

1-Citrate Regional Anticoagulation: Tobe PRIMSA M100 Protocol

Continuous Renal Replacement Therapy using the Prisma® M 100

Sunnybrook and Women's College Health Sciences Centre

University of Toronto

2075 Bayview Avenue

Toronto, Ontario, Canada M4N 3M5

Nephrology Office: 416-480-6901

Dialysis Unit: 416-480-4488

FAX: 416-480-6940

Continuous Renal Replacement Therapy using the Prisma® M 100

<u>1. ACCESS</u>	5
<u>2. Circuit Setup Guidelines</u>	5
<u>3. BLOOD FLOW RATE (BFR)</u>	5
<u>4. CVVH VS. CVVHD</u>	5
<u>5.0 SOLUTIONS</u>	6
<u>6.0 ANTICOAGULATION</u>	8
<u>6.1 Heparin Anticoagulation</u>	8
<u>6.2 Citrate Anticoagulation</u>	8
<u>6.3 CrCU Citrate Protocol For Use With CRRT Therapy (PRISMA)</u>	9
Post-filter ionized Calcium (iCa) mmol/L.....	10
Citrate Infusion Adjustment	10
< 0.25.....	10
↻ rate by 10 ml/hr (1.12mM/hr)	10
0.25 – 0.35	10
No adjustment	10
150ml/hr (16.8mM/hr)	10
0.36 – 0.45	10
↻ rate by 10 ml/hr	10
(1.12mM/hr).....	10
> 0.46.....	10
↻ rate by 20 cc/hr.....	10
(2.24mM/hr).....	10

7.0 REFERENCES	11
7.1 Prescription references	11
7.2 Access references	12
7.4 Anticoagulation references	12
7.5 Solution references	13
7.6 Nutrition references	13
7.7 Outcome references	13
7.8 Complication references	14
8.0 APPENDICES	15
8.1 Lactate vs. Bicarbonate for Dialysis or Replacement Solution	15
Substitution fluids and dialysate used in CRRT have been often primarily developed for intermittent hemofiltration or peritoneal dialysis. In CRRT techniques including dialysis also any ready-to-use dialysis solution may be employed. In nearly all commercially available fluids lactate (30 - 45 mmol/L), which is converted to bicarbonate on an equimolar basis under physiological conditions, is used as the buffer to correct acidosis. The lactate buffer has the advantage of greater stability over a physiologic bicarbonate buffer. However, lactate is thought to have negative effects on hemodynamic parameters, and on metabolic parameters, e.g. enhanced protein catabolism and decreased regeneration rate of ATP due to the fact that conversion from lactate to bicarbonate needs energy.	15
Only a few studies until now compare different buffers used in substitution fluids. From these data it seems to be common sense that acetate-buffered substitution fluids should be avoided, as a significantly reduced control of acidosis compared to a lactate-buffered solution has been recently reported during CVVH.....	15
Solutions used in peritoneal dialysis have also been recommended as an alternative, but their high glucose concentration can lead to incomplete metabolism, requiring additional insulin with concomitant metabolic alterations in MODS patients.	15
Some studies are dealing with bicarbonate-buffered compared to lactate-buffered solutions. Major goals in these studies had been: control of uremia, control of acidosis and lactate concentration, metabolic changes, hemodynamic parameters and the concentration of the important serum electrolytes.	15

Under stable clinical conditions 2000 mmol of lactate per day are metabolized to bicarbonate on an equimolar basis. Critically ill patients with ARF, especially with concomitant sepsis or circulatory shock have been reported to display a reduced lactate tolerance. In these cases or with the use of the high-volume hemofiltration using an exchange volume of 4-6L/hour the physiological capacity of the liver in converting lactate to bicarbonate may be exceeded. 16

In our first experience, nitrogen excretion was significantly increased in patients receiving lactate-buffer on day 1-4 of CRRT, a result we could not reproduce in a later study. But lactate- associated protein catabolism may be relevant using high amounts of substitution fluids..... 16

Bicarbonate-solutions must be stable for a 24 hour period without precipitation of calcium carbonate or magnesium carbonate. Therefore, the magnesium and calcium concentration is reduced compared to the lactate-buffered solution. To adjust ionic strength the chloride concentration must be increased. Possible precipitation does not allow a higher phosphate concentration in one of the solutions, so phosphate must separately be substituted to avoid phosphate depletion, as MODS patients with ARF tend to develop hypophosphatemia leading to decreased respiratory and cardiac function. The patients serum concentration of these electrolytes must therefore carefully be monitored and other electrolytes must be added if necessary. Especially the magnesium concentration in bicarbonate-solutions may be insufficient in patients with arrhythmias or depleted cardiac function..... 16

