Citrate Acid Concentrate Articles and Abstracts

Citrate acid concentrate represents the first major change in dialysate chemical composition in 30 years. The use of citric acid instead of acetic acid as the acidifier in the dialysate has been shown to produce better dialysis therapy by increasing the dialysis dose. Citrate dialysate can reduce clotting and increase dialyzer reuse which can save time and money for clinics. The following articles and abstracts speak to the benefits of a citrate acid concentrate.

1. Abstract: **Citrate dialysate in SLEDD is safe and effective in the presence of severe liver dysfunction.** Ahmad, S., Tu, A., Division of Nephrology, University of Washington, Seattle Wash. Long slow dialysis using citrate dialysate was successfully completed in 94% of the acute dialysis treatments for at least 6 hours without clots despite not using heparin on these advanced liver failure patients.
Citrate dialysate used for extended SLEDD treatments of as long as 24 hours duration was safe without any evidence of citrate accumulation or development of hypocalcemia in hepatic failure. Thus citrate dialysate in SLEDD is safe and effective in presence of severe liver dysfunction. Presented at the European Renal Association and European Dialysis and Transplant Association congress, Barcelona, Spain, June 2007.
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2. Abstract: **Heparin Free Slow Low Efficiency Dialysis (SLED) Using Citrate Dialysate (CD) Is Safe and Effective.** S. Ahmad, A. Tu, Department of Medicine, University of Washington, Scribner Kidney Center, Seattle, Wash., USA. Presented at the 12th International Conference on Continuous Renal Replacement Therapies (CRRT) March 7–10, 2007, San Diego, Calif.
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3. Abstract: **The use of citrate dialysate along with a 55% reduction in heparin was successful in decreasing the episodes of prolonged bleeding, was not associated with clotting of the system and an adequate dose of dialysis was maintained.** Kossmann, R. Nephrophiles, LLC (Fresenius Medical Care), Santa Fe, New Mexico, USA; Callan, R., Advanced Renal Technologies, Bellevue, Wash. USA; Ahmad, S., Division of Nephrology, University of Washington, Seattle Wash. USA Fifty-five percent heparin reduction is safe with citrate dialysate in chronic dialysis patients. Submitted to the American Society of Nephrology for presentation at ASN's 39th Annual Renal Week Meeting, San Diego, Calif., USA, November 2006.
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4. Abstract: **The anticoagulation effect of citrate dialysate keeps the dialyzer fibers and pores open and is responsible for the increased removal of urea**

and beta-2 microglobulin. Kossmann, R. Nephrophiles, LLC (Fresenius Medical Care), Santa Fe, New Mexico, USA; Callan, R., Advanced Renal Technologies, Bellevue, Wash. USA; Ahmad, S., Division of Nephrology, University of Washington, Seattle Wash. USA Increased dialysis dose and decreased concentration of beta-2 microglobulin with citrate dialysate. Submitted to the American Society of Nephrology for presentation at ASN's 39th Annual Renal Week Meeting, San Diego, Calif., USA, November 2006.
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5. Abstract: **Citrate dialysate (CD) is well tolerated in patients with advanced liver failure and bleeding risk, and CD resolves the dilemma of anticoagulation in these patients.** Ahmad, S., Tu, A., Division of Nephrology, University of Washington, Seattle Wash. Heparin-free citrate dialysis in end stage liver disease (ESLD) patients is well tolerated. Presented at the European Dialysis and Transplant Nurses Association congress, Madrid, Spain, September 2006.
Read Full Abstract

6. Abstract: **The use of citrate dialysate (CD) permitted a significant reduction in heparin (30% reduction) without any increase in clotting during the treatment, and without any decrease in the dose of dialysis as determined by Kt/V (urea).** Ahmad, S., Division of Nephrology, University of Washington, Seattle Wash.; Callan, R., Advanced Renal Technologies, Bellevue, Wash.; Kossmann, R., Nephrophiles, LLC (Fresenius Medical Care), Santa Fe, New Mexico, USA. Heparin reduction with citrate dialysate. Presented at the European Renal Association – European Dialysis and Transplant Association congress, Glasgow, Scotland, July 2006, and published in Nephrology Dialysis Transplantation, Volume 21 Supplement 4 2006.
Read Full Abstract

7. Stated conclusion: **"The use of Citrasate® in SLEDD or conventional hemodialysis treatments is an excellent alternative for an anticoagulant when heparin cannot be utilized."** Isaacs, P. Personal communication, April 2006.
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8. Stated conclusion: **"Citrasate® was more effective in maintaining the circuit than saline flushes, and appears to be safe for use in SLEDD in critically ill patients."** Madison, J., Depner, T., Chin, A., Division of Nephrology, University of California Davis Medical Center, and Renal Services Program, University of California Davis Medical Center, Sacramento, Calif., USA. Alternatives to heparin anticoagulation during slow extended daily dialysis in the ICU. Presented at the National Kidney Foundation Clinical Nephrology 2006 Meeting, Chicago, April 2006.
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9. Title: **"Citrate-containing dialysate is well tolerated during slow extended daily dialysis in the ICU"**

Madison, J., Ilumin, M., Chin, A., Division of Nephrology, University of California Davis Medical Center, and Renal Services Program, University of California Davis Medical Center, Sacramento, Calif., USA. Citrate-containing dialysate is well tolerated during slow extended daily dialysis in the ICU. Presented at the American Society of Nephrology, 38th Annual Renal Week Meeting, Philadelphia, Penn., USA November 2005.
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10. Stated conclusion: **"The results from this study show that citric acid-containing dialysate is associated with increase in dialyzer reuse and appears to be related to reduced clotting."** Ahmad S, Callan R, Cole JJ, Blagg CR Increased dialyzer reuse with citrate dialysate. *Hemodialysis International* 2005; 9: 264-267

11. Stated conclusion: **"Using dialysate containing citric instead of acetic acid increases the delivered dialysis dose."** Ahmad S, Callan R, Cole JJ, Blagg CR. Dialysate made from dry chemicals using citric acid increases dialysis dose. *Am J Kidney Dis.* 35(3):493-499, 2000.
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12. Stated conclusion: **"The use of citrate dialysate was associated with significantly less clotting than the regular dialysate, and can be a safe alternative to heparin in patients with high bleeding risk or who are intolerant to heparin."** Tu A, Ahmad S. Heparin-free hemodialysis with citrate-containing dialysate in intensive care patients. *Dial Transplant*. 29(10):620-626, 2000.

13. Abstract: **Heparin-free acute dialysis using citrate dialysate--this experience with citrate dialysate suggests it to be superior to regular dialysate in patients with a high risk of bleeding.** Tu A, Ahmad S. Div. of Nephrology, University of Washington, Seattle, Wash. Presented at the meeting of the American Society of Nephrology, Toronto, Ontario, Canada, October 2000.
Read Full Article

14. Presentation Summary: **Effect of citrate-containing dialysate on dialyzer reuse--results indicate that citrate dialysate reduces clotting of fibers and enables a significantly higher number of dialyzer reuses.** Ahmad S, Callan R, Cole JJ, Blagg CR. Div. of Nephrology, University of Washington, Seattle, Wash.; Advanced Renal Technologies, Inc., Kirkland, Wash. Presented at the meeting of the American Society of Nephrology, Toronto, Ontario, Canada, October 2000.

15. Abstract: **Increased dialyzer efficiency using a dialysate containing citric acid in place of acetic acid.** Ahmad S, Callan R, Cole JJ, Blagg CR. Div. of Nephrology, University of Washington, Seattle, Wash.; Advanced Renal Technologies, Inc., Kirkland, Wash. Presented at the meeting of the American Society of Nephrology, Miami, Fla., November 1999.
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16. **U.S. FOOD AND DRUG ADMINSTRATION 2006 Safety Alert: Heparin**
Heparin Sodium Injection [Posted 12/08/2006] FDA notified healthcare professionals of revisions to the WARNINGS section of the prescribing information for Heparin to inform clinicians of the possibility of delayed onset of heparin-induced thrombocytopenia (HIT), a serious antibody-mediated reaction resulting from irreversible aggregation of platelets. HIT may progress to the development of venous and arterial thromboses, a condition referred to as heparin-induced thrombocytopenia and thrombosis (HITT). Thrombotic events may be the initial presentation for HITT which can occur up to several weeks after the discontinuation of heparin therapy. Patients presenting with thrombocytopenia or thrombosis after discontinuation of heparin should be evaluated for HIT and HITT.
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Filename: 552109

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Abstract Categories: 20. M1) Extracorporeal dialysis: techniques and adequacy

Keywords: haemodialysis: technique, liver, calcium, haemodialysis: outcome

Title: Citrate Dialysate in Advanced Liver Failure

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INTRODUCTION AND AIMS: Citrate dialysate (CD) has been safely used for both acute and chronic dialysis. It has also been reported to be safe for use in both traditional intermittent and Slow Low Efficiency Diffusion Dialysis (SLEDD) in acutely ill patients. However, since the liver is a major site of citrate metabolism the safety of CD in liver failure patients needs to be evaluated. At University of Washington CD is routinely used for heparin free dialysis. The aim of this study was to assess the safety and efficacy of CD used for SLEDD in the presence of severe liver failure.

METHODS: CD was used in 23 patients (average age 53.6 $\pm$ 13.6 years, 14 male and 9 females) with advanced liver failure requiring heparin free SLEDD. The average pre-SLEDD INR and total bilirubin levels were 2.8 $\pm$ 1.2 and 26.3 $\pm$ 17.2 mg/dl, respectively. The patients underwent a total of 77 SLEDD treatments; the average blood and dialysate flows were 201 $\pm$ 70 and 269 $\pm$ 139 ml/min. (mean $\pm$ SD), respectively. The average duration of SLEDD was 9.5 $\pm$ 4.4 hours and ranged between 2 and 24 hours. Vascular access was through central venous catheters. Anion gap (increases with citrate accumulation) as well as the ratio of ionized calcium (iCa) to total calcium (tCa) were both used to assess the accumulation of citrate in blood; the latter has been reported to be a sensitive measure for citrate accumulation, the ratio declining as citrate increases.

RESULTS: Heparin free SLEDD was well tolerated by all patients and no complications related to CD were observed. Clot free treatments were completed for >4, >6, >8 and >12 hours for 98%, 94%, 64% and 25% of the treatments, respectively. Pre-SLEDD iCa and tCa and iCa to tCa ratios were 1.15 $\pm$ 0.13, 9.2 $\pm$

1.2 (mg/dl), and 0.12 ± 0.01, respectively and remained unchanged. Post-SLEDD values were 1.16 ± 1.1, 9.3 ± 1.1, and 0.12 ± 0.007, respectively (mean ± SD, p=ns). Similarly the anion gap decreased from pre-SLEDD to post-SLEDD, 14.8 to 12.6, respectively (p=0.007).

CONCLUSIONS: Long slow dialysis using CD was successfully completed in 94% of the treatments for at least 6 hours without clots despite using no heparin. CD used for extended SLEDD treatments of as long as 24 hours duration was safe without any evidence of citrate accumulation or development of hypocalcemia in hepatic failure. Thus CD in SLEDD is safe and effective in presence of severe liver dysfunction.

Blood Purification

Blood Purif 2007;25:183–208
DOI: 10.1159/000100029

Published online: February 23, 2007

The 12th International Conference on Continuous Renal Replacement Therapies (CRRT)

March 7–10, 2007, San Diego, Calif.

Abstracts

Editor

R.L. Mehta, San Diego, Calif.

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1

Impact of Acute Renal Failure in the Prognosis of the Critically Ill Obstetric Patient

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Introduction: Acute renal failure (ARF) was recently identified as an independent prognostic factor. This late discovery was partially caused by luck of consensus concerning ARF definitions. A huge step towards consensus was recently reached by wide adoption of the RIFLE criterions for ARF definition. In obstetrics, we face also widely disparate definitions for ARF. Some risk factors were clearly retrieved in the majority of studies. Meanwhile, no proof exists if ARF is a mortality risk factor in the critically ill obstetric patients. **Objective:** Try to determine if ARF is related to mortality in the critically ill obstetric population. **Patients and Methods:** Open prospective observational study. Setting: Medical surgical intensive care unit part of a university affiliated hospital. Inclusion criteria: critically ill obstetric patients. Exclusion criteria: Chronic renal failure and Kidney transplant. Study period: January 1996–September 2004. Collected data: Medical history, demographic, obstetric management (transfusion, cesarean section, hysterectomy, anesthetic complications etc.), Acute Physiology and Chronic Health Evaluation scores (APACHE II, APACHE III) at Day 1, organ dysfunction (SOFA score) and therapeutic interventions. Acute renal failure was defined as serum creatinine levels $\geq$100 μmol/l or doubling of serum creatinine level, and/or oliguria $<$150 ml/8 h or $<$500 ml/day. The main outcome of interest was vital status at time of ICU discharge. Data were computed on SPSS 11.5 XP-Windows compatible. Results were expressed as means ± standard deviation. Statistical analysis was based on χ^2 tests and Student t test corrected by Fisher exact test. $p < 0.05$ was considered for statistical significance. A multiple logistic regression determined if ARF was an independent risk factor of mortality. **Results:** 590 patients were enrolled in the study with an overall mortality of 10.5%. Mean age: 31 ± 6 years, 59% were multipara. Mean term: 34.7 ± 4.5 weeks. 70% of admissions were due to obstetric complications. 181 patients met the criteria of ARF. Patients with ARF were more severely ill as it was assessed by higher APACHE scores (APACHE II: 16 ± 8 vs. 7.5 ± 6) and a more important number of associated organ dysfunctions ($p < 0.01$). Pre-eclampsia and peripartum haemorrage were the leading causes associated with ARF. ARF patients got 34% mortality rate, with a relative risk of death increased by 5. Major risk factors for ARF development determined by a univariate analysis were: Persistant altered haemodynamics ($p = 0.02$), Disseminated Intra-vascular Coagulation ($p < 0.001$); Massive Transfusion ($p = 0.024$); and HELLP syndrome ($p < 0.001$). Running a univariate analysis, with mortality as the dependant variable and ARF as a co-variable, ARF as defined above was not an independent risk factor of mortality. A multivariate analysis using different levels of ARF depending on serum creatinine level and after Bonferroni statistical test correction, Severe acute renal failure (serum creatinine $\geq$ 300 μmol/l) and HELLP syndrome complicated by ARF were found to be independent risk factors of mortality. **Conclusion:** Severe acute renal failure is an independent mortality risk factor. The use of RIFLE criteria in the critically ill obstetric population could be pertinent. Use of low thresholds in ARF definitions must be maintained to diagnose ARF rapidly and treat aggressively with a clear goal: try to improve survival rate.

