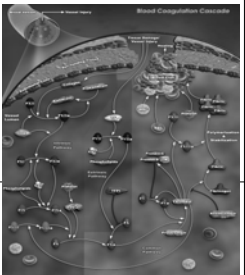


 Critical Care Medicine

Anticoagulation for Renal Support

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Disclosure

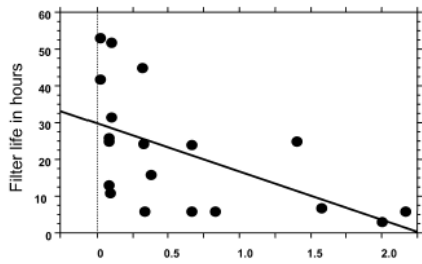
I have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Affiliation/Financial Interest: Member Expert Panel
 Name of Organization: Gambro

Why anticoagulation during RRT?

- To preserve life of extracorporeal circuit
- To maximize RRT dose
- To minimize blood loss caused by clotting during RRT
- To reduce nursing workload and complexity of care

Blood flow and hemofilter life



Flow reductions/hour: 34-66 % less than diastolic
Baldwin I et al. *Int Care Med* 2004;30:2074-2079

Role of access catheter

- Flow = $K \cdot \text{radius}^4 / \text{length}$
- For best flows catheter should be non-kinkable, thick and short.
- However, need to access large central vein
 - SVC 16-20 cm,
 - IVC 20-24 cm
- Consider flow interference by
 - High abdominal pressures
 - Low CVP
- Consider fibrin build up in poorly "locked" catheter

Anticoagulation options

- No anticoagulation
- Unfractionated heparin
- LMW Heparin
- Citrate
- Prostaglandins - PGI₂, PGE₁
- Danaparoid
- r-Hirudin
- Argatroban

Filtration fraction (FF)

The filtration fraction is the proportion of blood flow (QB) per min that is removed as plasma filtrate.

$$FF = QUF/QB$$

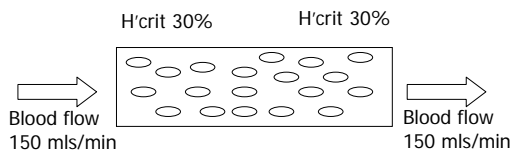
QUF = the total Ultrafiltration rate

QB = blood flow rate

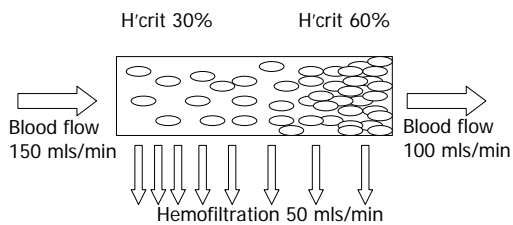
FF > 25% = Hemoconcentration ⇔ clotting

- Where is the FF displayed on the Prismaflex:
numerically % displayed on the set flow rate screen

Filtration fraction



Filtration fraction

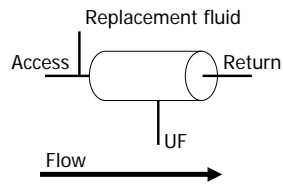


Filtration fraction is the proportion of blood flow/min that is removed as plasma filtrate.

Ideally keep < 25% and should not exceed 30%

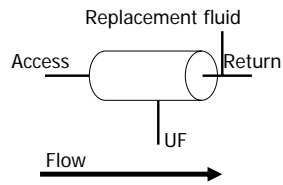
CVVH -predilution

- Fluid removal
- Solute clearance
- Convection
- Some of delivered replacement fluid lost by hemofiltration
- Lower anticoagulation requirements



CVVH -postdilution

- Replacement fluid delivered post-filter
- Higher delivered dose of hemofiltration

