

REFERENCES AND OVERVIEW FOR HEMOFILTRATION IN PEDIATRICS AND ADOLESCENTS

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Check out these web sites and dates!!

www.Adqi.net -web site for info on CRRT
www.Crrtonline.com -web site for info on Dr. Mehta's meeting
www.PCRRT.com Pediatric CRRT with links to other meetings, protocols, industry
4th International Conf on Pediatric CRRT February 24-25, 2006 Zurich, Switzerland
PCRRT list serve (contact Bunchman)

Education Objectives

1. Review of literature relevant to Pediatrics
 - a. Solutions for replacement or for dialysis
 - i. Dialysis
 1. Normocarb®
 2. Priskasate
 3. Baxter Hemofiltration solution
 4. Accusol
 5. Pharmacy made
 - Replacement solutions
 6. Normocarb®
 7. NS, LR
 8. Pharmacy Made
 - b. Anticoagulation protocols
 - i. Heparin
 - ii. Citrate
 - iii. none
 - c. Outcome
 - d. Prescriptions for
 - i. ARF
 - ii. Intoxications

Introduction

While the basic principles of continuous hemofiltration (HF) are similar for adults and children, the application of these modalities in children requires recognition of the unique properties of pediatric HF. Specific attention to detail such as, extracorporeal blood volume/blood priming (especially in patients < 10 kg), nutritional issues, etiological differences in disease processes (i.e. Inborn Errors of Metabolism), access, and line/membrane choice, must be given when dealing with problems in this population.

HF is indicated in the pediatric population for hypervolemic anuric acute renal failure (ARF), electrolyte abnormalities, catabolic patients with increased nutritional needs, patients with sepsis, poisoning (occasionally in combination with hemodialysis (HD)), inborn errors of metabolism, diuretic unresponsive hypervolemia, and hepatic or drug induced coma. Additionally, HF in conjunction with other therapies such as extracorporeal membranous oxygenation (ECMO), patients with cardiomyopathy on a left-ventricular assist device (LVAD) and the newer hepatic support therapies has also proven to be quite useful.

Machinery

Adaptive machinery (*i.e.*, the use of equipment designed for other purposes such as hemodialysis equipment) often includes a blood pump segment with an air leak detector. What adaptive machinery does not include is the ability to regulate either ultrafiltration control or thermic control. Commercially available machinery (Aquarius, Edwards Lifesciences, Mississauga, Ont; PRISMA, Gambro, Lakewood, CO; BM-25, Baxter, Deerfield, IL; Diapact™, B. Braun Medical Inc, Bethlehem, PA; 2008 Hemodialysis and CRRT machine, Fresenius, Fresenius, NA) offer a variety of blood flow rates (BFR), warming systems, accurate ultrafiltration controllers, venous and arterial pressure monitors and blood leak detectors. In addition these allow for local prescriptions of HF including continuous veno-venous hemofiltration (CVVH), continuous veno-venous hemofiltration with dialysis (CVVHD), and continuous veno-venous hemodiafiltration (CVVHDF (table 1).

Programs that have looked at transition from adaptive machinery to commercially available machinery have found that their nursing time and overtime, as well as their overall expense were often decreased. All systems can provide circuit volumes that offer the adaptability to sustain therapy for smaller and larger size individuals. The Baxter, Braun and the Fresenius machines allow for individual choice of hemofilter membrane while the PRISMA uses a single membrane (AN-69) that has been found in adult ARF HD data, to improve survival rate. The choice of HF machine is based on the local standard of care as opposed to clinical outcome (table 2).

Access

See table 3 and references

Anticoagulation

Pediatric protocols are available for both heparin and citrate anticoagulation as attachment A (heparin) and B (citrate)

Anticoagulation really should be thought about in three different ways. First, does the patient need it? Often patients with multi-organ system failure have a natural anticoagulation due to the underlying disease (e.g. sepsis with DIC). Those patients may have a “natural ACT” that may be in the range whereby anticoagulation is not necessary. In those patients obtaining a high BFR with a large size access may be sufficient to maintain HF without the use of anticoagulation.

The majority of studies to date have shown that heparin is relatively efficient in children. The use of heparin loading at 10-20 units/kg as an initial bolus and then 5-20 units/kg/hr maintaining a bedside ACT of 180-240 seconds is usually adequate in most patients. Bleeding secondary to systemic heparinization is always a potential complication.

Citrate anticoagulation is performed by adding citrate to the blood as it leaves the patient to flow to the machine. The result is a reduced ionized calcium ϕ (.35 to .45 mmol/l) within the circuit. A calcium infusion to the patient, independent of the HF circuit, results in the patient maintaining a normal systemic ionized calcium between 1.1 and 1.3 mmol/l. The overall result is HF system anticoagulation without patient anticoagulation. Citrate anticoagulation requires a calcium free dialysate and replacement solutions in order to reduce the potential risk of coagulation in the HF system

Citrate also requires a separate central line for Calcium replacement. Table 3 has included different triple lumen access for hemofiltration that has either a “pigtail” or an extra central line allowing for a calcium infusion line.