2

Clinical Effects of Early High Volume Hemofiltration on Acute Renal Failure in Post-Cardiotomy Patients

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Introduction: To evaluate the efficiency of HVHF in the treatment of ARF in post-cardiotomy patients. **Methodology:** HVHF was performed in 25 patients with ARF after cardiotomy, including 16 males and 9 females, with average age of 56.4 ± 16.80 (15–80) years. Except 6 of the patients quitted in early stage of HVHF, the remaining 19 patients were divided into two groups. Late HVHF group (Group I, n = 11) received HVHF treatment when urea levels were $\geq$30 mmol/l, creatinine levels were $\geq$250 μmol/l or potassium levels exceeded 6.0 mEq/l despite glucose-insulin infusion, regardless of urine output (polyuria, oliguria and anuria). While in early HVHF group (Group II, n = 8), HVHF was started when urine output was less than 100 ml within 8 h consecutively after surgery despite furosemide infusion. The levels of serum creatinine and potassium were not taken into account in Group II. HVHF was performed with AV600 hemofilter (polysulfone, 1.6 m^2) and the ultrafiltration (UF) flow rate at 4,000 ml/h, blood flow rate was 200–250 ml/min, and the substitute fluid was by a pre-dilution route. Low molecular weight heparin and/or citrate were used for anticoagulation in HVHF. The hemofilter was changed to a new one for clotting. Clinical conditions including blood pressure, heart rate, respiratory rate and temperature were monitored every 30 min, and blood gas analysis, serum biochemistry test were detected before and every 24 h after the initiation of HVHF. APCHE II scores were evaluated every 12 h during HVHF. **Results:** HVHF was well tolerated in all the patients. The hospital

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Table 1. Comparisons of body temperatures and the ratio of hypothermia between two groups (for Abstract 3)

	Base line	1 h	2 h	3 h	4 h	5 h	Proportion of hypothermia
BLW	37.2 (35.6–38.4)	36.6 (34.9–38.2)	36.3 (34.7–38.0)	36.1 (34.5–37.5)	35.8 (34.4–37.4)	35.5 (34.2–37.3)	20/25 (80.0%)
BLW + HRS	37.1 (35.2–38.0)	37.0 (35.1–38.0)	37.0 (35.4–38.1)	37.0 (35.2–38.0)	36.9 (35.2–38.3)	36.9 (35.5–38.2)	2/23 (8.7%)
p-value	NS	0.037	0.003	<0.001	<0.001	<0.001	<0.001
DW	37.2 (35.9–38.4)	36.6 (34.9–37.9)	36.4 (34.2–37.7)	36.3 (34.3–37.6)	35.9 (34.7–37.4)	35.7 (34.6–37.5)	17/23 (73.9%)
DW + HRS	37.0 (35.9–38.4)	36.8 (34.8–38.1)	36.7 (34.7–38.1)	36.6 (35.1–38.2)	36.7 (35.6–38.2)	36.8 (35.6–38.2)	2/21 (9.5%)
p-value	NS	NS	NS	0.008	0.001	<0.001	<0.001

mortality was 57.9%. In early HVHF group, the cardiopulmonary bypass (CPB) time (213.3 ± 137.33 vs. 138.4 ± 66.80) and x-clamp time (90.8 ± 33.31 vs. 80.7 ± 55.17) were both longer than the late HVHF group. After cardiatomy there was more patients accepted IABP in early HVHF group (77.8% vs. 30%). But in early group the mortality was lower than in the late one (44.4% vs. 70%). During HVHF, Body temperature, $p < 0.05$), heart rate and MAP were improved significantly in both groups. Urea and creatinine decreased to normal range rapidly ($p < 0.01$), and renal function was recovered in 10 patients. APACHE II score was decreased significantly ($p < 0.01$). And early HVHF group was better than the late one. **Conclusion:** HVHF is technically possible in ARF patients after cardiotomy, which could improve the general conditions, renal function and conduced to improve multiple organ disfunction. Early HVHF was better than the late one, which could improve the pathogenetic conditions in early stage after surgery, and had lower mortality.

3

The Easy and Effective Way to Prevent Hypothermia in Acute Renal Failure Patients on Continuous Venovenous Hemodiafiltration

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Acute renal failure (ARF) patients on continuous venovenous hemodiafiltration (CVVHDF) are vulnerable to hypothermia because the blood in the extracorporeal circuit is exposed 24 h/day. Hypothermia should be prevented to decrease the risk of cardiac, neurologic, hematopoietic and immunologic deterioration. We performed this study to investigate the usefulness of the method to warm the replacement fluid as an easy and effective method to maintain the isothermic status in patients on CVVHDF. CVVHDF was performed using a Prisma (Hospal-Gambro, Lyon, France) with an AN69 M60 filter (Hospal-Gambro, Lyon, France). To keep the blood temperature, we used a bloodline warmer (BLW, Prismaflo, Hospal-Gambro, Lyon, France) or a dialysate warmer (DW, Prismatherm, Hospal-Gambro, Lyon, France). We made the heated replacement solution (HRS) for 3 h just before using it in the peritoneal dialysis solution warmer (Bag warmer, Gambro, Korea). We measured body temperature for initial 5 h after applying HRS. Ninety-two consecutive patients with ARF were randomly assigned to four groups: only BLW (n = 25, M:F = 15:10), BLW + HRS (n = 23, M:F = 13:10), only DW (n = 23, M:F = 13:10), and DW + HRS (n = 21, M:F = 12:9). There was no significant difference between BLW and BLW + HRS and between DW and DW + HRS in age, sex, body weight, severity of acute illness such as APACHE II/CCF ARF score and mechanical parameters of CVVHDF. However, compared with the patients' body temperatures in BLW or DW groups, those in BLW + HRS or DW + HRS groups were significantly maintained within the isothermic range (table 1). In conclusion, the additional application of HRS to BLW or DW could be an easy and effective method to keep the patients' body temperatures on CVVHDF.

4

Outcome of Acute Renal Failure among Patients with CKD

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Aim: To study the outcome among patients admitted to Intensive Care for the management of acute renal failure on a background of CKD. **Design:** Prospective observational study. **Material and Methods:** All patients admitted into the intensive care unit with an acute worsening of CKD were followed through the ICU and Hospital stay to identify the predictors of outcome. Major outcome studied was ICU and in hospital mortalty. **Results:** A total of 30 patients were followed up for 3 months. 22 were male. The age of these patients ranged from 28 to 85 with a median of 62 years. Previous renal disease was known to be present in 23 patients. Nineteen were diabetic and 20 had either history or record of Coronary artery disease. Sepsis was the cause of the renal failure in 14 patients. The admission GFR ranged from 5.20 to 36 ml/min, with a mean of 28.3. The admission creatinine was between 1.3 mg% and 9.3 mg%. The overall ICU days were 11.7 days. However survivors stayed for only 10.04 days while non-survivors stayed for 19.8 days. Survivors spent about 9 days less on the ventilator. Some form of renal replacement therapy was needed in 25 patients. SLEDD was attempted in eight patients and CRRT followed by IHD among 6 patients. 22 patients survived the renal failure. Sepsis, Heart failure and prolonged ICU stay predicted those who were more likely to have an adverse outcome.

5

The DOse REsponse Multicenter International Collaborative Initiative (DO-RE-MI) in Intensive Care Units (ICU)

F. Mariano[1], M. Herrera[2], D. Kindgen-Milles[3], A. Marinho[4], D. Cruz[5], G. Monti[6]

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Background: Current practices for renal replacement therapy (RRT) in ICU remains poorly defined. The observational DO-RE-MI survey addresses the issue of how the different modes of RRT are currently chosen and performed. The primary end-point of DO-RE-MI will be delivered dose vs. in-ICU, 28-day, hospital mortality, and the secondary end-point, the hemodynamic response to RRT. The protocol has been published (Crit Care June 14, 2005). The Survey has been listed CRG110600093 in the Cochrane Renal Group. Here, we report the first preliminary descriptive analysis after 1 year recruitment. **Methods:** Data from 345 patients in need of RRT (M/F, mean age 61.2 + 15.9) from 25 centers in 5 countries (Spain, Italy, Germany, Portugal, France) were entered in electronic case report forms (CRFs) available via the acutewebsite.net. On admission, 50% patients had Crs >1.2 mg%, 48% came from Surgery, 30% from Emergency, and 14% from Internal Medicine. On admission, mean SOFA and SAPS 2 were 10 and 49, respectively. The first criteria to initiate RRT was the RIFLE in 33% (Failure: 62%, Injury: 19%, Risk: 10%), the second the high urea/creatinine, and the third immunomodulation. A total of 2,374 cumulative CRF were reported: CVVHDF, 50%; CVVH, 20%; IHD, 16%; HVHF, 8%; CVVHD, 2%; CPFA/CVVD, 2%. In 15% of cases, the patient was shifted to another modality. Mean blood flow rates (ml/min) in the different modalities were: 143 (CVVHDF), 194 (CVVH), 214 (IHD), 269 (HVHF), 167 (CVVHD). Downtime ranged from 7 to 25% of the total treatment time. Clotting of the circuit accounted for more than 60% of interruptions while a clinical reason was the case in 25%. **Conclusions:** Despite a large variability on the criteria of choice of RRT, the most used remains CVVHDF (49%). Clotting and clinical reasons were the commonest causes for RRT downtime. In CRRT, a large variability in the delivered dose is observed in the majority of patients and often in the same patient from one day to another. Preliminary analysis suggest that in a large number of cases the delivered dose is far from the 'adequate' 35 ml/h/kg.

6

Renal Failure in Leptospirosis in India

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Aim: To study the outcome among patients with Leptospirosis who develop renal failure. **Design:** Prospective observational study over 7 months in a tertiary care centre. **Material and Methods:** All patients admitted to the ICU for management of leptospirosis and its complications were followed throughout their ICU stay. Primary outcome studied was ICU mortality. Secondary outcomes studied were mode of RRT, effect of renal failure on outcome and effect of mode of RRT on outcome. Non-renal predictors of outcome were also assessed. **Results:** 23 patients were treated for leptospirosis in the time period mentioned. 21 were male. Average age of the patients was 56.4 years. The average APACHE of these patients was 26.4. 21/23 patients had a serum creatinine greater than 1.2 mg%. 11/21 were oliguric. 10/21 were non-oliguric. Average CPK was 9,200. Four patients had CPK values >10,000 IU/l. All 4 had oliguric renal failure. 7/21 patients needed RRT. 3 patients needed CRRT and HD. Six patients who needed RRT were oliguric. All patients with CPK >10,000 needed RRT. 6 patients died while undergoing treatment. Of these 2 did not need RRT. **Conclusion:** Oliguric renal failure, need for RRT, need for CRRT and CPK >10,000 were associated with adverse outcome among patients with leptospirosis.

7

Early Changes in Organ Failures Is Associated with the Outcomes of Critically Ill Patients in Need of Renal Replacement Therapy for Acute Kidney Injury

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Purpose: To evaluate the impact of changes in organ failures over the first three days of renal replacement therapy (RRT) on the outcomes of patients admitted to intensive care unit (ICU) with acute kidney injury (AKI). **Methods:** From November 2004 to May 2006, all patients admitted to the ICU of three tertiary care hospitals who required RRT for AKI for more than 48 h were studied. Patients with end-stage renal disease requiring chronic dialysis were excluded. AKD was classified according to RIFLE criteria. Organ failures were evaluated by the Sequential Organ Failure Assessment (SOFA) score (excluding renal points) on the first (D1) and third (D3) days of RRT. Absolute (D3–D1) and relative (delta SOFA) (D1–D3/D1) changes in SOFA score were calculated. Multivariate logistic regression analysis was used to identify predictors of hospital mortality. **Results:** Two hundred and sixty patients (80% medical admissions) with a mean age of 73 ± 15 years were studied. Mean SAPS II was 47 ± 11 points; mechanical ventilation was used in 81% and vasopressors in 72% patients. Continuous RRT was used in 84% patients. Overall ICU and hospital mortality rates were 71% and 75%, respectively. Median SOFA on D1 and D3 were 6 (4–8) and 7 (4–9) respectively. Associated organ failures worsened (D3–D1 > 0) in 48%, remained unchanged (D3–D1 = 0) in 17% and improved (D3–D1 < 0) in 30% patients, and mortality was lower for the last group (80% vs. 84% vs. 61%, $p = 0.003$). SOFA on D1 ($p < 0.001$), SOFA on D3 ($p < 0.001$),

absolute change ($p = 0.019$) and delta SOFA ($p = 0.016$) were significantly higher in non-survivors. In multivariate analysis, older age [Odds ratio (OR) = 1.03 (95% CI = 1.00–1.06), $p = 0.024$], presence of comorbidity [OR = 3.38 (1.41–8.08), $p = 0.006$], poor functional capacity [OR = 3.90 (1.74–8.75), $p = 0.001$], SOFA on D1 [OR = 1.31 (1.56–1.48), $p < 0.001$] and delta SOFA [OR = 1.84 (1.16–2.91), $p = 0.009$] were associated with increased hospital mortality. Adjusting for other covariates, patients in whom SOFA scores worsened [OR = 4.29 (1.45–12.72), $p = 0.009$] or remained unchanged [OR = 4.07 (1.91–8.66), $p < 0.001$] had a poorer outcome. **Conclusions:** In addition to baseline values, changes in SOFA scores over the first three days of RRT are associated with the outcomes of ICU patients with AKI.

8

Performance of Six Prognostic Scores in Critically Ill Patients Receiving Renal Replacement Therapy

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Purpose: To evaluate the performance of six prognostic scores in predicting hospital mortality in patients admitted to intensive care unit (ICU) in need for renal replacement therapy (RRT). **Methods:** All patients admitted to the ICU of three tertiary care hospitals who required RRT for acute kidney injury (AKI) from November 2004 to May 2006 were studied. Patients with end-stage renal disease requiring chronic dialysis and those with ICU stay less than 24 h were excluded. AKI was classified according to RIFLE criteria. Data from the first 24 h of ICU admission were used to calculate SAPS II and APACHE II scores and data from the first 24 h of RRT were used in the calculation of LOD, ODIN, Liaño and Mehta scores. Discrimination was evaluated using the area under ROC curve (AROC) and calibration by Hosmer-Lemeshow goodness-of-fit test (GOF). Standardized mortality rates (SMR) (observed mortality/predicted mortality) were also calculated for each model. **Results:** Three hundred and forty-seven patients with a mean age of 72 ± 15 years were evaluated. Type of admission was medical in 82%, scheduled surgical in 10% and emergency surgical in 8% patients. Mechanical ventilation was used in 81% and vasopressors in 73% patients. RRT was started in 49% of the patients within the first 24 h of ICU. The ICU and hospital mortality rates were 73% and 77%, respectively. Mean SAPS II, APACHE II and LOD scores were 43 ± 26, 21 ± 5 and 6 ± 2 points, respectively. Except for SAPS II ($p = 0.035$), all models were well fitted ($p > 0.05$ for GOF tests). However, discrimination was unsatisfactory for most of the models and AROC ranged from 0.61 (95% confidence interval (CI) = 0.54–0.68) for ODIN score to 0.74 (95% CI = 0.68–0.81) for APACHE II score. In addition, all models tended to underestimate hospital mortality and SMR ranged from 1.15 (95% CI = 1.05–1.27) for Mehta score to 2.42 (95% CI = 2.05–2.85) for LOD score. **Conclusions:** Organ dysfunction, general and renal-specific severity-of-illness scores are inaccurate in predicting outcome in ICU patients in need for RRT.

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Perioperative Factors Influencing Acute Kidney Injury in Patients following Cardiac Surgeries

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Background: Acute kidney injury (AKI) occurs in 1–30% of patients following cardiac surgeries and remains a cause of major morbidity and mortality. The influence of perioperative factors on the occurrence of AKI following cardiac surgeries is less well understood especially in the Asian population. **Methods:** A retrospective study of 623 consecutive patients who underwent open heart surgeries in a tertiary care centre in South India from January 2005 to July 2005. Preoperative, intraoperative and postoperative data of patients who underwent coronary artery bypass grafting (CABG), valvular surgeries and surgeries for correction of congenital cardiac defects were collected. AKI was defined as an elevation of 0.5 mg/dl of serum creatinine from baseline. The association between these variables was studied using bivariant analysis. This is an ongoing retrospective analysis with a total estimated study group of 3,000 patients to be completed before January 2007. **Results:** A total of 281 of the 623 patients underwent CABG, 123 patients underwent valvular surgeries, and 219 patients were operated for congenital heart disease. The incidence of AKI was 11.5% among CABG patients, 5.6% in patients with valvular surgeries, 2.28% in patients operated for congenital heart disease. The mortality of patients with AKI was 10.2%. Dialysis was initiated in 15.3% of the patients with AKI and the mortality among patients who required dialysis was 60.6%. Variables associated with the development of AKI included: age, diabetes mellitus, systemic hypertension, coronary artery disease, preoperative left ventricular dysfunction, preoperative renal dysfunction (serum creatinine > 1.2 mg/dl), use of vasopressors, redo surgeries, sepsis, duration of mechanical ventilation and prolonged intensive care unit stay. There was no significant association between these variables and the requirement of renal replacement therapy. **Conclusion:** AKI and AKI-dialysis are associated with a higher mortality in patients undergoing cardiac surgeries. We have studied perioperarive variables influencing the occurrence of AKI. A larger sample size would yield more valuable data. This would help in identifying patients for risk stratification before cardiac surgeries.