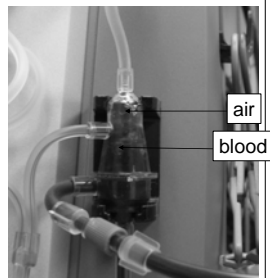


Clots in deaeration chamber

- Likely to happen in pre-filter replacement
- Blood/air interface in this chamber

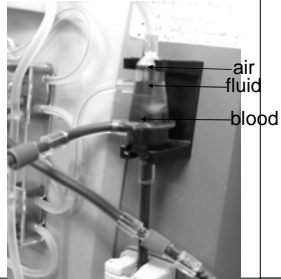
Resolution:

- Post-filter replacement
- 50%/50% pre/post replacement
- Citrate anticoagulant



Clots in deaeration chamber

- Post dilution replacement prevents clot formation in the deaeration chamber
- Blood/fluid/air interface is created rather than an air/blood interface



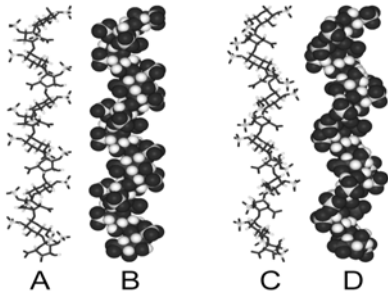
No anticoagulation

- Shorter hemofilter life 6-18 hrs unless severe coagulopathy
- Significant system down-time in CRRT
- Wasteful of nursing time
- Lower CRRT dose than prescribed
- Expensive at \$180 per ST100 Prismaflex hemofilter
- However may be valuable if significant coagulopathy

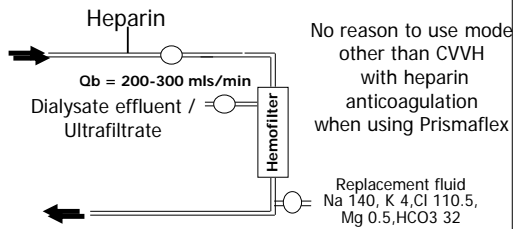
No anticoagulation-machine settings

- Catheter: fresh, no obstruction to flow
- Hemofilter: ST 150
- Mode: CVVH
- Filtration fraction: <25%
- Fluid: 50% prefilter and 50% postfilter replacement
- Blood flow: >200 mls/min

Heparin



Heparin anticoagulation



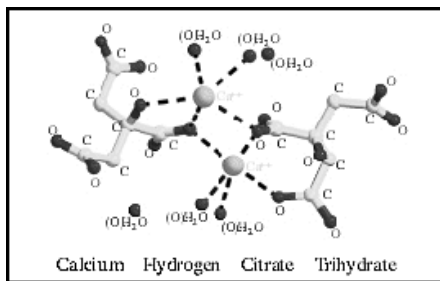
LMW Heparin

- 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

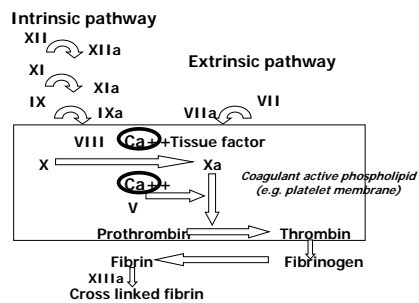
Complications of Heparin

- Bleeding
- Hemorrhage
- Heparin induced thrombocytopenia

Trisodium citrate

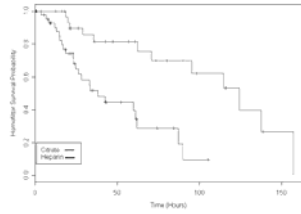


Citrate anticoagulation



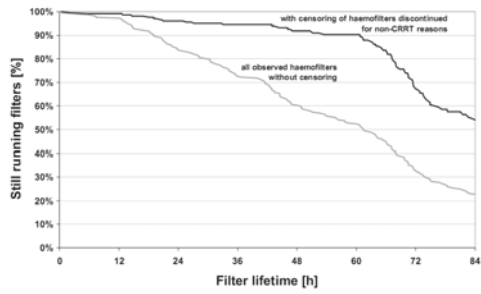
Why citrate?