8.2 Sample CRRT Orders..... 18

? FOR CORRECTED CA⁺⁺ < 2.0 MMOL/L, GIVE CACL 1GM IN 100ML NS OVER 2HRS VIA CENTRAL LINE. CANCEL ANY PREVIOUS CA⁺⁺ BOLUS ORDERS. 19

5-Citrate Regional Anticoagulation: Tobe PRIMSA M100 Protocol

1. Access

Vascular access will be placed by the ICU staff and should be preferably a dual lumen 12-14 Fr. access. Although flow and recirculation data is similar, it is preferable to have the access placed either IJ or subclavian as opposed to femoral but femoral access is acceptable if a catheter of sufficient length is used (20 cm). The preference that if the patient recovers and can switch to intermittent haemodialysis they can ambulate with out risk of bending a femorally placed catheter.

2. Circuit Setup Guidelines

Follow the manufacture guidelines. Priming of the circuit should be with normal saline. 5% albumin can be added if indicated. PRBC's should not be needed in adults for priming and may induce a "Bradykinin Release Syndrome" due to pH and membrane reaction.

3. Blood flow rate (BFR)

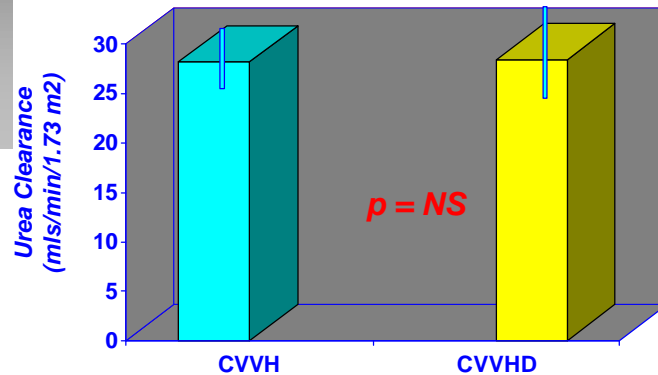
A blood flow rate of 100mls/min will allow for adequate flow. The maximum BFR of the PRISMA® is 180 mls/min. The higher the BFR, the potential for less clotting occurs but the trade off is more alarms. The use of citrate as an anticoagulant makes clotting less dependent upon blood flow (ie our local experience is that with citrate we have less clotting and therefore can run the patient at a slower blood flow rate). At 100 ml/min (6000 ml/hr) blood flow is much greater than dialysis and replacement flow rates (typically 1500-2000 ml/hr) so that clearance is NOT blood flow dependent and higher flow rates will not give higher clearances and will require greater volumes of citrate.

4. CVVH vs. CVVHD

Data has shown that if one keeps constant the amount of solution then urea clearance is similar in CVVH or in CVVHD.

Comparison of Urea Clearance: CVVH vs CVVHD

(Maxvold et al, Crit Care Med April 2000)



BFR = 4 mls/kg/min

Replacement Fluid/Dx FR = 2 l/1.73 m²/hr

SAM = 0.3 m²

In hemofiltration for sepsis, CVVH may have better cytokine clearance. We use a solution rate of 20 mls/kg/hr in either CVVH or CVVHD. The recent work of Ronco et al. suggests that there may be a survival benefit of higher flow rates but this was not confirmed by Bouman. Until this issue is resolved we recommend adjusting the patients clearance to at least prevent the urea and creatinine from rising and preferably fall to within a range of 1.5 - 2 x normal.

5.0 Solutions

Dialysis solutions choice can be bicarbonate based: Normocarb, Dialysis Sol'n Inc, Toronto, Canada (approved for dialysis in Canada and US); Hemosol BO, Hospal, Gottenberg, Sweden, (approved for dialysis in Canada), or lactate based: Hemofiltration sol'n by Baxter, Chicago, Illinois or peritoneal dialysis solution 0.5%(available in Canada only) or 1.5% PD solution, or pharmacy made solutions. Presently only pharmacy made solutions are "approved" for replacement solutions, but pharmacy made solutions run to the risk of ingredient error due to lack of standards that are adhered to by Industry.