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Hospitalization Duration Affects Hemodynamic Impact of CRRT in Trauma Patients

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Continuous renal replacement therapy (CRRT) is commonly employed for renal replacement in ICU patients. In addition, CRRT has also been examined as a potential therapeutic intervention for systemic inflammatory conditions. Despite increasing utilization, the optimal use of CRRT has not been completely characterized. In previous studies, we demonstrated that ICU admission diagnosis might affect response to CRRT. To further explore this question, the objective of this study was to determine how length of stay impacts the hemodynamic effect of CRRT in trauma patients. Specifically, trauma patients needing CRRT, as defined by nephrology consultation, were identified, placed on continuous venovenous hemodiafiltration (CVVHDF), and divided into 2 groups. The first group had CRRT initiated within the first week of admission. The second group consisted of patients started on CRRT after hospitalization day 7. At initiation of CRRT, APACHE II score was calculated. In addition, temperature (TEMP), heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded at baseline and at 4, 8, and 12 h after initiation. There were no significant baseline differences between the 2 populations. Percent change in TEMP, HR, SBP, DBP, and MAP were then calculated for each time point. A graph for the MAP result is shown. Our results demonstrate that trauma patients initiated on CRRT after 7 days of hospitalization experienced a greater change in SBP, DBP, and MAP than patients started on therapy before day 7 of hospitalization. However, HR decreased more in patients started on therapy before day 7. **Conclusion:** Trauma patients receiving CRRT experienced changes in overall hemodynamic profiles. However, trauma patients started on CRRT who were hospitalized more than 7 days experienced greater increases in SBP, DBP, and MAP. Trauma patients hospitalized less than 7 days experienced a greater decrease in heart rate. These results indicate that the etiology of acute renal failure may influence response to CRRT. Identifying characteristics of patients who experience the greatest improvement in hemodynamics may help to further define the optimal use of CRRT.

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Postoperative Acute Kidney Injury Is an Important Determinant of Long Term Survival of Surgical Patients

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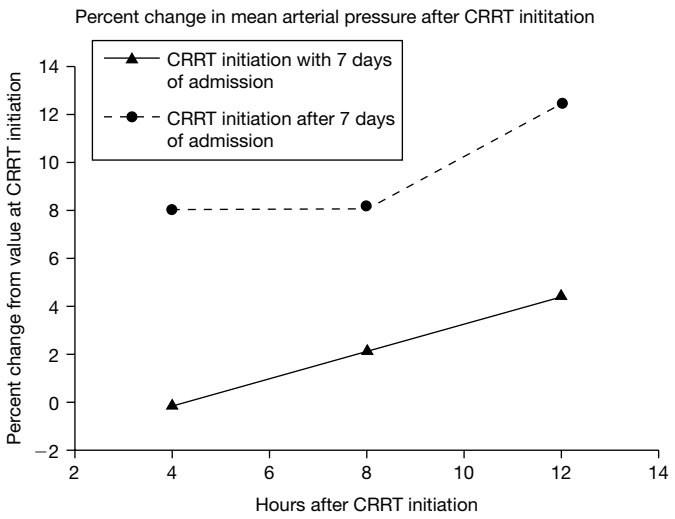
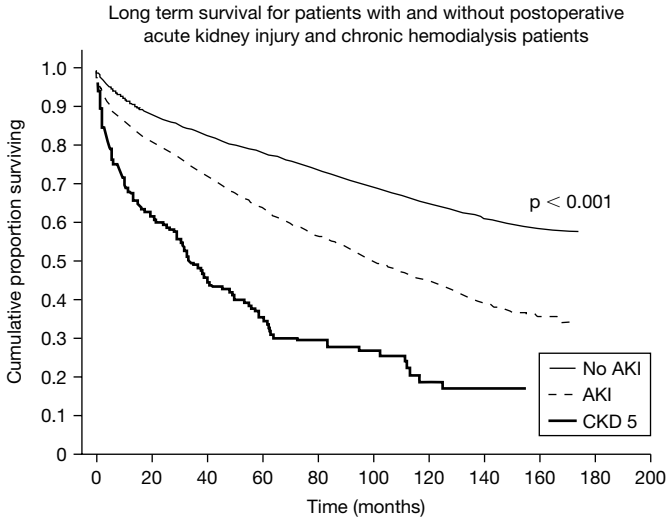
Acute kidney injury (AKI) is a common occurrence in surgical intensive care units (SICU). Long-term survival of patients with AKI who survive to leave the hospital is poorly studied. Our study reports the epidemiology and long-term outcome of surgical intensive care patients who developed post-operative AKI according to RIFLE criteria and survived to be discharged from the hospital. The administrative ICU database of Shands Hospital at the University of Florida was searched for all surgical patients discharged alive between 1992 and 2002. Medical records of patients were reviewed and AKI was determined using RIFLE classification. Patients were stratified according to the maximum RIFLE class (class R, class I or class F) reached during their hospital stay, based on glomerular filtration rate criteria, using changes in serum creatinine concentrations. Patients with end-stage renal disease (CKD 5) were analyzed separately. 10,678 patients had complete creatinine data. AKI was identified in 3,308 (31%) of patients who were discharged alive, while 7,076 (66%) patients had no episode of AKI. 156 CKD 5 patients who were hemodialysis-dependent prior to hospital admission were identified at the time of discharge. Patients with AKI were older (62 ± 14 vs. 55 ± 16, respectively, $p < 0.001$) compared to patients who did not





develop AKI; both groups were similar in regard to gender and ethnicity distribution. CKD 5 patients were more likely to be African-American (33% vs. 8%, respectively). Length of ICU and hospital stay was significantly longer among AKI patients (5 vs. 2 days and 16 vs. 9 days, respectively, $p < 0.001$). There was a significant difference in the AKI prevalence among the four major groups of surgery (General, Vascular, Cardiothoracic, and Neurosurgery). Five and ten year survival was significantly worse for patients with AKI (62% and 43% vs. 78% and 64%, respectively) (figure 1). Cox regression analysis confirmed AKI to be an independent predictor of long-term mortality when adjusted for patients' age, multiple co-morbidities on admission, post-operative sepsis and acute respiratory failure (RR 1.55, $p < 0.001$). We have demonstrated for the first time that postoperative AKI is not only an important complication in the immediate postoperative course, but also carries significant implications for long-term mortality.

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The Use of Radiocontrast Nephropathy Prophylaxis in Critically-Ill Patients

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Introduction: Radiocontrast nephropathy (RCN) is an important cause of acute kidney injury (AKI) in patients admitted to the intensive care unit (ICU). To date, intravascular volume expansion, sodium bicarbonate infusion, and N-Acetylcysteine (NAC) administration have been shown to reduce the incidence of RCN. Despite the benefit of these preventative strategies, the utilization rate for these prophylactic therapies in patients with AKI within the ICU is not known. **Methods:** We conducted a retrospective clinical and administrative database review to identify all patients admitted to the surgical or cardiac ICU at Shands Hospital (Gainesville, Fla.) between 01/01/05 and 12/31/05 that developed AKI during their ICU course. In this project, we used the Acute Dialysis Quality Initiative conference RIFLE criteria definition of AKI as a rise in serum creatinine concentration greater than 50% above baseline. Patients who received hemodialysis within 3 days of admission or were diagnosed with CKD on admission were excluded from this review. The subgroup of patients included in this study that received radiocontrast agents with or without prophylaxis with either sodium bicarbonate or NAC were then identified. **Results:** After review of the clinical and administrative databases, 2,436 patients were identified that matched inclusion and exclusion criteria (table 1). Of these patients, 533 (21.8%) developed AKI while in the ICU and 132 (4.7%) received radiocontrast agents after developing AKI. These 132 patients underwent 212 radiocontrast administrations, of which RCN prophylaxis was provided for 7 radiocontrast administrations (3.3%). There were 6 administrations of NAC and 1 administration of sodium bicarbonate. **Discussion:** This project demonstrates that patients who developed AKI while in the Surgical or Cardiothoracic ICU were routinely administered RCN prophylaxis at very low rates (3.3%). The possible reasons for the low rate of prophylaxis administration in this study include poor physician recognition of AKI, poor physician knowledge of RCN prophylaxis or incomplete data collection. Further study of this data may elucidate the cause of low prophylaxis rates. The use of routine guidelines by physicians in the ICU to identify and provide prophylaxis to patients with AKI may improve the apparent low utilization of RCN prophylaxis.

	n	%
Total number of patients admitted to the Surgical or Cardiac ICU	2,770	
Total number of patients included in review	2,436	87.9
Total number of patients excluded from review	334	12.1
Total number of patients with AKI in the ICU	533	21.8
Total number of patients with AKI in the ICU who received radiocontrast agents	132	4.7
Number of radiocontrast administrations to patients in the ICU with AKI	212	
Total number of prophylaxis administrations	7	3.3
NAC prophylaxis	6	2.8
Sodium bicarbonate prophylaxis	1	0.5

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AKI Classification Associated with the Severity of Renal Injury and In-Hospital Mortality in the Patients in a Cardiac Care Unit

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Purpose: In this study we evaluate whether the acute kidney injury (AKI) classification is associated with in-hospital mortality and the severity of renal injury in patients in the cardiac care unit (CCU). **Methods:** A retrospective cohort study was performed in Peking University First Hospital. Among 1,048 patients admitted CCU from 2002 to 2005, indicators of kidney injury and risk factors for death were evaluated. The observation end point of the study is the severity of renal injury (SKI) and mortality in the hospital. **Results:** Altogether 253 patients met criteria of AKI in 1,048 cases, and the prevalence of AKI stages 1, 2 and 3 was 12.4%, 2.9% and 7.2%, respectively. According to criteria of SKI as Scr > mol or RRT treatment, μ350 the percentage of AKI stages 1, 2 and 3 was 1.5, 3.3 and 50.7, respectively, while it was 0.4% in cases without AKI. The in-hospital mortality among AKI stages 1, 2 and 3 were 16.2%, 33.3% and 61.3%, respectively, compared to 2.1% in those without AKI. Kaplan-Meier analyses revealed that the in-hospital mortality increased progressively with advancement of AKI staging ($p < 0.0001$). Additionally, an almost linear increase in death odds ratios from AKI stage1 to stage 3 compared those without AKI (OR: 6.09, 12.91 and 19.51). There was a significantly different in SKI of AKI stage 3 patients compared to the other stage (OR: 87.09, $p < 0.05$). Univariate and multivariate COX analysis showed that AKI classification stage 2 and stage 3 were the independent risk factors for in-hospital mortality. The death odds ratios of AKI stage 2 and stage 3 (OR: 5.34 and 2.79) were associated with in-hospital mortality after adjusting all other risk factors for multiple covariates. AKI stage 3 was the independent risk factors for the SKI (OR: 18.11) after adjusting. **Conclusion:** In these CCU patients, AKI as the newly classification, its stage 2 and stage 3 is associated with increased risk of in-hospital mortality compared with those without AKI, even after adjusting for multiple risk factors. AKI stage 3 is closely associated with increased the severity of renal injury.

Emerging Concepts

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Cascade High Volume Hemofiltration: Preliminary Data in Septic Shock Patients

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During the early phase of septic shock, potentially toxic inflammatory mediators, mainly middle size molecules (5–55 kDa) are massively released and removed by high volume hemofiltration (HVHF). Nevertheless, the high permeability rate or high volume used during HVHF induces the loss of large amount of little and middle size molecules. We present here a new system: cascade HVHF, which allows a more efficient extraction of middle size molecules with restitution of small solutes by using sequential filters of different permeability. This pilot study aimed at the evaluation of the feasibility and the hemodynamic tolerance of this procedure. Septic shock patients with multiple organ failures requiring high doses of norepinephrine (>0.3 μg/kg/min) and extra renal epuration were included. Cascade HVHF (blood flow: 251.1 ± 25.4 ml/min) was performed for a maximum of 72 h, using a first high permeability filter (cut off of 69 kDa, area 2.15 m^2 (AN69 – Nephral ST 500)) and a filtration rate of 96.5 ± 19.3 ml/kg/h followed by a second filter of lower permeability (cut off: 5 kDa) but a larger area (3.6 m^2, GFS plus – HG 700). The second ultrafiltrate was reinfused at a rate of 73.0 ± 18.4 ml/kg/h. The unfiltered solutes were discarded and replaced by a substitution fluid at a rate of 23.6 ± 2.9 ml/kg/h. Unfractioned heparin was used unless contra indicated. Heart rate, blood pressure, lactate level, central venous pressure and respiratory variables were recorded before, during and after treatment. Nine patients (initial SOFA score 15.9 ± 3.1) were treated (duration 28.1 ± 17.8 h) by cascade HVHF followed by conventional hemofiltration. Among survivors at the end of the HVHF treatment (8/9), the hemodynamic variables were improved as suggested by the decrease in norepinephrine requirement from 0.65 ± 0.23 μg/kg/min to 0.36 ± 0.21 μg/kg/min, $p < 0.05$) and in serum lactate level (from 5.18 ± 4.54 mmol/l to 2.87 ± 2.88 mmol/l, $p < 0.05$). Cascade HVHF were well tolerated and improved hemodynamic status. These preliminary data support an assessment of this new therapeutic modality on a larger scale.

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Successful Treatment of Acute Renal Failure with Therapeutic Plasma Exchange

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Despite more than 50 years of research, acute renal failure (ARF) remains a serious problem. In the ICU, patients with ARF have mortality rates around 50%. Current therapies for ARF are largely supportive allowing time for the damaged tubular cells to regenerate. We report a case of a rapid reversal of ARF following therapeutic plasma exchange (TPE). At the time, TF was a 5-year-old boy who was status post orthotopic heart transplantation for complications following surgical palliation of hypoplastic left heart syndrome. An episode of gastroenteritis triggered uncompensated congestive heart failure. Following a cardiac arrest, he was placed on extra-corporeal membrane oxygenation (ECMO) for life support. Oliguric ARF developed with 50% fluid overload and an estimated GFR of 26 ml/min/1.73 m^2. Because of elevated panel reactive antibodies, Therapeutic Plasma Exchange (TPE) using the PRISMA system (GAMBRO, Lund, Sweden) was performed on ECMO days 4, 5, and 7. Starting on ECMO day 6, TF showed increasing response to diuretic therapies, and had urine output of 2 l/day (~4 ml/kg/h). By ECMO day 10, he had reached his dry weight, diuretics were held, and his GFR doubled to 50. He received additional plasma filtration sessions on ECMO days 11, 13 and 18. He was successfully weaned off ECMO after 21 days of support. We propose that the rapid improvement in TF's kidney function following TPE resulted from this therapy's ability to remove pro-inflammatory cytokines and/or pigment nephropathy components (from ECMO-induced hemolysis). This case highlights the ability of TPE as a potential new modality for the treatment of ARF and lends support for the peak concentration hypothesis, and to the increasingly recognized role that the kidney plays in regulating the global cytokine milieu.

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Effects of High Volume Hemofiltration on Severe Acute Pancreatitis in Pigs

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Introduction: To investigate the effects of different hemofiltration intensity on inflammatory response, hemodynamics and oxygen metabolism of SAP in pigs. **Methodology:** Pancreatitis was induced by pressure-controlled (100 mm Hg), intraductal injection of sodium taurocholate (4%, 1 ml/kg) and trypsin (2 U/kg). After induction 24 animals were randomly assigned to one of the three groups. Group I ($n = 8$) animals served as SAP controls received only saline. Group II ($n = 8$) animals accepted a low volume (20 ml/kg/h) CVVH and group III ($n = 8$) animals received HVHF (100 ml/kg/h) at the same time of the induction of SAP. Zero-balanced hemofiltration was performed with a blood flow rate of 80 ml/min in a predilution mode using AN69 (polyacrylonitrile, 1.2 m^2, Hospal, France), the machine was EQUA-smart (Medica, Italy). The filters were replaced daily. The heparin was used to avoid coagulation. After the instrumentation of the animals by arterial and Swan-Ganz catheters (5F, Arrow, USA), hemodynamic indexes were monitored intermittently. The serum concentrations of cytokines were measured using specific enzyme-linked immunosorbent assays (ELISA). Monocytes were separated and stimulated by LPS to detect cytokines production. **Results:** Survival time was significantly prolonged both by low-volume CVVH and HVHF; it was more pronounced in the latter ($p < 0.05$). HVHF was significantly superior compared with low-volume CVVH in systemic inflammatory reaction protection. The major hemodynamic finding was that pancreatitis-induced

hypotention was significantly attenuated by HVHF ($p < 0.05$). The development of hyperdynamic circulatory failure was simultaneously attenuated ($p < 0.05$), as reflected by a limited increase in cardiac output, an attenuated decrease in systemic vascular resistance ($p < 0.05$) and an elevation in oxygen extraction ratio ($p < 0.05$). The serum concentrations of cytokines such as IL-6, TNF-α and IL-10 decreased significantly in hemofiltration groups ($p < 0.05$), especially in HVHF group ($p < 0.05$). In the early phase of SAP, there was a significant reduction of TNF-α, IL-6 and IL-10 secreted by monocytes in the hemofiltration groups ($p < 0.05$). But 36 h after the induction of SAP, the activities of TNF-α and IL-6 secreted by monocytes in hemofiltration groups were higher than in controls ($p < 0.05$), while the activity of IL-10 in hemofiltraion groups were lower than in controls. **Conclusion:** HVHF might blunt the hyperdynamic circulatory failure and excess inflammatory response. HVHF was distinctly superior in preventing pancreatitis-related hemodynamic impairment and immune disorders compared with low-volume CVVH.