Solutions

Adult Studies by Zimmerman et al demonstrated that both lactate as well as the bicarbonate based solutions result in the same degree of effective clearance, but plasma lactate levels are higher in patients on lactate-based solutions. It is unclear whether elevated lactate levels, from lactate based solutions, may be detrimental to the patient. However, elevated lactate levels may offer confounding information to the clinician, especially in the setting of sepsis and/or organ under-perfusion. Furthermore, patients with hepatic failure may not be able to convert lactate to bicarbonate, and use of lactate based dialysis solution may produce or exacerbate lactic acidosis. Bicarbonate buffered dialysis solutions are therefore preferred for patients with hepatic failure. Barenbrock et al demonstrated improved care of the patient when receiving bicarbonate based solutions when compared to lactate. Essentially with the use of these products the use of lactate based solutions should be considered historical and potentially detrimental to the child needed CRRT.

Solutions for CVVH can be as uncomplicated as normal saline, lactated ringers, total parenteral nutrition (TPN), routine intravenous fluids or pharmacy made solutions (tables 4 and 5) or compounded solutions (Normocarb ®). Many programs will use saline or lactated Ringers as a relatively inexpensive form of replacement fluid in those patients who are having excessive ultrafiltration. The FDA modernization act of 1997 allows for pharmacies to compound fluids when no

alternative is available (<http://www.fda.gov/opacom/backgrounders/modact.htm>) allowing for those who wish to use bicarbonate replacement fluids to use either Normocarb® (Dialysis Solutions Inc, Richmond Hill, Ont, Canada) or solutions prepared by the hospital pharmacy. The decision to use replacement fluid is often based on the overall solute and ultrafiltration clearance requirements of the patient as well as the local standard of care.

FDA approved dialysis solutions are available both in lactate (Baxter, Deerfield, IL) and bicarbonate form (Dialysis Solutions Inc, Richmond Hill, Ont, Canada; Priskasate, Gambro Health Care, Lakewood, CO). Additionally, pharmacy made customized solutions (usually bicarbonate based) are also available. Further Normocarb® and Priskasate BGK 2/0 are calcium free dialysate solutions, providing a venue for the provision of either citrate or alternate anticoagulation.

Prescriptions

Classically, prescriptions for acute HF have been for the treatment of ARF. If one were to suggest a standard prescription, then a BFR for CVVH would be in the range of 4-6 mls/kg/min trying to keep a venous return pressure of less than 200 mm Hg. Further there is no absolute data to date on the rate of replacement fluid or dialysate fluid. Historically we have used a rate of 2000 ml per 1.73 m²/hr for this allows us to compare pediatric data based on body surface area to adult data. Thus in an 11 kilo child who has a .5m² body surface area, the dialysate or replacement fluid rate prescribed would be roughly 700 mls/hr. The standardization of BFR as well as replacement or dialysate rates allows a better appreciation of steady state drug kinetics, TPN clearance and/or intoxicant removal.

Nutrition and CRRT

When one looks at nutritional requirements of these children it is imperative to understand that HF prescriptions will result in significant amino acid loss across the hemofilter. Data by Davies et al in adults, Maxvold et al in pediatrics and by Zobel et al in neonates has showed that whether one does CVVH or CVVHD, one needs to consider the amount of protein calories given to a patient. In non-dialytic setting of ARF the standard recommendation for protein requirements is in the range of 1.5 grams/kilo/day. In patients on HF, in order to maintain adequate nitrogen balance, protein administration may be in the range of 3-4 grams/kg/day. Further in phosphorous deficient dialysate solutions (none have phosphorous unless added by local pharmacy) hypophosphatemia occurs frequently, requiring either a separate phosphorous infusion or additional phosphorous added to the TPN.

Outcome

A retrospective study by Goldstein et al examined outcome in 22 pediatric patients receiving CVVH(D) and controlled for patient severity of illness using the Pediatric Risk of Mortality (PRISM) score. Neither mean PRISM scores at the time of PICU admission nor time of CRRT initiation differed between survivors and non-survivors. Of the clinical variables studied (GFR, pressor number, mean airway pressure, patient size or % fluid overload), only the degree of % fluid overload at the time of CRRT initiation differed between survivors (16.4% +/- 13.8%) and non-survivors (34.0% +/- 21.0%, p =0.03), even when controlled for severity of illness by

PRISM score using a multiple regression model. This supports earlier data by Fargason et al suggesting that the PRISM score may not be predictive.

A database by Bunchman et al examined 226 children treated with RRT (HF, HD and PD) looking at predictors of outcome. Diagnosis in these groups varied from ARF to inborn error of metabolism, to intoxications. Similar to adult data, outcome appears to be related not to age, not to modality but to severity of illness (i.e. pressor requirement) and underlying cause of need for RRT. This points out that it is not the modality, but rather the underlying cause of the need for HF, as well as the overall hemodynamic status of the patient (including the presence or absence of vasopressor agents) that effects outcome. In children on CRRT and ECMO outcome is primarily related to need for ECMO not to the use of CRRT.

More recent single center data, as well as multi-center data from the Prospective Pediatric CRRT Registry Group support earlier findings that fluid overload at CRRT initiation is an independent risk factor for mortality in pediatric patients who receive CRRT.

Complications

Excessive Ultra-filtration

Data by Jenkins et al demonstrated up to a 30% ultrafiltration error rate when using intravenous pumps to regulate ultrafiltration. The only way to avoid the ultrafiltration error is to use industry made equipment that has been purposefully made for ultrafiltration regulation. This will not affect the individual IV pump error rate, but will minimize most of the error seen at bedside. Industry standards vary but experience with the PRISMA device in a 2.8 kg infant revealed an ultrafiltration error rate of only 2-4 mls/hr (personal communication Timothy Kudelka RN).