7-Citrate Regional Anticoagulation: Tobe PRIMSA M100 Protocol

Commercially Available Solutions for dialysis * or for dialysis or infusion

PREMADE SOLUTIONS ADDITIVES	RINGER'S LACTATE	1.5% PD FLUID	Normocarb *	Baxter Hemofiltration Solution *
Na (mEq/L)	130	132	140	140
K (mEq/L)	4	0	0	2
Cl (mEq/L)	109	96-102	106.5	117
HCO ₃ (mEq/L)	0	0	35	0
Lactate (mEq/L)	28	40	0	30
Ca (mmol/L)	1.5	1.5	0	1.5
PO ₄ (mmol/L)	0	0	0	0
Mg (mmol/L)	0	0.5-1.5	0.75	0.75
Dextrose (mmol/L)	0	83	0	55

*approved for dialysis only

Pharmacy Solutions for dialysis or infusion

CUSTOM MADE SOLUTIONS	CALCIUM-BASED infusate/ DIALYSATE	PHOSPHATE BASED infusate/ DIALYSATE
NaCl (mmol/L)	100	100
NaHCO ₃ (mmol/L)	40	40
KCl (mEq/L)	4	2
K ₃ PO ₄ (mmol/L)	0	1 **
Lactate (mmol/L)	0	0
CaCl ₂ (mmol/L)	1.75	0
MgSO ₄ (mmol/L)	0.75	0.75
Dextrose (mmol/L)	8	8
Solutions are mixed with sterile technique in the pharmacy BUT THERE IS RISK OF ELECTROLYTE ERROR TO DUE LACK OF STANDARDS		

8-Citrate Regional Anticoagulation: Tobe PRIMSA M100 Protocol

6.0 Anticoagulation

Many patients who require continuous renal replacement therapy (eg patients with sepsis, haem/onc patients) will need no anticoagulation due to their underlying coagulopathy. Some patients must be on heparin due to their medical condition. In these patients if heparin is incorporated into the CRRT protocol, if the dialysis is interrupted for any reason, the heparin will also be interrupted for the same period of time. For this reason if the patient requires heparin for a reason other than circuit anticoagulation it should be given separately from dialysis and adjusted by the appropriate most responsible physician. In those patients who require anticoagulation either citrate or heparin can be used. Both protocols are below. There is no contraindication for heparin to be given while the citrate regional anticoagulation protocol is running. For this reason all patients who require anticoagulation to maintain the extracorporeal circuit receive citrate according to the protocol below so that only one protocol is in use.

6.1 Heparin Anticoagulation

Place a syringe of 100 units/ml of heparin in the heparin syringe holder. Load the patient with 20 units/Kg, then begin an infusion at 10 units/Kg/hr. Check PTT systemically. Aim for a PTT of 1.5 to 2.0 times normal. We do not use ACT's due to the variability in this technique and the cost of maintaining this system.

A study by Van de Wetering, found that the coagulation of filters was clearly dependent on the PTT values but there was a similar close relation between the systemic PTT and the incidence of hemorrhage. When the PTT was twice the control between 45-55, the filter usage was 12.9 per 1000 hr. When the PTT was greater than 55, only 9 filters per 1000 hr were used. However, there was a threefold increase in the incidence of bleeding from 2.9/1000 hr in the normal ranges of PTT, to 7.4/1000 hr when the PTT was twofold prolonged between 45-55 and greater. Filter usage was not improved as PTT increased beyond 1.5 x normal, but bleeding consistently increased as PTT increased. He felt that a systemic PTT of 1.5 times (35-45 seconds), is associated with the best balance between filter life span and hemorrhagic complications.

6.2 Citrate Anticoagulation

Regional citrate anticoagulation. Regional citrate anticoagulation is a technique that enables only the extracorporeal circuit to be anticoagulated without systemic anticoagulation. Citrate infusion into the hemodialysis circuit prior to the dialyser leads to calcium chelation and prolongation of the clotting times when ionized calcium levels fall below 0.4 mmol/l. This requires a citrate concentration of approximately 5 mmol/l in the blood entering the dialyser. If a calcium containing dialysate or haemofiltration solution is used, much higher volumes of citrate are required leading to the risk of citrate block (systemic citrate accumulation, drop in systemic ionized calcium, rise in anion gap and risk of hypocalcemic complications, eg. tetany, ECG changes) (Karanicolaus et al). Regional citrate anticoagulation has been shown to be safe and effective in adult patients on haemodialysis but there are only 4 randomised-controlled (Flanigan, Weigmann

9-Citrate Regional Anticoagulation: Tobe PRIMSA M100 Protocol

and Janssen) trials. This technique offers the potential of hemodialysis without systemic anticoagulation and may also increase hemodialysis efficiency. Besides hemodialysis prescription, vascular access and clotting are the most important limits to hemodialysis adequacy. Haufbauer has shown that citrate results in significantly less thrombus formation and dialyser clotting than standard or low molecular weight heparin during intermittent hemodialysis. Coagulation activation presents one of the main determinants of biocompatibility. Calcium ions are a prerequisite for cellular activation of thrombocytes and neutrophils. Reducing the calcium concentration in the dialyser may ameliorate the adverse effects of neutrophil activation reducing leukopenia and release of proteolytic enzymes from neutrophils. Therefore regional citrate anticoagulation may be a superior form of anticoagulation for hemodialysis.