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Clinical Effects of High Volume Hemofiltration on Severe Acute Pancreatitis

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Introduction: To investigate the efficiency of HVHF in the treatment of SAP. **Methodology:** Totally 77 SAP patients were involved, 15.16 (13–18) years ± including 54 males and 23 females, with average age of 47.8. Diagnostic criteria for SAP standardized by the Chinese Medical Association were applied for inclusion. Except routine treatment of SAP, HVHF was given to the patients and sustained for at least 72 h, with AN69 (polyacrylonitrile, 1.6 m^2) and AV600 hemofilter (polysulfone, 1.6 m^2), and the ultrafiltration (UF) flow rate at 4,000 ml/h, blood flow rate was 200–250 ml/min, and the substitute fluid was by a pre-dilution route. Low molecular weight heparin and/or citrate were used for anticoagulation in HVHF. The hemofilter was changed to a new one every 24 h except for clotting. Clinical conditions including blood pressure, heart rate, respiratory rate and temperature were monitored every 30 min, and blood gas analysis, serum C-reactive protein (CRP), and serum biochemistry test were detected before and every 24 h after the initiation of HVHF. APCHE-II scores were evaluated every 12 h during HVHF. **Results:** HVHF was well tolerated in all the patients. Sixty-four of the patients survived, 8 patients died and 5 of the patients quitted for financial reason. The hospital mortality was 11.1%. Body temperature ($p < 0.01$), heart rate ($p < 0.01$) and respiratory rate decreased significantly after HVHF. During HVHF the hemodynamics was stable, and MAP was in normal range through the therapy. APACHE score was improved significantly after HVHF ($p < 0.01$). After HVHF, renal function of 12 ARF patients was recovered, and serum potassium, sodium, chlorine, glucose and PH were all kept in normal range. HVHF was well tolerated, and there were no severe fatal complications. **Conclusion:** When HVHF was used in SAP patients, it could not only improve the general conditions, APACHE II score but also keep the balance of electrolyte and acid base, improve the renal functions. HVHF, which seldomly disturbed the hemodynamics and caused few complications, was expected to become a beneficial adjunct therapy for SAP patients.

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Heparin Free Slow Low Efficiency Dialysis (SLED) Using Citrate Dialysate (CD) Is Safe and Effective

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Anticoagulation for continuous renal replacement therapies (CRRT) is a major problem, particularly when heparin is either contraindicated or is unsafe. Regional citrate anticoagulation is complex and often is associated with hypocalcemia, alkalosis, hypernatremia and accumulation of citrate. Citrate containing dialyaste has been reported to decrease clotting during intermittent acute dialysis, however its use in acutely ill patients with multi-organ failure and liver failure has not been reported with CRRT. We have used CD in this group for several years and have analyzed the data for most recent year, 2005. Forty-seven (31 male) patients underwent 117 SLED. Primary etiologies included 25 with advanced liver failure including liver transplantation (Tx) and/or rejection; 10 stem cell Tx and/or advanced malignancies; 6 with heart, lung, kidney, or pancreas Tx; and 6 others. Multi-organ failure including liver failure was present in 25 patients and 29 had sepsis; 6 patients had HIT and others were at increased risk of bleeding or were actively bleeding. Hemodynamic instability was the major reason for the use of SLED. Completion of treatment as ordered or lasting for greater than 12 h. without clotting was classified as 'Completed' otherwise 'Clotted'). Ninety percent of heparin free SLED using citrate dialysate were successful, 'Completed' (104 of 117). Table 1 shows changes in blood electrolytes with the SLED. The average blood and dialysate flows were 198 + 71 and 287 + 85 ml/min and net UF was 1.6 + 1.5 ml/procedure. All procedures were well tolerated and no complications were noted. Comparison of 'Completed' and 'Clotted' Rx shows that the blood flow (200 + 71 vs. 180 + 74 ml/min, $p = 0.02$) and dialysate flows (292 + 84 vs. 250 + 100 ml/min, $p = 0.02$) were higher in 'Completed' than in 'Clotted' procedures. There was no decline in ionized calcium however magnesium declined during the treatments but remained in normal range. CD appears to be effective and safe for heparin free SLED in acutely ill patients with multi-system failure including advanced liver failure.

Table 1 for Abstract 18

SLED	Sodium	Ionized Calcium (iCa)	iCa/Total Calcium	Magnesium	Bicarbonate	Anion Gap
Pre-	135 ± 4.7	1.14 ± 0.27	0.128 ± 0.012	2.0 ± 0.3	22.9 ± 5.8	13.9 ± 5
Post-	134 ± 2.9	1.13 ± 0.14	0.127 ± 0.001	1.8 ± 0.3	26.1 ± 4.4	11.9 ± 4.5
p	NS	NS	NS	<0.0001	<0.0001	NS

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Developing Nursing Expertise in Continuous Renal Replacement Therapy (CRRT)

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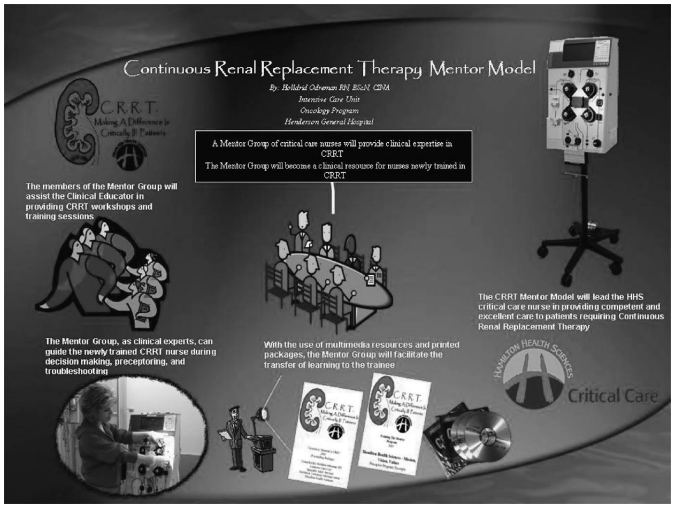
Purpose and Goals: The ICU at Hamilton Health Sciences-McMaster University Hospital had been running an adult CRRT program for approximately six years. This program had provided training to critical care nurses new to CRRT. In 2004, it was identified that there was a need to improve the teaching strategies of the existing program. As well, there was a need to develop an innovative model that would address the ongoing management of CRRT nursing skills and develop nursing leadership within the program in order to support newly trained nurses. The goals of such a model were to allow the ICU to become one of the leading centres for excellence in nursing care when providing CRRT and to improve job satisfaction and career empowerment as part of the recruitment and retention initiatives of the ICU. **Methods:** The 'CRRT Mentor Model' was developed by transferring knowledge in advanced principles of CRRT and adult teaching and learning principles to a select group of critical care nurses. The 'CRRT Mentor Group' was composed of ten nurses who would provide guidance and clinical expertise to nurses new to CRRT. The 'CRRT Mentor Group' eliminated the need for having one person responsible for the CRRT program but rather allowed a group of experienced nurses with the specialized training to run the program, devise ongoing learning opportunities, and provide subsequent training to future nurses hired in the ICU. Basic and advanced nursing skills in CRRT were included in the unit's annual critical care nursing skills review. **Summary:** Evaluation questionnaires taken before and after the implementation of the 'CRRT Mentor Model' from each member of the mentor group yielded positive responses about the effectiveness of the model. Annual nursing skill review in CRRT provided comfort to nurses new to CRRT by reviewing basic concepts in the modalities of the therapy. **Outcomes:** The mentor group became a key resource for the physician team in identifying appropriate patients and as part of the critical care team contributed to the decision making on treatment modalities within CRRT. The number of CRRT nurses in the ICU has increased to twenty. A CRRT 'Mentor Representative' from the mentor group was chosen to liaise between the mentor group, the clinical educator, and the clinical arranging quarterly CRRT mentor group meetings to review practice updates, literature reviews, and development of future learning activities for nursing. In 2006, the ICU of the Henderson Hospital, which is also part of Hamilton Health Sciences, started its own adult CRRT program and implemented the ideas and principles provided by the CRRT Mentor Model. Presently there are six mentor group members, six additional CRRT nurses, and plans for training four more critical care nurses. A joint collaboration in training and reviewing advanced nursing skills in the area of CRRT has been scheduled for the annual nursing skills review of each ICU for 2007. This collaboration will standardize the practice of nursing care in CRRT within the organization.



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Evaluation of On-line Monitoring of Dialysis Adequacy

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Purpose: To ensure that ESRD patients receive adequate treatments, the delivered dose of dialysis needs to be measured and monitored. There are various methods of estimating Kt/Vs, some are too complex for routine clinical use and create major inaccuracies. An on-line conductivity monitoring (using sodium flux as a surrogate for urea) determines Kt/V by measuring ionic dialysance on each dialysis treatment. The aim of this study is to evaluate the accuracy of on-line monitoring device in measuring the delivered dose of dialysis by comparing it to blood sampling method estimating Kt/V by obtaining pre and post urea samples. **Method:** We prospectively studied 20 stable chronic HD patients, age range from 30 to 75 years, dialyzed for 3–4 h, three times a week over a two-month period. Patients were dialyzed using Gambro Phoenix machine equipped with Diascan modules, which measures ionic dialysance to determine Kt/V. The volume of urea distribution volume is derived from Watson formula. Kt/V values are readily accessible in dialysis machine monitor every session. This method was supplemented and compared to every 6 weeks collection of pre and post dialysis serum samples to measure urea reduction. Post dialysis samples were obtained by using slow-flow technique to minimize effects of urea rebound. Kt/V was calculated using Daugirdas equation (second generation). **Results:** Preliminary findings of our study showed that the mean value of effective dialysance was lower than that of effective urea clearance by 5–15%. **Evaluation:** We conclude that in steady-state patients, effective urea clearance can be derived from ionic dialysance. On-line monitoring is an acceptable guideline for measuring dialysis adequacy. It's simple, readily accessible and cost effective without multiple blood sampling. However, other methods of measurement of dialysis dose are encouraged as to ensure dialysis patients receive not only the prescribed but the delivered dialysis treatment as well.

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The Effect of Hemofiltration on Adult Respiratory Distress Syndrome

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Objective: To analyze the effect of hemofiltration on adult acute respiratory distress syndrome. **Methods:** Thirty-three ARDS patients were involved whose average was 58.7 ± 16.6 years. Of the patients, 21 were male and 11 were female. The clinical characteristics of each patient met the diagnostic criteria of ARDS, which was established by the national ARDS annual meeting in 1999. Hemofiltration was performed by using the Baxter BM25 system. The substitute fluid was infused by a pre-dilution rout, the ultrafiltration rate was 6–8 l/h, blood flow rate was 250–350 ml/min. AN69 hemofilter (2.05 m^2) was applied without reuse. Low molecular weight heparin was continuously intravenously infused at a small dosage for pre-pump anticoagulation. Hemofiltration lasted 6–12 h each day. Patients' blood pressure, heart rate, CVP were recorded at the beginning of the treatment then followed every 30 min. Respiratory rate, SaO_2, FiO_2 Oxygenation index, end-expiratory positive pressure (PEEP) were recorded every 4 h. The tests of arterial blood gas and serum electrolytes were performed just before hemofiltration and after hemofiltration. **Results:** Totally 146 sessions of hemofiltration were performed. The average time of each session was 7.6 ± 2.6 h/day. The substitute volume was 49.2 ± 11.1 l/day (0.73 ± 0.21 l/kg/day). The removal of the fluid was 2.0 ± 1.41 in each session and its rate was 3.2 ± 2.8 ml/kg/h. Thirteen patients got better after hemofiltration, but the other 20 died although having intensive blood purification therapy, resulting in a mortality rate of 60.61%. Hemodynamic changes showed that the vital signs trend to be more stable and tachycardia ameliorated automatically (106.5 ± 20.5 vs. 98.9 ± 22.0 bpm, $p < 0.05$). MAP rose significantly without increase of vasoactive agent dose (71.6 ± 18.4 vs. 75.6 ± 21.8 mmHg, $p < 0.05$). Central vessel pressure decreased significantly after the therapy (6.5 ± 2.3 vs. 6.1 ± 2.2 mmH_2O, $p < 0.05$), but still within the normal range. Some other parameters such pH, PCO_2 and HCO_3- had no significant change after hemofiltration. The requirement of FiO_2 was lowered significantly (64.8 ± 22.6 vs. 60.8 ± 22.0, $p < 0.05$). Blood-gas analysis showed that both PaO_2 and oxygenation index were improved after therapy (93.9 ± 5.8 vs. 96.7 ± 3.8, $p < 0.05$; 121.0 ± 66.2 vs. 138.7 ± 77.7, $p < 0.05$). Serum electrolytes kept steady during the whole sessions. **Conclusion:** Hemofiltration can ameliorate pulmonary gas exchange function and improve SaO_2 in ARDS, so it contributes to the therapy of ARDS.

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A Randomized Prospective Study Comparing High Dose Continuous Venovenous Hemodiafiltration (CVVHDF) to Standard Dose CVVHDF in Critically Ill Patients with Acute Kidney Injury (AKI)

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Purpose: Several studies have demonstrated a survival benefit with dose of dialysis in acute kidney injury (AKI). We performed a prospective randomized study to determine the effect of the effluent rate of continuous venovenous hemodiafiltration (CVVHDF) on survival in critically ill patients with AKI. **Methods:** A total of 200 critically ill patients with AKI at the University of Alabama at Birmingham were randomized to receive CVVHDF at an effluent rate of 35 ml/kg/h (high dose) or CVVHDF at an effluent rate of 20 ml/kg/h (standard dose). The primary outcome measure was survival at either intensive care unit (ICU) discharge or 30 days, whichever came first. Renal recovery was a secondary outcome measure. Analysis was by intention to treat. **Results:** The two treatment groups were similar with respect to age, gender, AKI etiology, and Acute Physiology, Age, and Chronic Health Evaluation (APACHE) II score at initiation of CVVHDF. The overall ICU mortality among patients enrolled was 57%. At initiation of CVVHDF, the mean age was 60 years, mean APACHE II score 26, mean BUN 75 mg/dl, mean creatinine 4.3 mg/dl, and mean weight 91 kg. Fifty eight percent of the patients were male; 54% were septic, and 64% oliguric. Seventy eight percent of patients were intubated, and 59% were on pressors at initiation of CVVHDF. The mean duration of CVVHDF was 9.9 days, and 77% of patients obtained an effluent rate of at least 80% of the prescribed dose. Ninety one percent of patients were treated with citrate anticoagulation. ICU mortality at the earlier of 30 days or discharge from the ICU did not differ significantly between the two treatment groups: 44% in the standard dose arm died, as compared to 51% in the high dose arm ($p = NS$). Overall, 33% of patients had recovery of renal function at the earlier of 30 days or discharge from the ICU. Rate of renal recovery was 37% in the standard dose arm and 28% in high dose arm ($p = NS$). **Conclusion:** We observe no difference in mortality or rate of renal recovery between patients receiving high dose or standard dose CVVHDF.