Membrane Reactions

One of the more biocompatible membranes (PAN, AN-69) has been shown to cause a bradykinin release syndrome in patients who are acidotic at the onset of HF or in children who require a “blood prime” in the setting of one of these membranes. These membranes, in the face of interacting with an acidotic plasma environment generate bradykinin which may result in reactions from minor nausea to clinical anaphylaxis. Newer AN-69 membranes are now coming on market that will prevent these reactions. In the mean time in those patients who require blood priming, transfusing the blood post hemofilter with a generous administration of sodium bicarbonate, or use of a priming mixture of 75 ml PRBC, 75 ml sodium bicarbonate and 300 mg calcium gluconate makes this reaction virtually non existent. Alternate formulas exist for priming including; “The Jenkins formula”: pRBC’s = 80 ml; 5% albumin = 55 ml; heparin = 150 units; sodium bicarb = 12 mEq; 10% calcium gluconate = 2 ml. The prime must then be checked to be sure the pH is 7.3 – 7.5 and the ionized calcium is ≥ 1.0).

Thermic Control

Hypothermia is common however with the advent of thermic controllers this has become less of a clinical problem. In the smaller child on HF a thermic controller

will result in euthermia but may mask a fever, therefore a high index of suspicion of new or ongoing infection needs to be maintained even in the absence of a fever.

References (* Pediatric specific)

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; 34:486-92
3. *Bunchman TE, Maxvold NJ, Kershaw DB, et al: Continuous venovenous hemodiafiltration in infants and children. *Am J Kid Dis* 1995; 25:17; *Infants and Children, Pediatr Nephrol* 1994; 8:96-99.
4. *Braun MC, Welch TR: Continuous venovenous hemodiafiltration in the treatment of acute hyperammonemia. *Am J Nephrol* 1998;18(6): 531-3
5. Ronco C, Kellum JA, Mehta RL: Acute dialysis quality initiative (ADQI). *Nephrol Dial Transplant* 2001; 16(8):1555-8
6. *Brophy PD, Maxvold NJ, Bunchman TE: CAVH/CVVH in pediatric patients. In: Nissenson AR and Fine RN (eds.) *Dialysis Therapy*, 3rd Edition, Hanley & Belfus, Inc 2002
7. *Goldstein SL: Overview of pediatric renal replacement therapy in acute renal failure. *Artif Organs* 2003; 27(9):781-5
8. *Symons JM, Somers MJG, Baum MA, et al: Demographics of pediatric CRRT: A report of the Prospective Pediatric CRRT (ppCRRT) Registry Group. American Society of Nephrology Annual Conference, San Diego California, Nov 2003
9. *Barletta GM, Kershaw DB, Mottes TA, et al: Intraoperative continuous renal replacement therapy in pediatric intensive care unit patients. American Society of Nephrology Annual Conference, San Diego California, Nov 2003
10. *Brophy PD, Bunchman TE: CVVH in pediatric patients. In: Nissenson AR and Fine RN (eds.) *Clinical Dialysis*, Edition McGraw-Hill Inc., Medical Publishing Division, In Press.
11. Jiang HL, Xue WJ, Li DQ, et al: Pre- vs. post-dilution CVVH. *Blood Purif* 2005; 23(4):338
12. Meyer TW, Walther JL, Pagtalunan ME, et al: The clearance of protein-bound solutes by hemofiltration and hemodiafiltration. *Kidney Int* 2005; 68(2):867-77
13. *Harvey B, Watson AR, Jepson S: A renal critical care educator: the interface between paediatric intensive care and nephrology. *Intensive Crit Care Nurs* 2002; 18(4):250-4

Access references

14. *Bunchman TE, Gardner JJ, Kershaw DB, Maxvold NJ: Vascular access for hemodialysis or CVVH(D) in infants and children. *Nephrol Dial Transplant* 1994; 23:314-317

15. *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
16. *Jenkins RD, Kuhn RJ, Funk JE: Clinical implications of catheter variability on neonatal continuous hemofiltration. *Trans Am Soc Artif Intern Organs* 1998; 34:108-11
17. *Brophy PD, Mottes TA, Barletta GM, et al: Access for Pediatric CRRT (presented at the 8th CRRT, March 6-8, 2003, San Diego, CA)
18. Bunchman TE. Wilson SE (ed): Vascular access: principles and practice, 4th ed Mosby, St. Louis, 2002. *Pediatr Nephrol*. 2003 Sep;18(9):968. Epub 2003 Jul 22.

Anticoagulation references

19. *Geary DF, Gajaria M, Fryer-Keeze S, Willemsen J: Low dose and heparin free hemodialysis in children. *Pediatr Nephrol* 1991; 5:220
20. *Macdonald D, Martin R: Use of sodium citrate anticoagulation in a pediatric continuous venovenous hemodialysis patient. *ANNA J* 1995; 22(3): 21-4
21. *Bunchman TE, Maxvold NJ, Barnett J, et al: Pediatric hemofiltration: Normocarb® dialysate solution with citrate anticoagulation. *Pediatr Nephrol* 2002; 17:150-4
22. *Goldstein SL, Somers MJG, Symons JM, et al: Anticoagulation for pediatric CRRT: a report from the ppCRRT Registry Group (presented at the 8th CRRT, March 6-8, 2003, San Diego, CA)
23. *Chadha V, Garg U, Warady BA, Alon US: Citrate clearance in children receiving continuous venovenous renal replacement therapy, *Pediatr Nephrol* 2002; 17:819-24
24. *Brophy PD, Bunchman TE, Baum M, et al: Anticoagulation in pediatric hemofiltration: a report from the Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) Registry Group. American Society of Nephrology Annual Conference, San Diego, CA, Nov 2003
25. Tobe SW, Aujla P, Walele AA, et al: A novel regional citrate anticoagulation protocol for CRRT using only commercially available solutions. *J Crit Care* 2003; 18(2):121-9
26. Elhanan N, Skippen P, Nuthall, et al: Citrate anticoagulation in pediatric continuous venovenous hemofiltration. *Pediatr Nephrol* 2004; 19(2):208-12
27. Egi M, Naka T, Bellomo R, et al: A comparison of two citrate anticoagulation regimens for continuous veno-venous hemofiltration. *Int J Artif Organs* 2005; 28(12):1211-8
28. Bihorac A, Ross EA: Continuous venovenous hemofiltration with citrate-based replacement fluid: efficacy, safety, and impact on nutrition. *Am J Kidney Dis* 2005; 46(5):908-18. Review