Potential Adverse Effects: Hypocalcemia may occur when the systemic delivery of sodium citrate is greater than the patient's ability to metabolize citrate. The precise amount of citrate administered systemically will depend on citrate removal by the dialysis filter. The clearance of citrate is 60% of urea clearance with an extraction coefficient of 60% (van der Meulen J) The citrate concentration leaving the dialysis filter will be 50% of that entering the filter.

The metabolism of citrate results in the generation of bicarbonate. Accumulation of bicarbonate leads to systemic metabolic alkalosis with the use of citrate. As many patients on hemodialysis require bicarbonate supplements the development of metabolic alkalosis may be considered an adverse event only when excessive.

6.3 CrCU Citrate Protocol For Use With CRRT Therapy (PRISMA)

- 1.0 Prime in CVVHDF Mode using ordered dialysate and replacement solutions. Solutions will generally be as follows:
 - Dialysate – Normocarb 240mL in 3L Sterile Water for Irrigation
 - Replacement – NS 1LAdditives ordered by MD (eg. KCl 3 mmol/L for $K^+ < 3.5$ mmol/L, Phosphate is best added into TPN or enteral nutrition supplement).
- 2.0 Attach infusion set to blue arm of Y-connector and prime with the Citrate ACD(A) Solution (500 - 1000ml).
Attach red arm of Y-connector to Red Access Line on the PRISMA set. When ready to start the citrate the rate in ml's/hr will be 1.5 x the blood flow rate of the PRISMA machine at ml's/min (eg Start Citrate at 150 ml's/hr if the BFR is 100 ml's/min).
- 3.0 Set up the Ca^{++} infusion as ordered via central line (4gms Calcium Chloride in 1L D5W @ 50 ml/hr). DO NOT alter dilution volume or solution as this adjusts for the high sodium (224 mmol/L) in the ACD (A) citrate. Please note: If a central line is unavailable, Calcium Gluconate 9gm in 1L D5W must be used at the same rate. If the ACD (A) citrate rate is > 180 ml/hr or less than 120 ml/hr, the calcium/D5W rate can be adjusted to run at 1/3 of the citrate rate (eg. citrate rate = 195 ml/min then calcium/D5W rate = 65 ml/hr).
- 4.0 Connect the Prisma circuit to the dialysis catheter as per procedure and press start.

10-Citrate Regional Anticoagulation: Tobe PRIMSA M100 Protocol

- 5.0 Set the flow rates in PRISMA as ordered. The blood flow rate should be set at 100ml/hr.
- 6.0 Patient Fluid Removal Rate is calculated by:
 Net Ultrafiltration rate + Citrate rate + Calcium infusion rate = Pt. Fluid Removal Rate.
- 7.0 Connect the Prisma circuit to the dialysis catheter as per procedure and press start.
- 8.0 Start the Calcium Infusion at 50 ml/hr. Start the Citrate Infusion at 150 ml/hr. If the patient is hypotensive consider holding the citrate infusion for ½ hour until BP stabilized.
- 9.0 1 hour after initiation of therapy and every 6 hours thereafter, send the following blood work
- 10.0 Post-filter ionized Ca⁺⁺ (drawn from the return line, blue sample port)
 Systemic ionized Ca⁺⁺ (drawn from patient (true) arterial line or peripheral draw)
 Chemistries (eg Lytes, Bun, Cr, Ca, Phos, Albumin) Titrate the Citrate infusion according to the citrate sliding scale below* :

Post-filter ionized Calcium (iCa) mmol/L	Citrate Infusion Adjustment
< 0.25	↘ rate by 10 ml/hr (1.12mM/hr)
0.25 – 0.35	No adjustment 150ml/hr (16.8mM/hr)
0.36 – 0.45	↘ rate by 10 ml/hr (1.12mM/hr)
> 0.46	↘ rate by 20 cc/hr (2.24mM/hr)
NOTIFY MD IF CITRATE INFUSION RATE > 200 ml/hr	

?? From N. Gibney et al. 1999.

- 11.0 Adjust the Replacement Rate if the Serum Bicarb is > 26mmol/L and rising. Call Nephrologist to add NS as a replacement solution @ 200-400 ml/hr and decrease the dialysate rate by this amount. This will remove the excess bicarb in the ultrafiltered fluid and replace it with NS and reduce the HCO₃ from the bath at the same time. (eg. if replacement rate ? by 100 ml/hr, then ? dialysate rate by 100 ml/hr). Round the adjustment in replacement and dialysate rate to nearest 50ml/hr.