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Improved Serum Urea Control in Catabolic ICU Patients on CRRT using Adsorbent Based Partial Bicarbonate Dialysate Recycling is Related to Urea Clearance Independent Mechanisms

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Background and Aim: Appropriate treatment dosage is critical to improve outcome of ICU patients on CRRT (Ronco et al., 2000) and BUN is a predictor of outcome. In order to provide high treatment dosage with moderate use of cost intensive bicarbonate solutions, a new concept of partial dialysate recycling in CRRT was tested. **Method:** ICU Patients with at least one additional organ failure and indication for renal support were treated with Bicarbonate CRRT. Two alternative modes were applied: CRRT with 35 ml/kg/h Bicarbonate flow (Group A), and CRRT with a 130 ml/kg/h Bicarbonate flow which was partially recycled by a urease free adsorbent system (MaxiCyclerTM), reducing the net Bicarbonate use to 20 ml/kg/h (Group B). The endpoint was the regression of BUN during a course of 72 h. As a secondary parameter, the Urea clearance was calculated by the formula Clearance = BF × (CBI − CBO)/CBI; with BF being blood flow, CBI being Blood Urea concentration at Dialyzer inflow and CBO at dialyzer outflow. Because a minimum of 35 ml/kg/h is todays standard of care, groups A and B were also compared to a historical control group with comparable baseline urea and urea regression on CRRT with a bicarbonate flow of 20 ml/kg/h (group C). **Results:** At comparable blood flow rates (150 ml/min), the regression of urea concentration over time was 0.06 (SE 0.014) mmol/l/day in group A and −0.11 (SE 0.4) mmol/l/day in group B, indicating no significant difference in the time course of urea concentration between both groups. Both treatment modes (A and B) were significantly more effective in Urea control when compared to historical parameters (group C), when the regression of urea over time was 2 mmol/l/day. Interestingly, the urea clearance in group B was less (25 ml/min) than in group A (41 ml/min), indicating that urease free adsorbents exert urea control not via active urea clearance. **Conclusion:** Providing sufficient urea control by CRRT can be achieved at lower Bicarbonate use if partial Bicarbonate re-use is applied. The reduction of Bicarbonate Use to almost 50% may result in significant cost reduction for the provider. However, further controlled clinical trials need to confirm that this method results in the same favourable clinical outcome presented at 35 ml/kg/h.

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The Association Between the Variation of Serum Creatinine and the In-Hospital Mortality of Patients in a Cardiac Care Unit

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Purpose: To investigate which the variation of serum creatinine (Scr) can be considered as more predictable level for the in-hospital mortality of patients in CCU. **Methods:** From total of 1,048 patients in CCU of our hospital from 2002 to 2005, 259 patients without AKI and 130 patients of AKI stage 1 were included in this study, according to ΔScr level of Acute kidney injury (AKI) criteria. Patients were divided into 5 groups according to their maximum ΔScr level within 48 h: group 1 <0.2 mg/dl; group 2 0.2–0.29 mg/dl; group 3 0.3–0.39 mg/dl; group 4 0.4–0.49 mg/dl and group 5 >0.5 mg/dl. Using the Logistic Regression method, which the variation of serum creatinine (ΔScr) might be considered as more predictable level for the in-hospital mortality of patients in CCU was evaluated. **Results:** Among the total 389 patients, the in-hospital mortality was 4/171 (2.3%), 2/88 (2.3%), 3/59 (5.1%), 3/23 (13%) and 15/48 (31.3%) in groups 1, 2, 3, 4 and 5. ΔScr level of group 4 and group 5 was associated with the in-hospital mortality in these patients (OR 6.26, 18.98, $p < 0.05$). Multivariable analyses was done by adjusting other risk factors for death, such as: age, gender, the basal level of Scr, hypertension, diabetes mellitus, hypotension, multiple organ failure (MOF), heart failure, arrhythmia, circulate support, respiration support, coronary angiography and cardiac surgery. After adjusting, ΔScr level of group 5 was still significantly associated with the in-hospital mortality (OR 6.57, $p < 0.05$). **Conclusion:** In CCU patients of our hospital, ΔScr level more than 0.5 mg/dl within 48 h probably is the more predictable level for the in-hospital mortality. The criteria of AKI may need to be modified dependent on different type of clinical settings.

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Clinical Study of Blood Purification in Pediatric Critical Care

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We studied various factors for blood purification in only severe pediatric patients concerning with survival rate. **Methods:** Survival rate was an endpoint. There are 34 severe critical cases that were performed blood purification from 2002 to 2005. We excluded patients who had severe neurological problems or were performed ECMO, because we cannot calculate D-PELOD (PELOD). We analyzed effect of age, body weight, with or without CPR, cathecolamine index (CAI),

PELOD before blood purification on survival rate and blood purification. We used Fisher χ^2 test. **Results:** Patients mean age was 2 year and 6 month old. Mean body weight is 8.9 kg. About blood purification, there were 16 cases of CHF. There were 19 cases of CHDF. There were 8 cases of PEX. There were 6 cases of PMX-DHP. We found out that survival rate is statistically higher among the children who are one year or older, who are more than four kilograms in weight, who are supported by 5 μg/kg/min or less inotropes, whose PELOD score is less than twenty or who have never experienced cardiopulmonary resuscitation ($p < 0.01$). On the other hand, sepsis cases have much better survival than previously reported by us ($p < 0.05$). In PELOD, circulation factor and blood factor significantly made survival rate worse when those score was over ten points. On the contrary, when Kidney and Liver score of PELOD were higher, survival rate was lower. When Kidney and Liver score of PELOD were lower, survival rate was higher. **Conclusion:** Our study shows that we can achieve better survival before the deterioration of circulation status (below CAI 5) and we should perform blood purification earlier below PELOD 20. In severe sepsis patients, we can achieve significantly much better survival rate by using PMX-DHP.

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Innovative Use of CRRT; Low Flow ECLS

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Introduction: Extracorporeal life support (ECLS) is routinely offered for failed conventional management of neonatal meconium aspiration syndrome (MAS). **Background:** Pediatric ECLS is not offered at our institution. **Case Report:** A 4.5 kg male infant had MAS and persistent pulmonary hypertension of the newborn (PPHN). Severe hypoxemia required 100% oxygen, nitric oxide (NO), sedation, paralysis, surfactant and high frequency ventilation. Oxygen index (OI) was 40 to 80 for the first 7½ hours. Circulation was supported with dopamine and epinephrine. Ventilatory strategies and escalating inotropic support reduced OI over the next 7 hours. Indication for ECLS was to minimize end-organ damage from inadequate oxygen delivery (DO_2) and ventilator induced lung injury. Experimental therapy using an in-line oxygenator in the continuous renal replacement therapy (CRRT) circuit for 'low-flow' ECLS was proposed to the family and accepted. An 8 French double lumen (DL) catheter was placed in the right atrium (RA) (both lumens used as access ports) and a 7 French catheter in the left atrium (LA, return line). A Lilliput 902 oxygenator (Sorin) was placed in the patient return line of a PRISMA CRRT machine (pre-air detection sensor). Anticoagulation was maintained with heparin (ACT 250–300). Flow was initiated at 50 ml/min and increased to 80 ml/min. High return line and filter pressure prevented further increase in blood flow. Immediate and sustained improvement allowed weaning of FiO_2, inotropic support and normalization of pCO_2 and pH. Progressive fall in lactic acidosis suggested adequate DO_2. Return line was switched from LA catheter to RA DL catheter because of high return pressures. Flow of 150 ml/min with acceptable access and return pressures and minimal recirculation (visual AV difference) was achieved. Hemodynamic and respiratory parameters were unchanged. Uncomplicated ECLS was maintained for 57.35 hours. He was extubated 4 days later. **Conclusion:** 'Low flow' ECLS can be achieved using a CRRT circuit with an in-line oxygenator allowing modest improvement in DO_2 and CO_2 removal in neonates.

Technique Characteristics

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Safety and Efficacy of Low Cost Modified Plasmapheresis in a Perepheral Centre

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Background: Plasmapheresis is a costly procedure and economically not feasible for the most in developing countries. The aim of our study is to analyze the Safety and effectiveness of low cost modified plasmapheresis in a peripheral centre. **Material and Methods:** In this prospective study from 01 to 05, 20 patients were treated with modified plasmapheresis. Indications of plasmapheresis were myasthenia gravis (MG) 2 Guillaine-Barre syndrome (GBS) 18. Fresinious Dialog plus version 7.21 and GambroAK10 machines, PF 2,000 (Gambro) plasma filter, Ringer's lactate solution (potassium concentartion 4 mEq/l), fresh frozen plasma/5% human albumin, double lumen hemodialysis catheters placed in femoral or internal jugular vein as arterio venous access. Were the soft and hardware for our plasmapheresis. Prophylactic calcium gluconate and broad spectrum antibiotics were used in all. Unfractioned heparin in bolus and continuous infusion was used for anticoagulation. Catheter tip was sent for culture and sensitivity after the procedure. Neurogical assessment and nutritional assessment by the formula (usual wt – actual wt) ÷ (usual wt) × 100, for percent weight change over were done. **Results:** All were males. Average age was 32.15 years (17–68). Total number sessions and cycles of plasmapheresis were 20 and 91 respectively. The mean volume exchanged was 2,250 ml (1,750–2,800 ml). The mean duration of plasmapheresis, mean blood flow and mean TMP respectively were 116.6 min (80–150 m) 125 ml/m and 90 mm Hg. Plasmapheresis was scheduled daily for 3 consecutive days and later alternatively till the recovery. Plasma filter was reused in all. Filtered plasma was replaced by RL solution and FFP or 5% human albumin in 3:1 ratio. Adverse reactions noted-hypocalcaemia (15%), hypotension (10%), hypersensitivity reactions (5%), paraesthesiae (5%), infection (0%), bleeding (0%). Hypoalbuminemia (serum albumin <3.5 g%) in 60% and significant/severe percent weight change in 50% were noted at the end. Catheter tip culture was sterile in all. Concomitant immunosuppressive treatment was given to MG patients. Neurological improvement was noted in all the patients except one with an over all recovery rate of 95%. Mortality rate was 5%, which is not related to the procedure. Patients were discharged with a special emphasis on high protein diet. After six months follow up, nutritional status was restored to normal. Average cost was in between USD 371 (with FFP) and USD 482.8 (with 5% albumin) which is highly economical compared to IV Ig (USD 1,630.4–3,260.87). **Conclusions:** Our experience with modified plasmapheresis showed that procedure is safe, effective and highly economical and it is especially suitable for the poor developing countries and can be done in a peripheral centre. Except transient hypoalbuminemia and malnutrition no other significant complications were observed.

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Clinical Evaluation of Anticoagulation without Heparin during Continuous Venovenous Hemofiltration

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Objective: To evaluate anticoagulation without heparin during continuous venovenous hemofiltration. **Methods:** Forty-two critically ill patients for therapy of continuous venovenous hemofiltration (CVVH) were enrolled in our study. Nineteen patients with high risk of bleeding who had received anticoagulation without heparin were as observed group, the rest of the patients who had received anticoagulation with low molecular weight heparin were as control group. In the two groups, the replacement fluid rate was 3,000 ml/h, the therapy time was 12 h/day, the bicarbonate replacement fluid were infused by the mode of predilution. The decrease rate of solution was figured. Before and after each session of treatment, electrolytes, acid base, clotting index was tested and heart rate, mean arterial pressure, transmembrane pressure and the life of filter were recorded. **Results:** The serum level of urea, creatinine were significantly decreased after treatment in the two groups, but there were no difference in the decrease of solution between the two groups. After treatment, the level of securm electrolytes, acid base trend to stable. The clotting index were no significantly changed in observed group, while APTT was significantly extended in control group ($p < 0.05$). During the whole course of therapy, heart rate and mean arterial pressure of patients were stable. Transmembrane pressure was significantly increased at seventh hours in observed group and at ninth hours in control group. The mean life of filter in observed group was shorter than in control group ($p < 0.05$). **Conclusions:** Anticoagulation without heparin in CVVH with the advantage of high efficient, stable and safe is an important measure to ensure CVVH continuously for patients with high risk of bleeding.

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High-Volume Continuous Veno-Venous Hemofiltration Using Citrate Anticoagulation

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Background: Most citrate anticoagulation protocols reported in the literature for continuous renal replacement therapy (CRRT) are tailored for low-volume continuous veno-venous hemofiltration (CVVH). High-volume CVVH (HV-CVVH) is increasingly prescribed, but the safety and efficacy of citrate anticoagulation are not well established for this treatment modality. We developed a citrate anticoagulation protocol devised specifically for HV-CVVH and based on commercially available dialysis solutions. The aim of the present study was to evaluate the incidence of metabolic complications and filter life with this protocol. **Methods:** Blood flow (Qb)

was set at 150 ml/min and replacement fluid rate at 4 l/h with the Prism0cal solution (Gambro). Sodium citrate 4% was adjusted to maintain post-filter ionized calcium between 1.0 and 1.4 mg/dl (0.25 and 0.35 mmol/l). Calcium chloride 1.5% was adjusted to maintain systemic ionized calcium between 4.0 and 5.2 mg/dl (1.0 and 1.3 mmol/l). Laboratory values, including sodium, bicarbonate, creatinine and systemic ionized calcium were followed at least every 12 h. Post-filter ionized calcium was assessed at least every 4 h. The final solution content (Prism0cal with or without discarding the 250 ml of $NaHCO_3$) and its perfusion rate were adjusted to maintain electrolytes and acid-base status within normal. **Results:** Ten patients with acute renal failure and/or severe septic shock underwent the protocol. Average duration of the protocol was 60.3 ± 22.9 h. Mean filter life was 33.5 ± 23.4 h. Mean citrate and calcium perfusion rate were respectively 174.7 ± 32.3 ml/h and 50.9 ± 13.5 ml/h. Serum electrolytes (mean ± SD) were as followed (table 1). The following complications: hyponatremia (Na < 130 mmol/l), hypocalcemia (Ca < 3.6 mg/dl) and hypercalcemia (Ca > 5.2 mg/dl) occurred only in one patient and metabolic acidosis (bicarbonate < 15 mmol/l and pH < 7.4) occurred in two patients. All complications were quickly corrected. **Conclusion:** These preliminary results suggest that the present citrate anticoagulation protocol adapted for HV-CVVH and based on commercially available solutions is safe and effective.