29. Naka T, Egi M, Bellomo R, et al: Commercial low-citrate anticoagulation haemofiltration in high risk patients with frequent filter clotting. *Anaesth Intensive Care* 2005; 33(5):601-8
30. Naka T, Egi M, Bellomo R, et al: Low-dose citrate continuous veno-venous hemofiltration (CVVH) and acid-base balance. *Int J Artif Organs* 2005; 28(3):222-8
31. *Brophy PD, Somers MJ, Baum MA, et al: Multi-centre evaluation of anticoagulation in patients receiving continuous renal replacement therapy (CRRT). *Nephrol Dial Transplant* 2005; 20(7):1416-21

Solution references

32. Zimmerman D, Cotman P, Ting R, et al: Continuous veno-venous haemodialysis with a novel bicarbonate dialysis solution: prospective cross-over comparison with a lactate buffered solution. *Nephrol Dial Transplant* 1999; 14:2387-91
33. Roy D, Hogg RJ, Wilby PA, et al: Continuous veno-venous hemodiafiltration using bicarbonate dialysate. *Pediatr Nephrol* 1997; 11(6):680-3
34. Tobe SW, Murphy PM, Goldberg P, et al: A new sterile bicarbonate dialysis solution for use during cardiopulmonary bypass. *ASAIO J* 1999; 45(3):157-9
35. *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
36. Barenbrock M, Hausberg M, Marzkies F, et al: Effects of bicarbonate- and lactate- buffered replacement fluids on cardiovascular outcome in CVVH patients. *Kidney Int* 2000; 58:1751-7
37. *Bunchman TE, Benner KW, Rhodes RW, et al: Normocarb® as a replacement fluid for convective clearance in CVVH. Presented at the 8th CRRT, March 6-8, 2003, San Diego, CA.
38. *Bunchman TE, Maxvold NJ, Barnett J, et al: Pediatric hemofiltration: Normocarb® dialysate solution with citrate anticoagulation. *Pediatr Nephrol* 2002; 17(3):150-4
39. *Bunchman TE, Maxvold NJ, Brophy PD: Pediatric convective hemofiltration: Normocarb® replacement fluid and citrate anticoagulation. *Am J Kidney Dis* 2003; 42(6):1248-52

Nutrition references

40. *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; 28:1161-5
41. 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. *Crit Care Med* 1991 19(12):1510-5

42. *Maxvold NJ, Katz A, Bunchman TE: REE in pediatric rhabdomyolysis with acute renal failure on CRRT. Presented at the 8th CRRT, March 6-8, 2003, San Diego, CA
43. *Bunchman TE, Brophy PD, Somers MJG, et al: Protein and caloric delivery in pediatric CRRT: a report from the Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) Registry Group. Present at the American Society of Nephrology Annual Conference, San Diego, CA, Nov 2003.

Metabolic Disease References

44. McBryde KD, Kudelka TL, Kershaw DB, et al: Clearance of amino acids by hemodialysis in argininosuccinate synthetase deficiency. *J Pediatr* 2004; 144(4):536-40
45. Hmiel SP, Martin RA, Landt M, et al: Amino acid clearance during acute metabolic decompensation in maple syrup urine disease treated with continuous venovenous hemodialysis with filtration. *Pediatr Crit Care Med* 2004; 5(3):278-81
46. *McBryde KD, Kershaw DB, Bunchman TE, et al: Renal replacement therapy in the treatment of confirmed or suspected inborn errors of metabolism. *J Pediatr*, In press
47. *Deodato F, Boenzi S, Rizzo C, et al: Inborn errors of metabolism: an update on epidemiology and on neonatal-onset hyperammonemia. *Acta Paediatr Suppl* 2004; 93(445):18-21
48. *Picca S, Dionisi-Vici C, Abeni D, et al: Extracorporeal dialysis in neonatal hyperammonemia: modalities and prognostic indicators. *Pediatr Nephrol* 2001; 16(11):862-7

Outcome references

49. *Goldstein SL, Currier H, Graf JM, et al: Outcome in children receiving continuous hemofiltration. *Pediatrics* 2001; 107(6):1309-12
50. Mehta RL, McDonald B, Gabbai FB, et al: A randomized clinical trial of continuous versus intermittent dialysis for acute renal failure. *Kidney Int* 2001; 60(3):1154-63
51. *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
52. *Bunchman TE, McBryde KD, Mottes TE, et al: Pediatric acute renal failure: outcome by modality and disease. *Pediatr Nephrol* 2001; 16(12):1067-71
53. *Zobel G, Kuttig M, Ring E, Grubbauer HM: Clinical scoring systems in children with continuous extracorporeal renal support. *Child Nephrol Urol* 1990; 10:14-7
54. *Ronco C, Paganan L: Acute renal failure in infancy: treatment by continuous renal replacement therapy. *Inten Care Med* 1995; 21:490-9