11-Citrate Regional Anticoagulation: Tobe PRIMSA M100 Protocol

12.0 Alternatively the amount of replacement can be calculated as follows:

$$\frac{\text{Amount of bicarb to remove per hour mmol/hour}}{\text{Current bicarb concentration mmol/L}}$$

$$= \frac{(\text{bicarb current} - \text{bicarb previous}) \times 0.3 \times \text{patient weight(kg)}}{\text{Time between the bicarb samples (hours)} \times \text{current bicarb}}$$

ie. $(26-24) \times 0.3 \times 78 = 0.30 \text{ L/hr.} = 300 \text{ ml/hour}$

13.0 If the filter clots, stop the Citrate and Ca⁺⁺ infusions and discontinue the filter. If the therapy is terminated or to be disconnected, return blood according to procedure.

14.0 Notify MD for the following :

- a. Replacement rate > 1000 ml/hr.
- b. Systemic Ionized Ca⁺⁺ < 0.75 mmol/L. Consider holding citrate for 3 hours and resuming infusion at 150ml/hr
- c. Na⁺ > 150 mmol/L. Consider changing replacement solution to 0.45% NaCl.
- d. K⁺ < 3.5mmol/L. Consider adding KCL 3 mmol/L to replacement

15. Temperature Regulation:

When blood is outside of the body a tremendous heat loss occurs. The use of the PRIMSA THERM® on the infusion solution, the dialysis solution or the blood line will aid in keeping euthermic. Additional overhead warmer or external warmer may be needed.

7.0 References

7.1 Prescription references

1. Bellomo, R. Choosing a Therapeutic Modality: Hemofiltration vs. Hemodialysis vs. Hemodiafiltration Seminars in Dial, 1996; 9
2. Brunet S, Leblanc M, Geadah D et al Diffusive and Convective Solute Clearances During Continuous Renal Replacement Therapy at Various Dialysate and Ultrafiltration Flow Rates Am J Kid Dis 1999; 34:486-492
3. Bunchman TE, Maxvold NJ, Kershaw DB, Sedman AB, Custer JR: Continuous venovenous hemodiafiltration in infants and children, Am J Kid Dis. 1995; 25:17, 1995.
4. Bunchman TE, Donckerwolcke R: CAVH(D), CVVH(D), Modalities in Infants and Children, Pediatr Nephrol 1994; 8:96-99.

12-Citrate Regional Anticoagulation: Tobe PRIMSA M100 Protocol

5. Braun, M C et al Continuous Venovenous Am J Nephrol, 1998;18: 531-533
6. Ronco C, Bellomo R, Homel P et al: Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: A prospective randomized trial. Lancet 2000;356:26-30.
7. Bouman CSC, Oudemans-van Straaten HM, CRRT Meeting Presentation March 10, 2001, San Diego Ca.

7.2 Access references

8. Bunchman TE, Gardner JJ, Kershaw DB, Maxvold NJ: Vascular access for hemodialysis or CVVH(D) in infants and children, Dial Transplant. 1994; 23:314-317,.
9. Gardner JJ, Bunchman TE, Maxvold NJ et al. Flow characteristics of a new pediatric continuous renal replacement therapy catheter for acute renal failure management. Blood Purif 1997; 15, abstr #33
10. Jenkins RD, Kuhn RJ, Funk JE: Clinical implications of catheter variability on neonatal continuous hemofiltration, Trans Am Soc Artif Intern Organs 1998; 34:108-111

7.4 Anticoagulation references

11. Geary DF, Gajaria M, Fryer-Keeze S, Willemsen J: Low dose and heparin free hemodialysis in children, Pediatr. Nephrol. 1991; 5:220, 1991.
12. Macdonald D, Martin R: Use of Sodium Citrate Anticoagulation in a Pediatric Continuous Venovenous Hemodialysis Patient ANNA Journal 1995; 22: 21-24
13. Johnson PM, Maxvold NJ, Bunchman TE: Citrate anticoagulation for pediatric CRRT: (submitted to CRRT, San Deigo, CA March 8-10, 2001)
14. van de, Wetering J.; Westendorp, R.G.; van der Hoeven, J.G.; Stolk, B.; Feuth; JD; Chang, P.C. Heparin use in continuous renal replacement procedures: the struggle between filter coagulation and patient hemorrhage. JASN 7, 145-150, 1996.
15. Nuthall GA, Skippen PW, Daoust CR, Al Jofan FB: Citrate anticoagulation for continuous renal replacement therapy. Pediatr Nephrol 14:C138, 2000
16. Pinnick RV, Wiegmann TB, Diederich DA: Regional citrate anticoagulation for hemodialysis in the patient at high risk for bleeding. N Eng J Med 308:258-261, 1983
17. Hocken AG, Hurst PL: Citrate regional anticoagulation in hemodialysis. Nephron 46:7-10, 1987
18. Mehta RL: Regional citrate anticoagulation for CAVHD in critically ill patients. Kidney Int 38:976-981, 1990
19. Mehta RL: Regional citrate anticoagulation for CAVHD-An update after 12 months. Contrib Nephrol 93:210-214, 1991
20. Ward DM, Mehta RL: Extracorporeal management of acute renal failure patients at high risk for bleeding. Kid Int 43. Supp 41: S237-S244, 1993
21. Palsson, R.; Niles, J.L. Regional citrate anticoagulation in continuous venovenous hemofiltration in critically ill patients with a high risk of bleeding. Kidney International 55: 1991-1997, 1999.