- Regional anticoagulation
- No additional bleeding risk
- Longer hemofilter life



Kutsogiannis DJ et al. *Am J Kidney Dis* 2004

Citrate: hemofilter survival



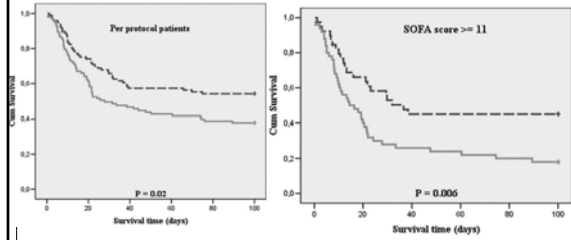
Morgera S et al. *Crit Care Med* 2009;37:2018-24

UF Heparin vs. LMW Heparin vs. Citrate



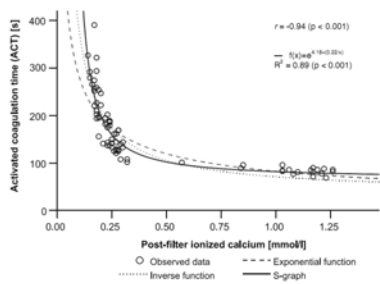
Hoffbauer R et al. *Kidney Int* 1999;56:1578-1583.

Citrate vs. Nadroparin (LMWH)



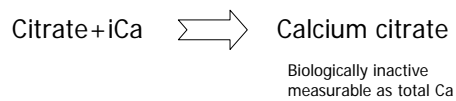
Oudemans van-Straaten HM et al. Crit Care Med 2009;37:545-552

Ionized calcium levels vs. ACT



Kreuzer M et al. Pediatr Nephrol epub March 2010

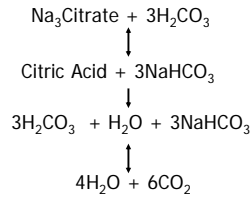
Citrate anticoagulation



- No clotting if serum ionized Ca^{++} is < 0.20 mmol/l
- Minimal clotting if serum ionized Ca^{++} is < 0.20 mmol/l
- On return to patient blood has normal serum ionized calcium levels

Citrate metabolism

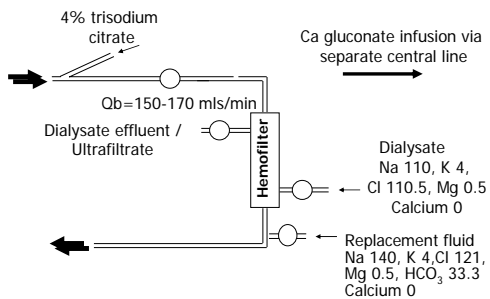
- Citric acid has plasma half life of 5 mins
- Rapidly metabolized by liver, kidney and muscle cells



Citrate formulations

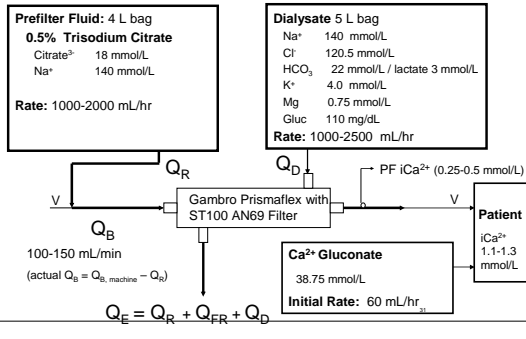
- Trisodium citrate (TSC) 4%
- Acid Citrate Dextrose (ACD)
 - Dextrose,
 - Citric acid 0.8%,
 - TSC 2.2%