55. *Zobel G, Ring E, Rödl S: Prognosis in pediatric patients with multiple organ system failure and continuous extracorporeal renal support. *Contrib Nephrol* 1995; 116:163-8
56. *Meyer RJ, Brophy PD, Bunchman TE, et al: Survival and renal function in pediatric patients following extracorporeal life support with hemofiltration. *Pediatr Crit Care Med* 2001; 2:238-42
57. *Goldstein SL, Somers MJG, Symons JM, et al: Pediatric multi-organ system failure: a report from the ppCRRT Registry Group. Presented at the 8th CRRT, March 6-8, 2003, San Diego, CA.
58. *Symons JM, Bunchman TE, Baum M, et al: Technical characteristics of pediatric CRRT: a report from the ppCRRT Registry Group. Presented at the 8th CRRT, March 6-8, 2003, San Diego, CA.
59. *Symons JM, Brophy PD, Gregory MJ, et al: Continuous renal replacement therapy in children up to 10 kg. *Am J Kidney Dis* 2003; 41(5):984-9
60. *Goldstein SL, Somers MJG, Symons JM, et al: Pediatric multi-organ dysfunction syndrome (MODS) outcomes: a report from the Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) Registry Group. American Society of Nephrology Annual Conference, San Diego CA, Nov 2003.
61. *Somers MJG, Baum MA, Symons JM, et al: Continuous renal replacement therapy in children <10 kg: a report from the Prospective Pediatric Continuous Renal Replacement Therapy Registry Group. American Society of Nephrology Annual Conference, San Diego CA, Nov 2003.
62. *Fortenberry J, Somers MJG, Symons JM, et al: Pediatric multi-organ dysfunction syndrome (MODS) outcomes: a report from the Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) Registry Group. Critical Care Medicine 33rd Congress, Orlando FL, Feb. 2004.
63. Chen CY, Tsai TC, Lee WJ, et al: Outcome prediction for critically ill children with acute renal failure requiring continuous hemofiltration. *Ren Fail* 2004; 26(4):355-9
64. Foland JA, Fortenberry JD, Warshaw BL, et al: Fluid overload before continuous hemofiltration and survival in critically ill children: a retrospective analysis. *Crit Care Med* 2004; 32(8):1771-6
65. Askenazi DJ, Goldstein SL, Chang IF, et al: Management of a severe carbamazepine overdose using albumin enhanced continuous venovenous hemodialysis. *Pediatrics* 2004; 113(2):406-9
66. DiCarlo JV, Alexander SR, Agarwal R, Schiffman JD: Continuous veno-venous hemofiltration may improve survival from acute respiratory distress syndrome after bone marrow transplantation or chemotherapy. *J Pediatr Hematol Oncol* 2003; 25(10):801-5
67. Lin MC, Fu YC, Fu LS, et al: Peritoneal dialysis in children with acute renal failure after open heart surgery. *Acta Paediatr Taiwan* 2003; 44(2):89-92

68. Goldstein SL, Somers MJ, Baum M, et al: Pediatric patients with multi-organ system failure receiving continuous renal replacement therapy. *Kidney Int* 2005; 67(2):653-8
69. Piccinni P, Dan M, Barbacini S, et al: Early isovolaemic haemofiltration in oliguric patients with septic shock. *Intensive Care Med* 2006; 32(1):80-6
70. *Askenazi DJ, Feig DI, Graham NM, et al: 3-5 year longitudinal follow-up of pediatric patients after acute renal failure. *Kidney Int* 2006; 69(1):184-9
71. Tan HK, Uchino S, Bellomo R: Electrolyte mass balance during CVVH: lactate vs bicarbonate-buffered replacement fluids. *Ren Fail* 2004; 26(2):149-53
72. *Bellomo R, Honore PM, Matson J, et al: Extracorporeal blood treatment (EBT) methods in SIRS/Sepsis. *Int J Artif Organs* 2005; 28(5):450-8. Review
73. Elahi MM, Lim MY, Joseph RN, et al: Early hemofiltration improves survival in post-cardiotomy patients with acute renal failure. *Eur J Cardiothorac Surg* 2004; 26(5):1027-31
74. *Gillespie RS, Seidel K, Symons JM: Effect of fluid overload and dose of replacement fluid on survival in hemofiltration. *Pediatr Nephrol* 2004; 19(12):1394-9
75. *Goldstein SL, Somers MJ, Baum MA, et al: Pediatric patients with multi-organ dysfunction syndrome receiving continuous renal replacement therapy. *Kidney Int* 2005; 67(2):653-8