13-Citrate Regional Anticoagulation: Tobe PRIMSA M100 Protocol

22. C. Barbour, L. Devenish, J. Locke, T. Rogovein, S. Karanicolas. Regional anticoagulation using anticoagulant citrate dextrose solution in conjunction with commercially prepared dialysate solutions containing calcium in continuous venovenous hemodiafiltration. *Blood Purification* 1999; 17: 19-49
23. Flanigan MJ, Pillsbury L, Sadewasser G, Lim VS: Regional hemodialysis anticoagulation: Hypertonic tri-sodium citrate or anticoagulant citrate dextrose-A. *Am J Kid Dis* 27:519-524, 1996
24. Wiegmann TB, MacDougall ML, Diederich DA: Long-term comparisons of citrate and heparin as anticoagulants for hemodialysis. *Am J Kid Dis* IX:430-435, 1987
25. Janssen MJFM, Deegens JK, Kapinga TH, Beukhof JR, Huijgens PC, van Loenen AC, van der Meulen J: Citrate compared to low molecular weight heparin anticoagulation in chronic hemodialysis patients. *Kidney Int* 49:806-813, 1996
26. Hofbauer R, Moser D, Frass M, Oberbauer R, Kaye AD, Wagner O, Kapiotis S, Druml W: Effect of anticoagulation on blood membrane interactions during hemodialysis. *Kidney Int* 56:1578-1583, 1999
27. van der Meulen J, Janssen MJFM, Langendijk PNJ, Bouman AA, Oe PL: Citrate anticoagulation and dialysate with reduced buffer content in chronic hemodialysis. *Clin Nephrol* 37:36-41, 1992

7.5 Solution references

28. Zimmerman D, Cotman P, Ting R, Karanicolas S, Tobe SW: Continuous veno-venous haemodialysis with a novel bicarbonate dialysis solution: prospective cross-over comparison with a lactate buffered solution *Nephrol Dial Transplant* 1999 14:2387-2391
29. Roy, D., et al Continuous veno-venous hemodiafiltration using bicarbonate dialysate *Pediatr Nephrol*, 1997; 11:680-683
30. Maxvold NJ, Flynn JT, Brophy PD, et al. Prospective, crossover comparison of bicarbonate vs lactate-based dialysate for pediatric CVVHD. *Blood Purif* 1999; 17; abst :#27

7.6 Nutrition references

31. Maxvold NJ, Smoyer WE, Custer JR, Bunchman TE. Amino acid loss and nitrogen balance in critically ill children with acute renal failure: A comparison between CVVH and CVVHD therapies. *Crit Care Med*, 2000; 28:1161-1165
32. Davies SP, Reaveley DA, Brown EA, Kox WJ: Amino acid clearance and daily losses in patients with acute renal failure treated by continuous arteriovenous hemodialysis *Critical Care Med* 1991 19:

7.7 Outcome references

33. Goldstein SL, Currier H, Graf JM, Cosio CC, Brewer ED, Sachdeva R: Outcome in children receiving continuous hemofiltration (In Press *Pediatrics*)
34. Fargason CA, Langman CB: Limitations of the pediatric risk of mortality score in assessing children with acute renal failure. *Pediatr Nephrol* 1994; 7:703-7

14-Citrate Regional Anticoagulation: Tobe PRIMSA M100 Protocol

35. Bunchman TE, Brophy PD, Flynn JT, Kershaw DB, Maxvold NJ, Smoyer WE. Pediatric renal replacement therapies: Diseases, modalities and outcome. JASN 1999; 10: abst # 138
36. Zobel G, Kuttinig M, Ring E, Grubbauer HM: Clinical scoring systems in children with continuous extracorporeal renal support. Child Nephrol Urol 1990; 10: 14-17
37. Ronco C, Parenzan L. Acute renal failure in infancy: Treatment by continuous renal replacement therapy Intensive Care Med 1995; 21: 490 – 499
38. Zobel G, Ring E, Rödl S. Prognosis in Pediatric Patients with Multiple Organ System Failure and Continuous Extracorporeal Renal Support Contrib to Nephrol Basel, Karger, 1995, Vol. 116, pp 163-168
39. Meyer RJ, Brophy PD, Bunchman TE et al Survival and renal function in pediatric patients following extracorporeal life support with hemofiltration. (In press Pediatric Critical Care)