Citrate anticoagulation: CVVHDF



Dilute RCA for CVVHDF

Tolwani et al, CJASN 2006



Calcium replacement

- Progressive depletion of iCa with continuous TSC/ACD infusions
- Risk of hypocalcemia
- Calcium infusion - either CaCl_2 or Ca gluconate
- Must be via CENTRAL LINE if CaCl_2
 - Risk of severe local tissue necrosis
 - Preferably NOT via CRRT circuit
- Titrate to maintain systemic iCa 0.90-1.00 mmol/L



Complications of citrate anticoagulation for CRRT

- Metabolic alkalosis
- Hyponatremia
- Ionized hypocalcemia
- Total hypercalcemia
- Ionized hypercalcemia

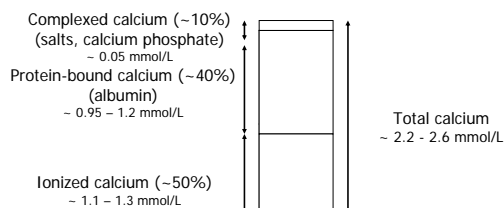
Citrate accumulation/toxicity

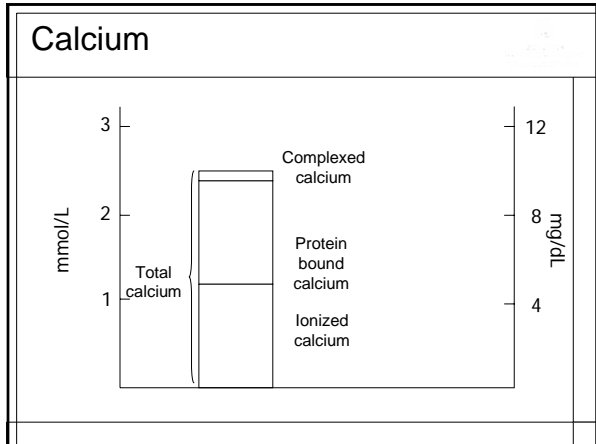
- Progressive ionized hypocalcemia with increasing serum total calcium
- Cardiac arrhythmias-exceptionally rare with CRRT
- Avoid by
 - Keeping blood pump speed 150 mls/min
 - Keeping TSC infusion below 200 mls/hr
 - Monitoring Cai/Total Ca ratio

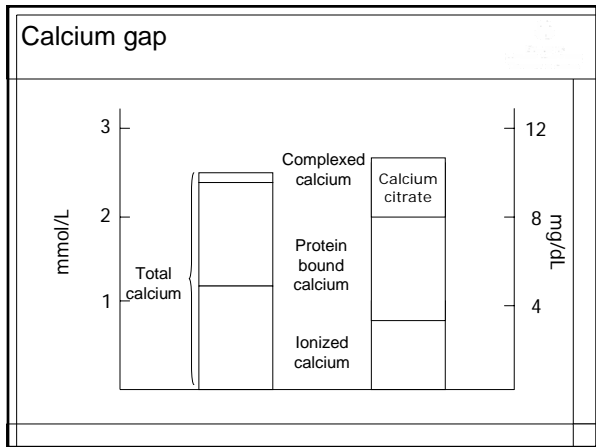
Total to ionized calcium gap

- If high rate of citrate infusion or hepatic dysfunction
 - Accumulation of calcium citrate (total)
 - Progressive decrease in systemic Cai level (ionized)
 - Indicative of citrate accumulation/toxicity
 - Manage by reducing citrate infusion and blood pump speed (Qb) and reducing citrate and calcium infusions to starting levels

Calcium distribution in plasma







Monitoring

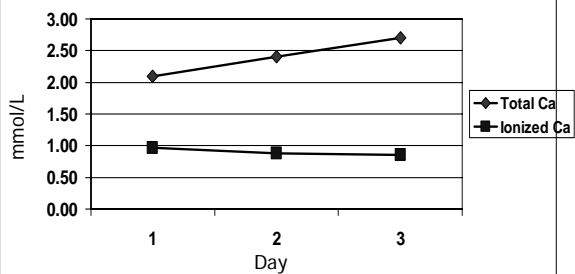
- Circuit serum ionized calcium q 6-8^H
 - keep 0.25-0.35 mmol/l
- Systemic serum ionized calcium q 6-8^H
 - keep 0.90-1.0 mmol/l
- Serum Total Ca, PO₄ and Mg q 12 -24^H