Complication references

76. Lacour F, Maheut H: AN-69 membrane and conversion enzyme inhibitors: prevention of anaphylactic shock by alkaline rinsing? *Nephrologie* 1992; 13(3):135-6
77. *Brophy PD, Mottes TA, Kudelka TL, et al: AN-69 membrane reactions are pH-dependent and preventable. *Am J Kidney Dis* 2001; 38(1):173-8
78. *Jenkins R, Harrison H, Chen B, et al: Accuracy of intravenous infusion pumps in continuous renal replacement therapies. *Trans Am Soc Artif Intern Organs J* 1992; 38:808-1
79. *Lane PH, Mauer SM, Blazar BR, et al: Outcome of dialysis for acute renal failure in pediatric bone marrow transplant patients. *Bone Marrow Transplant* 1994; 13:613-7
80. Bunchman TE: Fluid overload in multiple organ dysfunction syndrome: a prediction of survival. *Crit Care Med* 2004; 32(8):1805-6
81. Gillespie RS, Seidel K, Symons JM: Effect of fluid overload and dose of replacement fluid on survival in hemofiltration. *Pediatr Nephrol* 2004; 19(12):1394-9
82. *McBryde KD, Bunchman TE, Kudelka TL, et al: Hyperosmolar solutions in continuous renal replacement therapy for hyperosmolar acute renal failure: a preliminary report. *Pediatr Crit Care Med* 2005; 6(2):228-9

83. *Hackbarth RM, Eding D, Gianoli-Smith C, et al: Zero balance ultrafiltration (Z-BUF) in blood-primed CRRT circuits achieves electrolyte and acid-base homeostasis prior to patient connection. *Pediatr Nephrol* 2005; 20(9):1328-33

Acute Renal Failure Review Articles

84. *Williams DM, Sreedhar SS, Mickell JJ, Chan JC: Acute kidney failure: a pediatric experience over 20 years. *Arch Pediatr Adol Med* 2002; 156:893-90
85. *Andreoli SP: Acute renal failure. *Curr Opin Pediatr* 2002; 14:183-8
86. *Flynn JT: Choice of dialysis modality for management of pediatric acute renal failure. *Pediatr Nephrol* 2002; 17:61-9
87. *Parekh RS, Bunchman TE: Dialysis support in the pediatric intensive care unit. *Adv Ren Replace Ther* 1996; 3:326-3
88. Ronco C, Pohlmeier R, Tetta C: Intermittent or continuous treatment of acute renal failure? *Crit Care Med* 2003; 31(9):2417
89. Bellomo R, Kellum JA, Ronco C: Defining acute renal failure: physiological principles. *Intensive Care Med* 2004; 30(1):33-7
90. Wan L, Bellomo R, Di Giantomasso D, Ronco C: The pathogenesis of septic acute renal failure. *Curr Opin Crit Care* 2003; 9(6):496-502
91. Tetta C, D'Intini V, Bellomo R, et al: Extracorporeal treatments in sepsis: are there new perspectives? *Clin Nephrol* 2003; 60(5):299-304
92. Ronco C, Tetta C, Mariano F, et al: Interpreting the mechanisms of continuous renal replacement therapy in sepsis: the peak concentration hypothesis. *Artif Organs* 2003; 27(9):792-801
93. *Gregory MJ, Bunchman TE, Brophy PD: Continuous renal replacement therapies for children with acute renal failure and metabolic disorders. In: Warady BA, Fine RN, Alexander SR and Schaefer F (eds.) Pediatric Dialysis, 1st Edition In Press.
94. Andreoli SP: Acute renal failure in the newborn. *Semin Perinatol* 2004; 28(2):112-23
95. Strazdins V, Watson AR, Harvey B; European Pediatric Peritoneal Dialysis Working Group: Renal replacement therapy for acute renal failure in children: European guidelines. *Pediatr Nephrol* 2004; 19(2):199-207
96. Barletta GM, Bunchman TE: Acute renal failure in children and infants. *Curr Opin Crit Care* 2004; 10:499-504
97. *Hui-Stickle S, Brewer ED, Goldstein SL: Pediatric ARF epidemiology at a tertiary care center from 1999 to 2001. *Am J Kidney Dis* 2005; 45:96-101
98. *Goldstein SL, Somers MJ, Brophy PD, et al: The Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) Registry: design, development and data assessed. *Int J Artif Organs* 2004; 27(1): 9-14
99. *Ronco C, Bellomo R, Brendolan A (eds): Sepsis, kidney and multiple organ dysfunction (Contributions to Nephrology series, vol 144) and R.M. Lindsay (ed); U. Buoncristiani, R.S. Lockridge, A. Pierratos, G.O. Ting (co-eds): Daily and nocturnal hemodialysis (Contributions to Nephrology series, vol 145) Ronco et al.: Karger, Basel, 2004 (ISBN 3-8055-7755-9),

- US\$ 260.00 and Lindsay et al.: Karger, Basel, 2004 (ISBN 3-8055-7808-3), US\$ 207.25. *Pediatr Nephrol* 2005 Dec 6; [Epub ahead of print]
100. *Barletta GM, Bunchman TE: Acute renal failure in children and infants. *Curr Opin Crit Care* 2004; 10(6):499-504