7.8 Complication references

40. Lacour F, Maheut H: AN-69 membrane and conversion enzyme inhibitors: prevention of anaphylactic shock by alkaline rinsing? Nephrologie 1992; 13:135-136
41. Brophy PD, Mottes TA, Kudelka TL, McBryde KD, Gardner JJ, Maxvold NJ, Bunchman TE: AN-69 Membrane Reactions are pH-dependent and Preventable (In press Am J Kid Dis)
42. Jenkins R, Harrison H, Chen B. Arnold D. Funk J: Accuracy of intravenous infusion pumps in continuous renal replacement therapies, Trans Am Soc Artif Intern Organs J 1992;38:808-811

8.0 Appendices

8.1 Lactate vs. Bicarbonate for Dialysis or Replacement Solution

From Dr. Horst Kierdorf, Syllabus: Workshop on Replacement and Dialysate Solutions for CRRT, Sixth International Conference on CRRT, San Diego, 2001.

Continuous renal replacement therapies (CRRT) are well accepted for critically ill patients with acute renal failure (ARF). To fulfill the three major aims of RRT in ARF: detoxification, fluid elimination and compensation of acidosis, today, daily fluid exchange in CRRT reaches 30-40 L and more. Therefore, the composition of the substitution-/ dialysate-fluid becomes more relevant.

Substitution fluids and dialysate used in CRRT have been often primarily developed for intermittent hemofiltration or peritoneal dialysis. In CRRT techniques including dialysis also any ready-to-use dialysis solution may be employed. In nearly all commercially available fluids lactate (30 - 45 mmol/L), which is converted to bicarbonate on an equimolar basis under physiological conditions, is used as the buffer to correct acidosis. The lactate buffer has the advantage of greater stability over a physiologic bicarbonate buffer. However, lactate is thought to have negative effects on hemodynamic parameters, and on metabolic parameters, e.g. enhanced protein catabolism and decreased regeneration rate of ATP due to the fact that conversion from lactate to bicarbonate needs energy.

Only a few studies until now compare different buffers used in substitution fluids. From these data it seems to be common sense that acetate-buffered substitution fluids should be avoided, as a significantly reduced control of acidosis compared to a lactate-buffered solution has been recently reported during CVVH.

Solutions used in peritoneal dialysis have also been recommended as an alternative, but their high glucose concentration can lead to incomplete metabolism, requiring additional insulin with concomitant metabolic alterations in MODS patients.

Some studies are dealing with bicarbonate-buffered compared to lactate-buffered solutions. Major goals in these studies had been: control of uremia, control of

16-Citrate Regional Anticoagulation: Tobe PRIMSA M100 Protocol

acidosis and lactate concentration, metabolic changes, hemodynamic parameters and the concentration of the important serum electrolytes.

Uremia and acidosis (pH, base-excess) are sufficiently controlled during CRRT with an exchange volume of in average 30 L using either buffer. If patients with severe liver failure and lactic acidosis were excluded, no difference in hemodynamic and metabolic parameters between the solutions occurred. Plasma lactate concentration was elevated during lactate use in some cases, but lactate levels remained within normal limits in patients without liver impairment. Bicarbonate concentration in the solutions should exceed 35-40 mmol/L as in some cases the buffer capacity of the solutions were inadequate. In patients with severe liver failure or lactic acidosis solutions with lactate buffer were shown not to be indicated.

Under stable clinical conditions 2000 mmol of lactate per day are metabolized to bicarbonate on an equimolar basis. Critically ill patients with ARF, especially with concomitant sepsis or circulatory shock have been reported to display a reduced lactate tolerance. In these cases or with the use of the high-volume hemofiltration using an exchange volume of 4-6L/hour the physiological capacity of the liver in converting lactate to bicarbonate may be exceeded.

In our first experience, nitrogen excretion was significantly increased in patients receiving lactate-buffer on day 1-4 of CRRT, a result we could not reproduce in a later study. But lactate-associated protein catabolism may be relevant using high amounts of substitution fluids.