Citrate toxicity

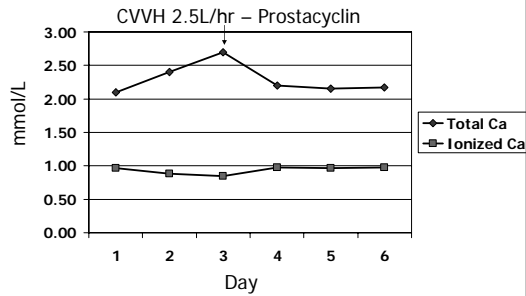
- 49 year-old male with acute on chronic liver failure due to Hepatitis C. Esophageal varices and previous GI bleeding.
- Spontaneous bacterial peritonitis with septic shock and oliguric renal failure. No improvement in renal function with fluid resuscitation and elevation of MAP with vasopressors.
- Creatinine 286, urea 29, Na 138, HCO₃ 14, Plt 60, INR 1.8, PTT 52
- CVVHDF
 - Dialysate 1.5L/hr, replacement fluid 1.5L/hr
 - Citrate 170 ml/hr, calcium gluconate
 - Blood flow 150 ml/min

- Settled with stabilization of urea, creatinine
- 48 hrs later:
 - Dialysate 1.5L/hr, replacement fluid 1.5L/hr
 - Citrate 130 ml/hr, calcium gluconate 110 mls/hr
 - Blood flow 150 ml/min
 - Na 129, HCO₃ 20
 - Total Ca 2.5

Calcium gap



Calcium gap



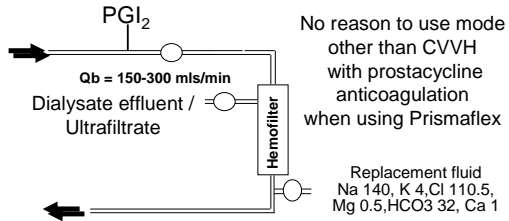
Management of citrate accumulation

- Reduce blood flow rate if possible
- Reduce citrate infusion
- Increase clearance dose -increase dialysate ± replacement fluid flow
- Consider using no anticoagulation if marked coagulopathy
- Consider prostacycline if heparin undesirable

Prostacyclin PGI₂

- Vasodilator
- Inhibits platelet function
 - aggregation
 - activation
 - adhesion
- No effect on on intrinsic clotting system
- Short acting
- Main indication – CRRT in hepatic failure
- 4ng/kg/min

Prostacycline



Prostacyclin issues

- Vasodilator
 - Hypotension, especially if inadvertent bolus given
 - Slight increased risk of cerebral edema
 - Slight increased risk of variceal bleeding
- Slower gastric emptying

Prostacycline challenges

- Must be mixed in supplied diluent-high concentration.
- Must be infused via narrow non-compliant "heparin" tubing using external syringe pump.
- Costly but no more so than citrate.

Management of patients with HIT

- Direct thrombin inhibitors
 - Danaparoid
 - r-Hirudin
 - Argatroban
- Use with extreme caution- non-reversible
- High incidence of severe bleeding

Summary

- Must have good IV access
- Keep blood pump speed > 150 mls/hr
- No anticoagulation is a viable option if severe coagulopathy (e.g. INR>3, PTT>60) or rAPC
- Citrate is safe default if no need for systemic heparin
- Caution with citrate in liver disease
- Heparin if need for systemic anticoagulation
- Prostacyclin if significant hepatic failure and hemofilters clotting
- Argatroban, Lepirudin or Danaparoid if HIT

Thank you for your attention!