	Baseline	48 h	p-value
Sodium (mmol/l)	137.3 ± 3.0	136.5 ± 2.3	0.83
Bicarbonate (mmol/l)	19.6 ± 2.2	22.9 ± 1.6	0.09
Systemic ionized calcium (mg/dl)	4.10 ± 0.49	4.58 ± 0.27	0.28

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Safe and Rigorous Implementation of Pulse-HVHF in ICU (100 ml/kg/h): A Combined Medical and Nursing Approach

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Objectives: Describe all the rigorous education process performed inside the nursing and the medical team in order to make the use of Pulse-HVHF (100 ml/kg/h) a safe and rigorous technique available at any time of the day but this time Indexed to the body weight. **Background:** In the early 90, we decide to implement 100 ml/kg/h as a standard dose of Pulse-HVHF in all our patients reaching the entry criteria while being in Catecholamine Resistant Septic Shock (CRSS). For the past 10 years, we have been using Pulse-HVHF at 100 ml/kg/h regardless of the body weight using Gambro AK 10 devices. Since 2001 (after the Ronco Study), we applied 100 ml/kg/h and indexed it according to the body weight. Also, since 2001, we are performing Pulse-HVHF using Edwards Aquarius Devices. A nursing cell specially dedicated to CRRT/HVHF has been created in our unit more than 12 years ago. This cell allows us to have dedicated nurses to CRRT/HVHF in nearly every nursing shift. This is very helpful also when we do need to implement new machines or new techniques. Such a change needs a rigorous education process in the nursing cell first and than to the whole nursing team as well concerning physicians including ICU colleagues. **Setting:** General Hospital, Regional Centre of 450 beds, Interland population of 150,000 inhabitants and a medical-surgical general ICU of 15 beds having 1,000 admissions a year. The Unit is performing from 40 CRRT patients up to 50 CRRT patients per year. **Design:** Descriptive study and reported single centre experience. **Changes Made in the Daily Practice:** (1) Vascular Access: Need of a co-axial catheter of 14 french. The catheter site had to be exclusively a right internal Jugular Approach (Posterior one) with a 20 cm length and the tip of the catheter placed in the right atrium. Indeed, in order to perform 100 ml/kg/h in each patient regardless of the body weight (from 50 kg to 150 kg), we need a blood flow of 450 ml/min in order to keep the filtration fraction (FF) around and 30% but below 32%. The clothing and clogging problems are really minimized as it is a short term procedure and last for only 4 h despite a FF around 30%. The choice of the RIJ approach needs a very large consensus within all the ICU consultants and again very strict rules have to be applied. (2) Pre- and Post-Dilution Policy: According to the latest literature, we did choose 33% of pre-dilution and 66% of post-dilution. This policy allows us to prevent some clotting and some clogging by the use of a certain amount of predilution. This policy also permits us to sustain a good convection rate. Indeed, the loss of convection by the concomitant use of pre-dilutiuon reduces the risk of fouling and protein cake formation and finally preserve further loss of convection. The short term procedure obviously minimize this type of problems. (3) Pre-determination of the Exchange rate according the body weight: In order to reduce the workload at the beginning of the CRRT, we did introduce full tables which can give automatically the amount of pre- and post for a given body weight eliminating the need of sophisticated calculation that can lead to further mistakes. Additional tables do exist also regarding the adaptation of antibiotics to 100 ml/kg/h and other drugs as well. Control of prescribed dose is crucial and will need this type of table. (4) No further need of associate dialysis: During the last three years, even in very severe rhabdomyolysis cases, no need of associate dialysis was required whatever the release of potassium was. This allows us to use the Edwards-Aquarius with combined pre- and post-dilution and also to save money regarding additional cost of fluids also during Pulse-HVHF. **Conclusions:** This descriptive and reporting study is showing that the implementation of new technique as the 100 ml/kg/h Pulse-HVHF adapted to the body weight can not be decided in one day. This will need a rigorous longstanding educational process as well for the nursing staff and for the medical team. A nursing cell can be of help in order to achieve this. We will embark soon upon the implementation of citrate using the same implementation and educational process.

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Use of High-Flow Continuous Veno-Venous Hemofiltration with Citrate Anticoagulation for Maintaining Hypernatremia in a Patient with Acute Brain and Kidney Injury

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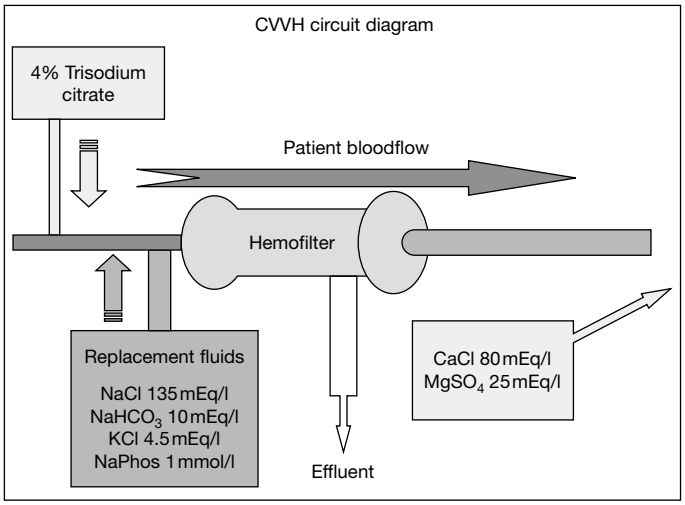
The use of high flow continuous renal replacement therapy (CRRT) for renal replacement therapy in acute kidney injury has grown in popularity. Citrate anticoagulation in CRRT has also grown in popularity given its remarkable success as a regional anticoagulant. However, utilizing citrate anticoagulation with continuous veno-venous hemofiltration (CVVH) has been less frequently described. Concerns about electrolyte abnormalities including hypernatremia have limited its use. There are increasing reports of inducing hypernatremia in the context of traumatic brain injury to acutely lower elevated intraicranial pressure (ICP). We describe an otherwise healthy 18-year-old man who presented with traumatic brain injury whose case was complicated with persistently elevated ICP's, acute respiratory distress syndrome, marked ECF expansion and acute kidney injury. CVVH was implemented utilizing regional citrate anticoagulation with the goal of inducing and maintaining hypernatremia to lower ICP. Accounting for the sodium load from the trisodium citrate, the replacement fluid was adjusted to maintain hypernatremia. Within days of CVVH initiation the patient's ICP improved, hemodynamics improved, and respiratory status also improved. The serum sodium was maintained at goal and furthermore there were no episodes of alkalosis due to the citrate metabolism. We report the first case of CVVH induced hypernatremia successfully used in acute kidney injury specifically for the correction of elevated ICP following acute traumatic brain injury.



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Treatment Efficiency Related to Filter Lifespan, Heparine Use, Education and Machine Available

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Abstract: The Intensive Care Unit at Hvidovre University Hospital is a multidisciplinary department with 7 high intensive beds. Patients primarily come from the Gastro surgical Department and the Department of Infectious Diseases. In addition to this, patients come from the Orthopedic Department, Internal Medicine, Department of Endocrinology, Department of Obstetrics and Gynecology, and the Pediatric Department. The ICU treats 70–80 patients a year with CRRT and uses 4 Edwards Aquarius dialysis machines. We have implemented a structured education plan where all nurses are taught by seniority. The following modes of dialysis are applied: CVVH and CVVHD, and, in a few cases, SCUF. Visitation of patients for treatment happens according to a fixed treatment strategy. In case of CVVH treatment, replacement fluid in the amount of 45 ml/kg is employed. In general, dialysis treatment is always started without Heparin, and filter change 1–2 times every 8 h is accepted. In case of CRRT treatment, we usually have an assembled machine ready and recirculating. An inexperienced nurse often sets up this machine with the help of a more experienced colleague, and this serves as good practice. Despite this, the ICU's expenses for CRRT treatment are decreasing. With this poster, we wish to establish filter lifespan as well as the number of efficient hours of treatment per 24 h. We believe that efficient and structured education as well as the presence of an extra-assembled dialysis machine makes the pauses in treatment short…

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Heparin-Free High Volume Venovenous Hemofiltration Treatment for Perioperative Patients of Orthotopic Liver Transplantation

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Background: Acute renal failure developing after orthotopic liver transplantation (OLTxs) requiring renal replacement usually heralds a poor prognosis. Many patients have the high risk of bleeding. We under took this study to determine whether we can improve the survival of these patients and decrease the complications of renal replacement. **Methods:** OLTxs performed between January 1999 and January 2006. 42 patients (the mean age was 47.2 years old and 5 was female) develop acute renal failure and received heparin-free high volume venovenous hemofiltration treatment. The primary disease for 42 patients was tumor for 8 and liver cirrhosis for 34. The machinery we use was ACCURA (Baxter), the hemofilter was F60 and the ultrafiltration rate was 60–80 ml/kg/h. The ratio of pre-dilution to post-dilution was 3:1. **Results:** The mean treatment time was 10.5 (1–110) days. 8 patients with tumor all died. Among the 34 patients

with liver cirrhosis 12 patients survived and all recover renal function. Among the survival patients, treatment time was 1–15 days, only one patients last 110 days. The hemofilter mean life span was 12 h (6–24). The There was no patients dying of complications of renal replacement. **Conclusions:** For acute renal failure patients after orthotopic liver OLTxs, heparin-free high volume venovenous hemofiltration can avoid the use of heparin and decrease the complications of renal replacement and can improve the survival of these patients.

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Cost-Effectiveness of Commercially Available Solutions in Continuous Veno-Venous Hemo-Diafiltration

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Continuous Veno-Venous Hemo-Diafiltration (CVVHDF) is increasingly used in critically ill patients with acute renal failure. The CVVHDF prescription should be easy to implement by pharmacy and nursing staff to avoid medical errors and to decrease preparation time. The prescription should also be cost effective and provide optimal metabolic control and solute clearance. At our center, we routinely use commercially available Prismasate (Gambro) solutions as replacement and dialysate fluids. Prior to change over, the replacement fluids (RF) were custom-made and usually included NaCl 0.9% (NS) or NaCl 0.45% (1/2NS) with 50–75 mEq of $NaHCO_3$ in one-liter bags. We collected data in 29 patients undergoing CVVHDF using the Prisma M100 set with AN69 hemofilter. The mean age of the patients was 57 +11 years (22 males, 7 females). Prismasate BGK 2/0 or BGK 4/0 was delivered as replacement fluid at a rate of 1,500 ml/h. Prismasate BGK 4/2.5 was delivered as dialysate at 500 ml/h. Calcium Chloride was administered as continuous intravenous infusion to maintain systemic ica between 4.0 and 4.5 mg/dl. Anticoagulant Citrate Dextrose Formula A (ACD-A) was initiated at 150 ml/h. The rate was adjusted to maintain post filter ica between 1 and 1.4 mg/dl. We calculated the total nursing and pharmacy time and cost to prepare and change the Prismasate (Gambro) replacement solution bags for each patient, and the total cost of purchasing the replacement fluids per patient. We compare this to the total time and cost of delivering custom-made replacement fluids for each patient. Data (mean + SD) are summarized below (table 1). Use of commercially available replacement fluids is cost-effective, and may reduce medication errors in CVVHDF. However, larger custom-made bags and on-line replacement solutions may be less expensive.

Variables	Prismasate Replacement Fluids 5 l bags	Custom-made Replacement fluids 1 l bags	p-value
Days on CVVHDF	5.76 ± 4.15	5.76 ± 4.15	
RF rate ml/h	1,508 ± 46	1,508 ± 46	
No. RF bags per Pt	40.2 ± 31.5	207.3 ± 149.2	
Cost RF fluids $	1,204.5 ± 946.7	313.0 ± 225.3	<0.0001
Pharmacy time (min)	0	4,146.2 ± 2,985.1	<0.0001
Pharmacy cost $	0	3,455.9 ± 2,488.1	<0.001
Nursing time (min)	190.2 ± 142.9	414.6 ± 298.5	<0.0001
Nursing cost $	100.8 ± 75.7	219.8 ± 158.2	
Total cost per Pt $	1,305.3 ± 1,020.6	3,988.7 ± 2,871.7	<0.0001

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Sustained Low Efficiency Dialysis (SLED) Using Regional Citrate Anticoagulation (RCA) is without Metabolic Complications

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Patients that may benefit from SLED therapy, particularly in the ICU, are at risk for bleeding. Thus, anticoagulation strategies that are safe to use via nursing staff would be of great benefit. Regional citrate anticoagulation can be complicated by citrate accumulation, metabolic alkalosis, and hypernatremia. We proposed that the modification of pre-existing RCA protocols to our increased SLED dose will not cause significant metabolic abnormalities. We used Fresenius® 2,008H or K machines for 8 h SLED treatments at a blood flow (Qb) rate of 250 ml/min and dialysate flow (Qd) rate of 300 ml/min. The circuit was anticoagulated prefilter with a 4% Sodium Citrate solution provided by Baxter© (Citrate 136 mmol/l and Sodium 408 mmol/l) and a Calcium Chloride ($CaCl_2$) infusion postfilter. Standard Bicarbonate (37 mEq/l) dialysate without Calcium was used. Every two hours a BMP, ionized circuit Calcium and ionized patient Calcium was monitored. There were 7 patients representing 36 treatments after an initial titration period. The initial protocol was titrated to maintain patients ionized Ca of 4.0–4.8 mg/dl and circuit ionized Ca levels between 0.8 and 01.6 mg/dl. The serum Sodium did not change from baseline 138.8 mEq/l to the final 139.5 mEq/l ($p = 0.52$). Serum HCO_3 did predictably increase from the baseline of 25.9 mmol/l to a final 29.7 ($p < 0.05$). Serum pH also predictably increased from a baseline of 7.33 to a final 7.39 ($p < 0.05$). The change in total serum Calcium was not statistically significant from 9.17 mg/dl to 8.73 mg/dl ($p = 0.37$). Citrate anticoagulation can be performed on our 8 h SLED therapy without metabolic complications. The infusion of 4% Sodium Citrate delivers both a higher dose of Citrate and Sodium which in our population did not cause hypernatremia, alkalosis/acidosis or citrate toxicity. An explanation for the lack of significant metabolic complications is the higher dose of dialysis used within our SLED system stabilizes the electrolytes to within a narrow normal target range. Thus, our regime requires no addition lab surveillance and becomes very easy to perform.

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Sustained Low Efficiency Dialysis (SLED) Using Regional Citrate Anticoagulation (RCA) Requires a Larger Infusion of Calcium Chloride

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Patients that may benefit from SLED therapy, particularly in the ICU, are at risk for bleeding. Thus, anticoagulation strategies that are

simple and effective would be of great benefit. We propose that modifying pre-existing RCA protocols to our increased SLED dose will provide effective anticoagulation but at a cost of increased Calcium infusions. We used Fresenius® 2,008H or K machine for 8 h SLED treatments at a blood flow (Qb) rate of 250 ml/min and dialysate flow (Qd) rate of 300 ml/min. The anticoagulant used was a 4% Sodium Citrate Baxter© solution prefilter and Calcium Chloride ($CaCl_2$) postfilter. Standard Bicarbonate (37 mEq/l) dialysate without Calcium (Ca) was used. Every two hours a BMP, ionized circuit Calcium and ionized patient Calcium was monitored. There were 7 patients representing 36 treatments after an initial titration period. The initial protocol was titrated to maintain patients ionized Ca of 4.0–4.8 mg/dl and circuit ionized Ca levels between 0.8–01.6 mg/dl. The Citrate infusion was constant throughout the treatment with a baseline 33.9 mmol/h and final at 33.5 mmol/h ($p = 0.024$). This maintained the circuit ionized calcium 2 h level at 0.82 mg/dl and final at 0.84 mg/dl ($p = 0.8$). The Ca ion infusion baseline was 38.3 mmol/h, which increased to a final 43.3 mmol/h ($p < 0.05$). The Ca infusion was able to maintain the patients ionized Ca at 4.2 mg/dl by 8 h from the baseline of 4.7 mg/dl ($p < 0.05$). No Calcium boluses were required to keep patients ionized calcium above 4.0 mg/dl. The total serum Ca baseline was 9.17 mg/dl with final 8.73 mg/dl ($p = 0.37$). Citrate anticoagulation can be performed on our 8 h SLED therapy with stable circuit and peripheral calcium levels. Thus, the initial Ca infusion should be increased as in our patients or monitoring continued during the 8 h of high clearance. We prefer the former approach. This larger dose of Ca infusion is a consequence of a higher dose of dialysis being delivered and Ca-complex removal within our system.

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Filter Patency Is Maintained Using Regional Citrate Anticoagulation (RCA) for Sustained Low Efficiency Dialysis (SLED), but at the Cost of Increased Citrate Dose

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Patients that may benefit from SLED therapy, particularly in the ICU, are at risk for bleeding. Thus, anticoagulation strategies that are safe and simple to use via nursing staff would be of great benefit. We propose modifying pre-existing RCA protocols to our increased SLED dose will provide an effective anticoagulation to the dialysis circuit. We used Fresenius® 2,008H or K machine for 8 h SLED treatments at a blood flow (Qb) rate of 250 ml/min and dialysate flow (Qd) rate of 300 ml/min. The circuit was anticoagulated with 4% Sodium Citrate solution provided by Baxter© (Citrate 136 mmol/l and Sodium 408 mmol/l) and Calcium Chloride ($CaCl_2$) infusion. Standard Bicarbonate (37 mEq/l) dialysate without Calcium was used. Every two hours a BMP, ionized circuit and patient Calcium was monitored. Overall there were 7 patients representing 36 treatments after an initial titration period. The initial protocol was titrated to maintain patients ionized Ca of 4.0–4.8 mg/dl and circuit ionized Ca levels between 0.8–01.6 mg/dl. The circuit was anticoagulated with a Citrate infusion baseline of 33.9 mmol/h and final 33.5 mmol/h ($p = 0.024$). This maintained the circuit ionized calcium 2 h level at 0.82 mg/dl and final at 0.84 mg/dl ($p = 0.8$). The circuit being anticoagulated from 0.82 to 0.84 mg/dl provided 245 h of open circuit time. Of the 36 treatment sessions 12 had the 8 h time shortened due to staffing and/or transportation needs. No treatments were shortened due to circuit clotting. Citrate anticoagulation can be performed on our 8 h SLED therapies without the filter clotting. Our regimen fully anticoagulates the circuit for at least 8 h and does so without requiring lab surveillance. However, the infusion rates of both Citrate and Ca are high. To lower the infusion rates will require more surveillance and higher risk of circuit clotting.

