24^H$
- Daily AST, Bilirubin

Hemofilter life

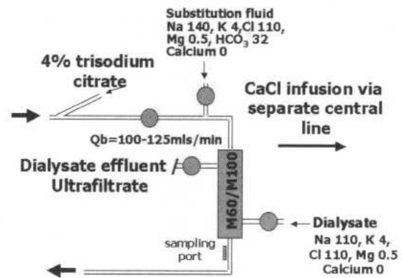


What do you want to do about anticoagulation?

- Platelets 41
- PTT 95
- INR 1.9
- About to start on Activated Protein C infusion

- 24:00 hrs commenced on rAPC (Xigris) 24 mcg/kg/hr infusion
- 24:00 hrs Commenced on CVVH - initially no anticoagulation.
- Hemofilter clotted after 4 hours
- CRRT recommenced - mode CVVHDF with trisodium citrate (TSC) anticoagulation
  - Replacement fluid 1.5 l/hr
  - Dialysate fluid 1.5 l/hr
  - Qb 125 mls/min
  - Fluid balance +200 mls/hr
  - Trisodium citrate 4% infused into circuit at 170 mls/hr
  - Calcium chloride 0.75% infusion via central line at 60 mls/hr - monitored and titrated with systemic whole blood ionized calcium levels every 8 hrs
  - Citrate infusion monitored and titrated using circuit whole blood ionized calcium levels every 8 hrs

Citrate anticoagulation: CVVHDF



Kutsogiannis DJ, Mayers I, Chin WDN, Gibney RTN. Am J Kidney Dis 2000, 35:802-811

- Subsequent steady improvement in hemodynamic status, oxygenation, acid base and coagulopathy
- Noradrenaline weaned off 15:00 hrs day 2, Adrenaline progressively reduced
- Learned that drama group colleague had died
- FiO2 0.4, Lactate 3 nmol/l by 16:00 day 2
- Remained anuric and on CVVHDF
- Adrenaline weaned off and extubated day 3
- Ischemic terminal digits 5th toes
- CVVHDF discontinued on day 3 but remained anuric, requiring IHD for 3 weeks
- Transferred to medicine unit day 6

"I have learned that good HD is like good lovemaking: It should be performed:

- as often as possible
- as long as possible
- as gently as possible
- with a maximum of safety"

Gluserix, Nephrol listserv 1999