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101. *Nguyen TC, Stegmayr B, Busund R, et al: Plasma therapies in thrombotic syndromes. *Int J Artif Organs* 2005; 28(5):459-65
102. *Tissieres P, Sasbon JS, Devictor D: Liver support for fulminant hepatic failure: Is it time to use Molecular Adsorbents Recycling System in children? *Pediatr Crit Care Med* 2005; 6(5):585-591
103. *Askenazi DJ, Goldstein SL, Chang IF, et al: Management of a severe carbamazepine overdose using albumin-enhanced continuous venovenous hemodialysis. *Pediatrics* 2004; 113(2):406-9
104. Naka T, Wan L, Bellomo R, et al: Kidney failure associated with liver transplantation or liver failure: the impact of continuous veno-venous hemofiltration. *Int J Artif Organs* 2004; 27(11):949-55
105. Wigg AJ, Padbury RT: Liver support systems: promise and reality. *J Gastroenterol Hepatol* 2005; 20(12):1807-16
106. Sen S, Rose C, Ytrebo LM, et al: Effect of albumin dialysis on intracranial pressure increase in pigs with acute liver failure: a randomized study. *Crit Care Med* 2006; 34(1):158-64
107. Pless G, Sauer IM: Bioartificial liver: current status. *Transplant Proc* 2005; 37(9):3893-5
108. Novelli G, Rossi M, Pretagostini M, et al: One hundred sixteen cases of acute liver failure treated with MARS. *Transplant Proc* 2005; 37(6):2557-9
109. Naruse K: Artificial liver support: future aspects. *J Artif Organs* 2005; 8(2):71-6
110. Du WB, Li LJ, Huang JR, et al: Effects of artificial liver support system on patients with acute or chronic liver failure. *Transplant Proc* 2005; 37(10):4359-64
111. Van de Kerkhove MP, Poyck PP, Deurholt T, et al: Liver support therapy: an overview of the AMC-bioartificial liver research. *Dig Surg* 2005; 22(4):254-64

Table 1 AVAILABLE HEMOFILTRATION MACHINES

Company	Machine	Lines
Edwards Lifesciences	Aquarius	Adult PEDS (in development)
GAMBRO	PRISMA	ADULT/ PEDS (in development)
BAXTER	BM 11* BM 11a* BM 25 Accura	ADULT/PEDS
FRESENIUS	2008	ADULT/PEDS
B BRAUN	Diapact	ADULT/PEDS

* blood pump only; need the additional of the BM 14 to make the total of a BM 25 for the blood and ultrafiltration monitor all in one

TABLE 2 Pediatric Hemofilter Properties

HEMOFILTER	PROPERTIES/ SURFACE AREA	PRIMING VOLUME
AMICON Minifilter Plus	Polysulfone 0.07m ²	15 ml
RENAFLO II HF 400 HF 700 HF 1200	Polysulfone 0.3m ² 0.7m ² 1.25m ²	28 ml 53 ml 83 ml
Gambro Multiflow 60 Multiflow 10	AN-69 0.6m ² 0.3m ²	44 mls
ASAHI PAN 0.3 0.6 1.0	Poly Acrylonitrile 0.3m ² 0.6m ² 1.0m ²	33 ml 63 ml 7 ml

(Note Veno-Venous HF requires larger circuit volume depending on the pumps utilized. For the non-adapted systems such as the PRISMA, the filter is the Multiflow 60 and the circuit volume is fixed at around 90 ml and the Multiflow 10 and circuit volume is 45 mls.)

TABLE 3 Suggested Size and Selection of HF Vascular Access for Pediatric Patients

PATIENT SIZE	CATHETER SIZE & SOURCE	SITE OF INSERTION
NEONATE	Single-lumen 5 Fr (COOK)	Femoral artery or vein
	Dual-Lumen 7.0 French (COOK/MEDCOMP)	Internal/External-Jugular, Subclavian or Femoral vein
3-6 KG	Dual-Lumen 7.0 French (COOK/MEDCOMP)	Internal/External-Jugular, Subclavian or Femoral vein
	Triple-Lumen 7.0 Fr (MEDCOMP)	Internal/External-Jugular, Subclavian or Femoral vein
6-30 KG	Dual-Lumen 8.0 French (KENDALL, ARROW)	Internal/External-Jugular, Subclavian or Femoral vein
>15-KG	Dual-Lumen 9.0 French (MEDCOMP)	Internal/External-Jugular, Subclavian or Femoral vein
>30 KG	Dual-Lumen 10.0 French (ARROW, KENDALL)	Internal/External-Jugular, Subclavian or Femoral vein
>30 KG	Triple-Lumen 12.5 French (ARROW, KENDALL)	Internal/External-Jugular, Subclavian or Femoral vein

TABLE 4 Commercially Available Solutions for dialysis * or for dialysis or infusion

PREMADE SOLUTIONS ADDITIVES	Normocarb®	Hemofiltration Solution *	Prismasate BK 0/3.5 *//BGK 2/0	Accusol * (multiple options)
Na (mEq/L)	140	140	140	140
K (mEq/L)	0	2	0//2	0,2,4
Cl (mEq/L)	105	117	109.5	109-115
HCO ₃ (mEq/L)	35	0	32	30-35
Lactate (mEq/L)	0	30	3	0
Ca (mEq/L)	0	3.5	3.5//0	3.5
PO ₄ (mEq/L)	0	0	0	0
Mg (mEq/L)	1.5	1.5	1	1
Dextrose (g/L)	0	1	0	1

*only FDA approved solution for dialysis

TABLE 5 Pharmacy Solutions for dialysis or infusion

CUSTOM MADE SOLUTIONS	CALCIUM-BASED infusate/ DIALYSATE	PHOSPHATE BASED infusate/ DIALYSATE
NaCl (mEq/L)	100	100
NaHCO ₃ (mEq/L)	40	40
KCl (mEq/L)	4	2
K ₃ PO ₄ (mEq/L)	0	2 **
Lactate (mEq/L)	0	0
CaCl ₂ (mEq/L)	3.5	0
MgSO ₄ (mEq/L)	1.5	1.5
Dextrose (g/L)	1.5 (0.15%)	1.5 (0.15%)
** Provides 2 mEq/L of potassium & 4 mg/dl of phosphorous		
Solutions are mixed with sterile technique in the pharmacy BUT THERE IS RISK OF ELECTROLYTE ERROR DUE TO LACK OF STANDARDS		