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Premature CVVH Hemofilter Failure: The Role of Severe Hyperlipidemia Complicating Total Parenteral Nutrition

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Despite an average filter life of over 2 days in a busy CVVH program using regional citrate anticoagulation, rare patients experience very frequent filter clotting. Two such patients were on intravenous lipids as part of their total parenteral nutrition (TPN), raising a possible causative role of severe hyperlipidemia. We investigated in depth one patient who had hypotension, multi-organ failure, anuria, and TPN treatment with Intralipid® (a fat emulsion of soy bean oil, egg phospholipids and glycerol). The CVVH therapy was started with a blood flow rate of 100 ml/min and pre-filter replacement fluid at 3 l/h using PrismaSate BGK2/0®. The post-filter blood iCa++ was <0.3 mmol/l and there was excellent catheter flow, yet the high-flux F160 polysulfone hemofilters 'clotted' every 2–3 h. The patient's blood was noted to be grossly lipemic, and triglyceride levels returned 1,700 mg/dl. The lipid solution was stopped and filter life gradually prolonged, coinciding with improved hyperlipidemia. One of the short-lived filters was studied in detail. It was sectioned and an oily substance was noted to leak out of some of the cut fibers. Light microscopy revealed that most fibers were filled with fibrin in an amorphous matrix, generally without prominent numbers of red blood cells. Many fibers contained highly unusual spherical particles of approximately 70–80 micron diameter having a similar fibrin appearance, and some were surrounded by a lucent halo. Electron microscopy of their substructure showed a typical appearance of variably sized lipid droplets and disorganized aggregates of fibrin. We hypothesize that the parenteral lipid, by a chemical and/or mechanical effect that is yet to be determined, induced fibrin deposition and plugging of the hollow fibers. This mechanism may be an unappreciated and preventable cause of premature filter failure in CRRT patients undergoing aggressive hyperalimentation.

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Removal of Water Soluble Toxins as One Mechanism of MARS at Different Secondary Dialysate Flow Rates

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MARS was recently shown to result into significant improvement of advanced stages of HE (grades 3 and 4). It is hypothesized that albumin bound cofactors (middle chain fatty acids, tryptophane, benzodiazepines etc.) are removed along with ammonia as the key factor of hepatic encephalopathy during albumin dialysis. Whereas reports are consistent about the efficacy of MARS to eliminate albumin bound toxic cofactors, reports about the efficacy of MARS to control serum ammonia levels are conflicting. **Aim:** We investigated the effect of different flow rate parameters utilizing ECAD on removal of nitric sources (ammonia and urea). **Method:** A complete model of ECAD using a MARS device was used to investigate the removal of urea and ammonia from a patient model as suggested by Cordoba et al. containing a baseline ammonia concentration of 800 μmol/l and being supplied with an ammonia dose reflecting the ammonia and urea generation rate in vivo. After passing the dialysis side of the patient's dialyzer (MARSFlux) the albumin enriched dialysate is recycled by passing a secondary dialyzer, a charcoal adsorbent and an ion exchanger. Blood and albumin flow was adjusted as reported in the MARS-HE study (250 ml/min) and 3 dialysis flow rates were used, starting at 50 ml/min (as used in continuous devices) up to the maximum of 250 ml/min. Urea and ammonia samples were taken in blood and additionally between cartridges in the albumin circuit in order to locate and quantify the mechanism of urea and ammonia removal. In parallel, the same measures were performed for Bilirubin and Bile acids as albumin bound markers. **Results:** The mechanism by which urea and ammonia are affected in ECAD is not in the adsorbents but via the secondary dialyzer. Urea and ammonia clearance was significantly affected by dialysis flow up to 200 ml/min. **Conclusion:** Maximum clearance for ammonia and urea reached by ECAD will not increase significantly by dialysis flow more than 250 ml/min but will be reduced significantly by dialysis flow below 200 ml/min. Modulating flow parameters will result into different efficacy and may impact clinical outcome.

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Solute Clearance Comparison between Diffusion and Pre-dilution Filtration Using Large Surface Area Dialyzers: In Vitro Studies

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Purpose: Continuous hemofiltration (HF) achieves maximal clearances of middle molecular weight solutes for a given volume of replacement fluid in critical care applications. We recently reported that urea and β_2-microglobulin (11.8 kDa) clearances during hemodialysis (HD) using large surface area dialyzers were comparable to solute clearances achieved using conventional equipment. The current study compares small solute (urea) and middle molecule (cystatin C, 13.3 kDa) clearances during HD with those achieved during pre-dilution HF using a large surface area dialyzer (PUREMA, 1.46 square meter, Membrana GmbH) at several replacement fluid flow rates. **Methods:** Clearances were determined for urea and cystatin C (Cys C) during purely diffusive (HD) and purely convective (pre-dilution HF) therapies from blood and effluent sampling using a bovine blood model after addition of urea and human Cys C. Blood flow rate was 250 ml/min; HD dialysate and pre-dilution HF flow rates were 2, 3 and 4 l/h. Net ultrafiltration was zero, and all experiments were repeated 5 times under each condition. **Results:** Determined mean (SEM) clearances (ml/min) for urea and Cys C are shown in the table 1. ANOVA demonstrated urea clearances were larger at higher flow rates ($p < 0.0001$) and were larger for HD than HF ($p < 0.001$). Further, Cys C clearances were larger at higher flow rates ($p < 0.005$) but not statistically different between HD and HF. Averaged together, Cys C clearances during HD were 85% of those during pre-dilution HF. **Conclusions:** At equivalent dialysate and pre-dilution HF replacement fluid flow rates, urea clearances during HD were larger than during pre-dilution HF as expected. Further, Cys C clearances during HD were comparable to those during pre-dilution HF. Middle molecule clearances during HD using large surface area dialyzers are comparable to those during pre-dilution HF.

	2 l/h	2 l/h	3 l/h	3 l/h	4 l/h	4 l/h
Modality	Urea	Cys C	Urea	Cys C	Urea	Cys C
HD	36.7 (0.7)	14.0 (0.6)	51.4 (0.5)	18.3 (3.1)	67.3 (1.4)	21.7 (2.1)
HF	30.3 (0.4)	14.2 (1.7)	40.2 (1.3)	24.6 (2.7)	50.8 (1.0)	26.2 (1.9)

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Use of Commercially Available Solutions in Continuous Veno-Venous Hemo-Diafiltration

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Continuous Veno-Venous Hemo-Diafiltration (CVVHDF) is being increasingly used in critically ill patients with acute renal failure. The CVVHDF protocol should provide optimal metabolic control, solute clearance and minimal disruption of the CVVHDF treatment. At the same time the protocol should be simple for implementation. We use commercially available Prismasate (Gambro) solutions as replacement and dialysate fluids for CVVHDF. We collected data in 29 patients undergoing CVVHDF using the Prisma M100 set with AN69 hemofilter from January to September 2006. The mean age of the patients was 57 + 11 years (range 34–76, 22 males and 7 females). Prismasate BGK 2/0 or BGK 4/0 was delivered as replacement fluid at a rate of 1,500 ml/h. Prismasate BGK 4/2.5 was delivered as dialysate at 500 ml/h. Calcium Chloride was administered as continuous intravenous infusion to maintain iCa between 4.0–4.5 mg/dl. Anticoagulant Citrate Dextrose Formula A (ACD-A, Baxter) was initiated at 150 ml/h. The rate was adjusted to maintain post filter iCa between 1–1.4 mg/dl. Data (mean + SD) are summarized below at 0 and 48 h of CVVHDF (table 1). Commercially available solutions as replacement

and dialysis fluids in CVVHDF provide adequate metabolic control. These solutions are easy to implement and may decrease medical errors.

Variables	0 h	48 h	p-value
Replacement fluids ml/h	–	1,508 ± 46	–
Serum BUN mg/dl	63.6 ± 25.7	43.3 ± 19.2	<0.001
Serum Creatinine mg/dl	3.8 ± 1.8	2.5 ± 1.2	<0.001
Serum Sodium mEq/l	139.5 ± 6.3	139.5 ± 4.0	NS
Serum Potassium mEq/l	4.7 ± 0.9	4.1 ± 0.5	<0.01
Serum Chloride mEq/l	104.0 ± 8.9	100.9 ± 5.7	<0.05
Serum Bicarbonate mEq/l	22.0 ± 5.4	26.1 ± 4.5	<0.001
Serum Anion Gap mEq/l	13.4 ± 8.5	12.3 ± 7.2	NS
Serum Phosphorus mg/dl	5.8 ± 2.0	3.8 ± 1.6	<0.001
Serum Magnesium mg/dl	2.3 ± 0.4	2.0 ± 0.2	<0.01

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The Increased Efficacy of Citrate over Heparin Catheter-Locking in Reducing Catheter Thrombosis in Hemodialysis Patients

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Heparin containing catheter-locking solutions are the most common used method to prevent clotting in hemodialysis catheters. Despite this, thrombosis of hemodialysis catheters remains a significant problem. The aim of this study was to compare the efficacy on thrombotic complications of an alternate catheter-locking solution, trisodium citrate, to the standard heparin solution. In June of 2006, the catheter locking solution was changed from 5,000 units of heparin to 4% trisodium citrate in a dialysis unit that accommodates 103 patients. The incidence of clotting related complications (tPA administrations, reduced catheters flows, and clotted accesses) was then examined in the 5 months before and after the change in the 30 patients that had hemodialysis catheters during this time period. Baseline characteristics of the dialysis patients included a mean age of 53.4 + 18 years, 50% diabetic, 53% male and 30% Caucasian, 29% Hispanic, and 24% African-American. Table 1 shows the number of patients with each of the clotting related complications. The absolute risk reduction for patients treated with trisodium citrate was 37% for tPA administration, 39% for reduced catheter flows, and 33% for clotted access. This data suggests that the use of trisodium citrate catheter-locking solution is more effective than heparin in reducing clotting related complications in hemodialysis catheters. These findings need confirmation in a prospective clinical trial.

	Heparin	Trisodium citrate
tPA administrations	27	17
Reduced catheter flows	28	17
Clotted access	4	3

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Intra-Operative (IO) Continuous Renal Replacement Therapy (CRRT) utilizing Regional Citrate Anticoagulation (RCA) during Liver Transplantation: Technical Considerations

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Liver transplant is associated with large volume shifts and metabolic changes during the course of the surgery. We have used CRRT for anuric patients undergoing liver transplantation for hypervolemia and metabolic derangements that occur during the anhepatic phase. We have evaluated the technical issues for using RCA CRRT intraoperatively (IO-CRRT) during liver transplantation. **Study Design:** Retrospective review of medical records and intraoperative charts of 27 patients who received IO-CRRT during liver transplantation from 1999 to 2006 at a tertiary care hospital. **Results:** CRRT was exclusively veno-venous hemodiafiltration. Venous access was via 12F dual lumen hemodialysis catheter inserted in femoral/internal jugular veins or tunneled permacath. Blood flow rates varied between 100 and 200 ml/min. RCA, 4% tri-sodium citrate, administered via 3-way stop cock inserted at arterial port of venous line at rates of 125–210 ml/h (16.6–27.9 mmol/h). Normal saline (NS) or saline + bicarbonate ($NAHCO_3$) was administered pre-filter at a rate of 500 ml/h. Ultrafiltration rate (UFR) was set at 1,000–2,000 ml/h. Dialysate flow was consistently 1,000 ml/h. Dialysate composition varied. Potassium (K) concentration (a) kept at a low range (2–4 mEq/l for the pre-anhepatic phase), switched to no K during the anhepatic and immediate neo-hepatic phase, then switched back to low K; or (b) kept at a constant level varying from 0–5 mEq/l; the choice to use one over the other was nephrologist dependent. NaCl and $NaHCO_3$ concentrations were varied depending on degree of pre-existing acidosis. No instances had dialysate devoid of bicarbonate. Replacement fluid was given as NS or saline + $NAHCO_3$ based on pH sliding scale. Peripheral ionized calcium was monitored on an hourly to half hourly basis. Calcium was replaced by the anesthesiologist to maintain systemic ionized calcium between 1.00 and 1.2 mmol/l (mean 1.01 + 0.19). Post-filter ionized calcium was monitored every 2–3 h, goal being <0.3 mmol/l (mean 0.37 + 0.09); citrate rate adjusted up or down in 5–10 ml/h increments to reach this goal. A dialysis nurse was present during IO-CRRT to manage citrate administration and complications with CRRT procedure in conjunction with the nephrology service. Barring two procedures where filters had to be changed, circuit patency was achieved in all the sessions ranging from 240 to 900 min. **Discussion:** RCA can be safely and effectively used for CRRT AC during liver transplantation and can provide circuit patency without complications. The procedure itself takes considerable multidisciplinary planning with the nephrology, anesthesiology, nursing, pharmacy and transplant services. A protocol driven approach with standardized orders is required and constant communication between anesthesiology and nephrology in managing the procedure particularly with respect to acid-base, electrolyte and calcium homeostasis. Availability of an adequate supply of customized dialysate with added bicarbonate is a major factor, however feasible with in-house pharmacy. Maintaining a large effluent volume to compensate for multiple rapid blood and other product administration can accommodate the large shifts in volume. Further research is required to identify the efficacy of alternate modes of CRRT including hemofiltration using citrate anticoagulation.

CRRT Research

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Clinical Research of Prevention and Cure of Hypophosphatemia During Continuous Venovenous Hemofiltration

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Objective: To approach and investigate the prevention and cure of hypophosphatemia for critically ill patients during continuous renal replacement therapy. **Methods:** Thirty critically ill patients enrolled in our study were divided into two groups according to APACHE II score, (thirteen patients whose score were less than fifteen were A group, seventeen patients whose score were more than fifteen were B group). The mode of CVVH were used in two groups. The rate of replacement fluid in A group is 2,000 ml/h and 4,000 ml/h in B group, Therapy time were eight to twelve hours every day. A group patients were supplemented to 10–20 ml/day glycophos, while B group were 30–40 ml/day glycophos. The level of securm phosphorus and APACHE II score were tested before treatment and at twenty-fourth hour, forty-eighth hour, seventy-second hour during therapy. The correlate analysis between serum phosphorus and APACHE II score were performed and the clearance of phosphorus were figured. **Results:** The clearance of phosphorus of B group is larger than that of A group [(42.76 ± 2.39) vs. (23.84 ± 3.05), $p < 0.05$] before therapy. The level of securm phosphorus of B group was lower than that of A group [(0.78 ± 0.19) vs. (1.25 ± 0.27), $p < 0.05$]. At twenty-forth hour, the level of securm phosphorus of the two groups were decreased. After adding to glycophos, the level of securm phosphorus of a group were normal and that of B group were slight hypophosphatemia. After adjusting the dose of glycophos, the level of securm phosphorus of B group were normal at seventy-second hour. APACHE II score in the two groups had the tread of decrease after CVVH. Serum phosphorus and APACHE II score had direct correlation. **Conclusions:** Hypophosphatemia often occur in critically ill patients and have direct correlation with severity of illness, while CVVH aggravate hypophosphatemia. So the supplement of phosphorus are individualization and not adhere to the routine dose, meanwhile the level of securm phosphorus should be monitoried closely to adjust the dose of glycophos.