Bicarbonate-solutions must be stable for a 24 hour period without precipitation of calcium carbonate or magnesium carbonate. Therefore, the magnesium and calcium concentration is reduced compared to the lactate-buffered solution. To adjust ionic strength the chloride concentration must be increased. Possible precipitation does not allow a higher phosphate concentration in one of the solutions, so phosphate must separately be substituted to avoid phosphate depletion, as MODS patients with ARF tend to develop hypophosphatemia leading to decreased respiratory and cardiac function. The patients serum concentration of these electrolytes must therefore carefully be monitored and

17-Citrate Regional Anticoagulation: Tobe PRIMSA M100 Protocol

other electrolytes must be added if necessary. Especially the magnesium concentration in bicarbonate-solutions may be insufficient in patients with arrhythmias or depleted cardiac function.

Two other major problems may occur in daily use of bicarbonate-solutions:

- a) The solution has to be mixed immediately before use from a buffer-free electrolyte solution and the bicarbonate-buffer. It must be realized that the administration of the buffer-free electrolyte solution may endanger the patients and it must be secured that the lone application of either the buffer or the buffer-free solution is impossible.
- b) The readily mixed bicarbonate-buffered solution has to be prepared in bags of special plastic sheeting to prevent evaporation of carbon dioxide. The solution must be stable for at least 24 hours without precipitation of calcium carbonate or magnesium carbonate.

References:

Morgera S, Heering P, Szentandras T, Manassa E, Heintzen M, Willers R, Passlick-Deetjen J, Grabensee B. Comparison of a lactate- versus acetate-based hemofiltration replacement fluid in patients with acute renal failure. *Renal Fail* 19:155-164, 1997

Thomas AN, Guy JM, Kishen R, Geraghty IF, Bowles BJM, Vadgana P: Comparison of lactate and bicarbonate buffered haemofiltration fluids: use in critically ill patients. *Nephrol Dial Transplant* 12:1212-1217, 1997

Kierdorf HP, Leue C, Arns S: Lactate- or Bicarbonate-buffered Solutions in Continuous Extracorporeal Renal Replacement Therapies. *Kidney Int* 56 (Suppl.72): S37-S40, 1999

Zimmerman D, Cotman P, Ting R, Karanicolas S, Tobe SW. Continuous veno-venous haemodialysis with a novel bicarbonate dialysis solution: prospective cross-over comparison with a lactate buffered solution. *Nephrology, Dialysis, Transplantation* 1999;14:2387-91.

18-Citrate Regional Anticoagulation: Tobe PRIMSA M100 Protocol

8.2 Sample CRRT Orders

Yes	No	Doctor must check off appropriate orders
Signature _____		
1.		Priming : ? M100 filter ? Other _____ ? CVVHDF Mode ? Other _____
2.		Prime Solution : (please choose one) ?? Heparin 5,000U in 1L NS, total prime volume 2L ?? NO HEPARIN, N/S 2L for HIT patients
3.		Solutions : Dialysate : ? Normocarb 240mL/3L bag Sterile Water for Irrigation ?? Other : _____ Replacement : ? _____
4.		Flow Rates : Blood Flow Rate : ? 100 mL/min ? Other : _____ mL/hr Dialysate Rate : _____ mL/hr (approx. 20mL/Kg) Replacement Rate : _____ mL/hr (for citrate protocol, start at 0mL/hr) Patient Fluid Removal Rate Calculation : (please fill in all spaces) Net Ultrafiltration rate _____ mL/hr + citrate rate _____ mL/hr + Ca++ rate _____ mL/hr + NS flush rate _____ mL/hr = _____ mL/hr Patient Fluid Removal Rate
5.		Anticoagulation (please choose one) ?? Citrate as per CrCU Citrate Protocol (as printed on reverse) ?? Heparin : (Not to be ordered if on systemic heparin) Initial Heparin Bolus _____ Units IV Heparin 1000U/mL via 20mL syringe to run at _____ U/hr Maintain PTT in range _____ secs.(recommend 35-45s) Monitor PTT q6h. Notify physician if out of range ?? NS flush _____ mL, q ____ hour ?? None
6.		Lab Work : ? Electrolytes, BUN, Cr q6h ? Ca++ profile, BS, CBC q12h
7.		Other : ? CaCl infusion 4gms in 1L D5W at 50mL/hr via central line

19-Citrate Regional Anticoagulation: Tobe PRIMSA M100 Protocol

? If $K^+ < 3.5$ mmol/L, add KCl 3 mmol/L to dialysate (ie.

9mmol in 3L bag)

? For Corrected $Ca^{++} < 2.0$ mmol/L, give CaCl 1gm in 100mL NS
over 2hrs via central

line. Cancel any previous Ca^{++} bolus orders.

8. For temporary disconnection, maintain dialysis catheter with :
(choose one)

?? Heparin 1,000U in 500 mL NS

?? NO HEPARIN, NS 500 mL (for HIT patients)