Attachment A-Heparin Protocol

Standardize your protocol PATIENT COAGULATION/ANTICOAGULANT THERAPY:

(before initiating therapy)

1. Obtain PT/PTT, Platelet count, *ACT baseline (by dialysis nurse).
2. In the absence of coagulopathy (patient's ACT <150), give bolus of ___ units heparin (25 units/kg) to patient and recheck ACT. Repeat heparin bolus and ACT check until ACT >180 (maximum: repeat x 2)

(during hemofiltration)

1. Heparin infusion: When ACT > 180, start heparin drip 10 units/ml in CRRT circuit at 10 units/kg/hr = ___ units/hr or ___ ml/hr. Check system ACT.
2. Titrate heparin drip to keep post-filter ACT between 180-220 seconds
 - If ACT is <180, increase heparin drip by 1 unit/kg/hr.
 - If ACT is >220, decrease the heparin drip by 1 unit/kg/hr

Anticoagulation monitoring: **With each circuit change and when platelets or blood are administered to the patient**, obtain postfilter (blue port) ACT q 20 minutes until stable.

Monitor ACTs q 20-30 min. for an hour after any heparin changes.

Monitor ACTs every four hours once stable

Attachment B-Citrate Protocol

1. Prime in CVVHDF Mode using ordered dialysate and replacement solutions.
 Dialysate : HCO₃-based without Ca (Normocarb® or pharmacy-prepared;
 Replacement: normal saline or bicarb-based Normocarb or pharmacy-prepared.
2. Place a 3 way stop cock to both the “arterial” and venous ports of the dialysis access. Attach the Citrate ACD(A) Solution 1000cc to a regular IV pump and then attach it to the “arterial” stop cock.
3. When ready to start the citrate rate in ccs/hr will be 1.5 x the blood flow rate of the PRISMA machine at ccs/min. (eg Start Citrate at 150 mls/hr if the BFR is 100 mls/min)
4. Set up the Ca⁺⁺ infusion (ie. 8gms Calcium Chloride in 1L NS) as ordered via central line other than the dialysis access. This will run at 40% of the citrate flow rate. (eg citrate rate = 150 mls/hr then CaCl rate = 60 mls/hr)
5. Set the flow rates in Hemofiltration machine as ordered.
6. Patient Fluid Removal Rate is calculated by:
 Net Ultrafiltration rate + Citrate rate + Calcium infusion rate = Pt. Fluid Removal Rate.
7. Connect the Hemofiltration machine circuit to the dialysis catheter as per procedure and press start.
8. 2 hour after initiation of therapy and every 6 hours thereafter, send the following blood work
 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, Albumen)
 (see # 14 for citrate and calcium adjustment)
9. Metabolic alkalosis occurs due to citrate metabolism to bicarbonate and due to bicarbonate in the Dialysate. Call Peds Nephrologist if the Serum Bicarb is > 35 meq/l In that case the Peds Nephrologist will add in NS as a replacement soln by 200-400 cc/hr and decrease the dialysate rate by the same amount. This will give an acid load from the NS and diminish the HCO₃ from the bath at the same time
10. Notify MD for the following :

- a. Systemic Ionized $\text{Ca}^{++} < 0.75$ mmol/L. (Consider holding citrate for 1 hours and resuming infusion at 30% of the citrate flow rate and bolus with 10 mg/kg of CaCl and increase Ca infusion by 10%)
- b. $\text{Na}^+ > 150$ mmol/L. Consider changing replacement solution to 0.45% NaCl.

11. If the filter clots, stop the Citrate and Ca^{++} infusions and discontinue the filter.

12. **In children less than 10 kg who require a blood transfusion when going on, avoid the use of citrate for the first 15 minutes for it may exacerbate the Bradykinin release syndrome seen in some children.**

13. Citrate Lock occurs when the total calcium rises with a dropping ionized calcium. This is due to the fact of the citrate infusion exceeds the clearance on dialysis and from hepatic metabolism. When this is seen, stop the citrate for 2-4 hours then restart at 70% of the previous dose. Watch the ionized calcium during this time to avoid inadequate anticoagulation of the circuit (i.e. the ionized calcium of the system rising causing system clotting).

14. Titrate the Citrate infusion according to the citrate sliding scale below :

Prisma ionized Ca^{++} (mmol/L)	Citrate Infusion Adjustment	
	> 20 kg	< 20 kg
< 0.35	↓ rate by 10 ml/hr	↓ rate by 5 ml/hr
0.35 – 0.5 (Optimum Range)	No adjustment	
0.5 – 0.6	↑ rate by 10 ml/hr	↑ rate by 5 ml/hr
> 0.6	↑ rate by 20 ml/hr	↑ rate by 10 ml/hr
NOTIFY MD IF CITRATE INFUSION RATE > 200 ml/hr		

Titrate the Calcium infusion according to the calcium sliding scale below :

Patient ionized Ca^{++} (mmol/L)	Calcium Infusion Adjustment	
	> 20 kg	< 20 kg
> 1.3	↓ rate by 10 ml/hr	↓ rate by 5 ml/hr
1.1-1.3 (Optimum Range)	No adjustment	
0.9-1.1	↑ rate by 10 ml/hr	↑ rate by 5 ml/hr
< 0.9	↑ rate by 20 ml/hr	↑ rate by 10 ml/hr
NOTIFY MD IF Calcium INFUSION RATE > 200 ml/hr		