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Outcome of Acute Renal Failure in Those Needing Continuous Renal Replacement Therapy

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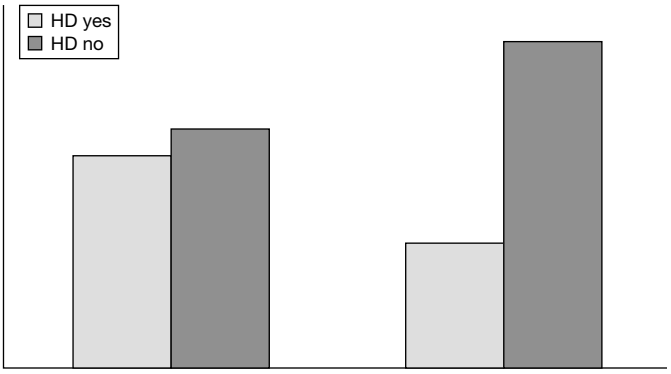
Outcome of ARF and use of CRRT, in studies, have shown a consistent higher mortality. We reviewed ARF outcome and the use of CRRT at our institute. **Aims:** (1) To evaluate the short-term (ICU discharge to with in 30 days) patient survival. (2) To evaluate dialysis free survival (from ICU discharge to last follow up). (3) To evaluate risk factors associated with overall survival and the continued need for intermittent dialysis. **Hypothesis:** Outcome of ARF needing CRRT at our center follows the national trend. **Data Source:** Froedtert Medical and Lutheran Hospital (FMLH) data. **Primary Endpoint:** Death during hospitalization. **Secondary Endpoint:** Hemodialysis (HD) dependant after discharge. **Material and Methods:** We identified adults (>18 years), with ARF needing CRRT, treated in the critical care units of FMLH from 1st January 2003 till 31st December 2005. Patients were divided into dead and alive. Survivors were analyzed depending on their continued need for intermittent dialysis. CRRT was performed with a 21 replacement fluid exchanges/hour, heparin was used when not contraindicated. Data was analyzed by using chi-square and t-test, non-parametric tests were utilized when necessary. **Results:** A total of 86 patients with ARF received CRRT. Over all mortality was 63%. Patients who received CRRT for ARF and survived, 47% needed IHD on dc from ICU and 28% continued to need HD on last follow-up (6 months–1 year). **Conclusion:** Patients with ARF needing CRRT have a high mortality. Significant percentage of patients remained dialysis dependant on last follow-up.

	Dead	Alive	p-value
Total #86	54	32	
Male	25	23	
Female	29	9	0.04
White/Non-white	40/14	21/11	0.049
Mean age @ CRRT start	56	60	0.57
Mean Cr @ CRRT start	33	39	0.16
Days on CRRT	5.1	5.3	0.18
Days in hospital	17.5	29	0.003



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The Therapeutic Effect of High Volume Hemofililtrition in Severe Acute Pancreatitis

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Objects: To observe the therapeutic effect and to investigate the mechanisms of high volume hemofililtrition (HVHF) in the assistant to aid the severe acute pancreatitis (SAP). **Methods:** 31 patients with SAP were included. These patients were divided into two groups: group 1 (group of accepting the conventional therapy) and group 2 (accepting the combined therapy which adding HVHF on the basic of the conventional therapy). Blood flow range from 200 to 250 ml/min, exchange fluid flow range from 60 to 65 ml/min. All the patients used AN69 and changed every 12 h. The therapeutic time 72–168 h. To comparing the achievement ratio of salvaging and the adverse effect. To observe the diversity of the clinical symptom and the indicator of acute Physiology between pretherapy and posttherapy. Simultaneously observing the changes in biochemical indicator and arterial blood gas analysis and inflammatory factor and the indicator of the acute physiology and chronic health evaluation II (APACHE II). **Results:** 14/16 patients were recovery in group 2, 10/15 patients were recovery in group 1. The survival rate was (87.5%) in group 2 vs. in group 1 (66.7%). Comparing with the conventional therapy, the clinical symptom, the APACHE, the ALT (alanine aminotransferase), the serum total bilirubin, the serum creatinine, the blood urea nitrogen, the TNF-α (tumor necrosis factor-α) and the interleukin-6 were well improved ($p < 0.05$). Simultaneously the acidosis and the hypoxemia also got well rectification. The adverse effect in the two groups have no obviously difference ($p > 0.05$). **Conclusions:** The combined therapy can improve the survival rate and ameliorate the pathogenetic condition of the SAP patients. The mechanism possibly is blocking the inflammatory reaction and clearing the mediators of inflammation such as TNF-α and interleukin-6.

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The Effect of Artificial Liver on Serum Cytokines in Pig Model of Fulminant Hepatic Failure

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Objective: Artificial liver is a technique, which have gained great progress in the past few years. Yet there is great difficulty in evaluating it objectively. Therefore we established animal model of fulminant hepatic failure to investigate the effect of plasma exchange combined with continuous hemofiltration on the dynamic change of serum cytokine through the determination of the variant of cytokines in the treatment group and control group. And then to evaluate the effectiveness, possible mechanism and optimal treatment intervals of artificial liver. **Methods:** Eleven minipigs were divided into two groups at random: control group ($n = 5$) and treatment group ($n = 6$). And another five minipigs are selected to provide the normal plasma needed for plasma exchange. All of the control group and treatment group animals were induced fulminant hepatic failure with administration of D-galactosamine (dosage, 1.2 g/kg) through the intubation remained in external jugular vein. 24 h and 48 h later the treatment group was given plasma exchange combined with hemofiltration. The volume of plasma exchanged was the 1.3 fold of plasma volume of the animal itself. Continuous hemofiltration was performed shortly after the plasma exchange with the volume of 8,000–10,000 ml. The control group was not given the treatment of artificial liver. Clinical data were recorded and blood was drawn at definite intervals for laboratory determinations after centrifugalization. Liver tissues were sampled for pathological examination. To compare the difference of survival time, improvement in manifestation, pathological and biochemical parameters, serum cytokines and tissue pathology between the two groups, t-test is performed. **Results:** After the artificial liver therapy, the treatment group's manifestation was improved obviously and its mean survival time was 116.4 ± 10.7 h, which was much longer than the control group (73.5 ± 11.8 h, $p < 0.05$). Compared with the control group, there were significant differences in cytokines, biochemical parameters and histological manifestation. **Conclusion:** Early and enough plasma exchange combined with continuous hemofiltration can efficiently affect the dynamic change of cytokines, prolong the mean survival time of the animals, improve biochemical parameters, histological manifestation and prognosis in the near future and then earns time for liver regeneration or liver transplantation.

Future Trends

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Establishment of a Community-Wide Continuous Renal Replacement Therapy Center of Excellence Program: A Team Approach using Data Collection

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Background: Approximately one-thousand fourteen dialysis treatments a month are performed which include apheresis, continuous renal replacement therapy, hemodialysis, and peritoneal dialysis. On average, seventy continuous renal replacement therapies are initiated and maintained a month. The program services seven hospitals, four in which continuous renal replacement therapies are prescribed in eleven intensive care units by a group of eleven physicians. **Purpose:** To improve patient outcomes with continuous renal replacement therapy through identifying best practices and best practices in our community. **Methods:** Initial data collection on the use and problems encountered in four hospitals lead to the design of a strategic plan to identify best practices. The strategic plan included developing relationships with all the disciplines involved in the care of the patient on continuous renal replacement therapy. This included nephrologists, surgeons, intensive care staff, and nephrology nursing staff. The bottom line of these discussions was that fundamental education was needed in each group. Communication was the true basis of continuous renal replacement therapy failures. Traditional classroom instruction was initiated, however, this education was only successful if reinforced one to one at the bedside. Also, giving monthly feedback on best practices and statistics to all involved has improved outcomes. **Summary:** Implementation of this strategic plan has allowed the establishment of a community-wide continuous renal replacement therapy program. Therapies averaged six to eight hours prior to the strategic plan. Therapies now average thirty-five to forty-seven hours post intervention with overall increased therapy system patency and a decrease in anticoagulation use by eighty-five percent.

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Nursing Education and Competency Verification for CRRT

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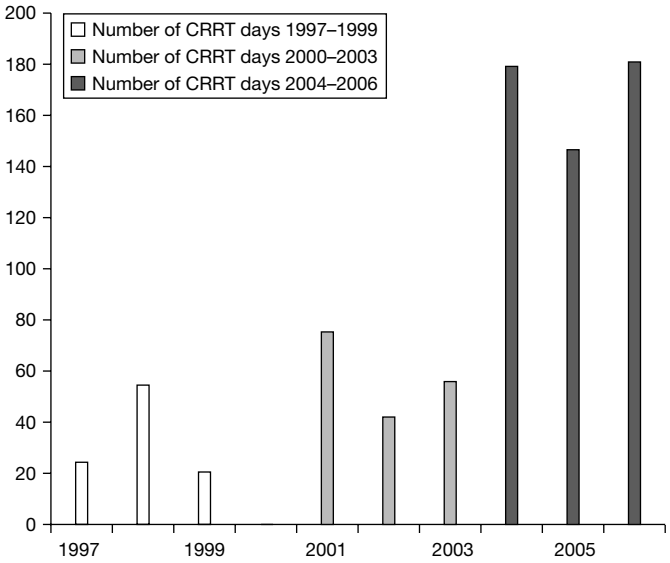
ICU, St. Jude Children's Research Hospital, Memphis, Tenn., USA

St. Jude Children's Research Hospital is a 60 bed facility specializing in the treatment of pediatric hematology/oncology patients. The facility houses an 8 bed pediatric intensive care/step down unit. From January 2004 to November 2006, the pediatric intensive care unit performed 507 days of continuous renal replacement therapy on 32 patients. Of the 32 patients 70% were stem cell transplant patients. Our service is unique in that renal replacement therapy is managed by the pediatric intensivist and performed by the intensive care nurse. Continuous renal replacement therapy education is part of the Critical Care Curriculum and offered bi-yearly. Each nurse is required to attend the Critical Care Course. On day 5 of the Critical Care Course, CRRT is covered. The topics are: CRRT and the different modes of therapy, machine dynamics, basics of CVVHD (our primary therapy), use of citrate as anticoagulation, troubleshooting, and documentation. The course consists of lecture, on line education, care mapping and literature review. The competency verification program at St. Jude consists of staff nurses yearly identifying new, changing, or problematic issues. The competencies that are chosen fall into one of three categories, technical, interpersonal or critical thinking. The CRRT/hemofiltration process, because it is complex and a high risk treatment, is chosen each year as a competency. It would be considered in the technical and critical thinking categories of the competency program. As a chosen competency, this requires the nurse to perform the elements of the competency either in a simulated setting (CRRT class) or in observation of daily work. The process of understanding CRRT, setting up and running the machine, and documenting hemofiltration is very complex. Education is key in minimizing problems with this process. By requiring each ICU nurse to attend the CRRT course and offering the course as a refresher for the ICU nurses and by evaluating yearly competencies, the ICU at St. Jude Children's Research Hospital is able to successfully offer this therapy. This poster presentation will illustrate the educational process and competency verification for nurses working in the intensive care unit.



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A Study of Bilirubin Kinetics During the Molecular Adsorbent Recirculating System Therapies

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Introduction: This study observed the kinetics of bilirubin in serum and albumin dialysate during molecular adsorbent recirculating system (MARS) therapies, and aimed to find the possible factors affecting the removal of bilirubin by MARS therapy. **Methodology:** Five patients received total 10 treatments of MARS due to hyperbilirubinemia, in which 60 ml of 20% human albumin was used as circulating dialysate and regenerated by two adsorbents columns built-in the circuit. At the 0, 3rd, 6th and 8th hour (the end) of MARS therapy, the concentration of total, direct, indirect bilirubin (TB, DB, IDB) and albumin in serum and albumin dialysate were measured. Besides standard MARS therapy, a modified treatment was performed in one patient, in which the two adsorbents columns were bypassed in the first 4-hour term, until in the second 4-hour term, they were then connected into the circuit and standard MARS was performed. **Results:** The reduction rate of TB, DB and IDB was 26.6 ± 9.0%, 29.5 ± 9.6% and 14.8 ± 12.3%, respectively. The concentration of bilirubin in albumin dialysate was between 21.6–22.5 μmol/l. Albumin concentration in albumin dialysate reduced by 34.6 ± 16.6% after treatments (table 1). The molar ratio of TB to albumin in serum and dialysate varied during MARS, and existed great gaps at the end of the treatments. For the modified treatment, during the first 4 h, in which only albumin dialysis was performed, the TB concentration, molar ratio of TB to albumin in albumin dialysate elevated markedly (table 2), and the latter increased from 0.03 to 0.15, comparable with the value in serum (0.26). During the second 4 h, which standard MARS was performed, the TB concentration and molar ratio decreased rapidly. **Conclusion:** The removal of bilirubin by MARS is not satisfying and may be due to that the MARSflux filter can not effectively transfer the bilirubin from the blood to the albumin dialysate. The reduction of albumin concentration in dialysate during treatment is obvious and possible due to the adsorption onto or blocked in the adsorbent columns.

Table 2. One patient switched from albumin dialysis to MARS

	Albumin dialysis only			MARS	
	5 min	2 h	4 h	6 h	8 h
serum TB (μmol/l)	162.1	131.8	124.7	117.5	108.4
TB in albumin dialysate	42.8	134.8	195.8	36	31.6
molar ratio (TB/albumin) in serum	0.38	0.29	0.26	0.25	0.22
molar ratio (TB/albumin) in dialysate	0.03	0.1	0.15	0.03	0.03

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Dose Predictions for Combined Treatment of Hemofiltration with Hemodialysis

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HD therapy is used to treat chronic renal failure (CRF). Several decades of clinical experience has indicated that HD therapy three-times-weekly has sufficient efficacy to remove small molecules such as urea and creatinine. However, according to recent reports, the quality of life of a CRF patient treated with HD is still poor and their mortality rate is quite high. HF therapy, which was first introduced in the mid 70s, is based on the convective principle and has been suggested as an alternative to HD. However, its high cost and complex equipment were the main obstacles to making HF an alternative treatment to CRF, and HF was developed into continuous renal replacement treatment for treating acute renal failure (ARF) in intensive care units (ICU). A combined treatment (CT) of HF several-times-weekly with HD weekly was suggested to combine the diffusive and convective efficacies. Various CT modalities were mathematically modeled and calculated in order to compare the adequacy in removing small and middle molecules to those of other renal treatments. The corrected equivalent renal clearance (EKRc) and standard Kt/V (std Kt/V) were used as dose measuring parameters for comparing the efficacy with respect to the different molecular sizes. The CT, achieving a weekly total exchange volume of 160% of the total body water, can reduce the frequency of sessions and the volume of replacement fluid compared with daily HF (DHF), and provide satisfactory treatment efficiency for patients with CRF.

Table 1. Decrease of total, direct and indirect bilirubin (TB, DB, IDB) during MARS (n = 10) (for Abstract 50)

	0 h	3 h	6 h	8 h	Reduction (%)
Serum TB (μmol/l)	237.8 ± 69.2	203.5 ± 69.2	185.5 ± 64.1	171.3 ± 64.0	26.6 ± 9.0
Serum DB (μmol/l)	190.9 ± 51.8	157.3 ± 53.9	141.2 ± 51.5	128.0 ± 46.8	29.5 ± 9.6
Serum IDB (μmol/l)	46.9 ± 19.2	42.3 ± 21.5	44.2 ± 18.1	44.28 ± 17.3	14.8 ± 12.3
TB in dialysate (μmol/l)	0	21.6 ± 10.3	21.5 ± 13.6	22.5 ± 16.2	–
Albumin in dialysate (g/l)	132.0 ± 41.8	101.8 ± 27.5	93.1 ± 31.0	84.7 ± 33.68	34.6 ± 16.6

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Access for Wrist and Forearm Wearable Artificial Kidney, Pancreas and Liver

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Purpose: Purpose of this study is to propose for discussion: That with no more than prophylactic anticoagulation of the patient resulting from full anticoagulation of the extracorporeal blood circuit, wrist and forearm wearable CRRT could become a safe, effective, chronic therapy. **Methods:** Methods used by us in the 1970s consisted of treating large plastic trash container 'artificial patients' with either conventional intermittent REDY dialysis, or with miniaturized dialyzers and miniature adsorbents cartridges, continuously, 24/7. **Summary of the Results:** The 'square meter-hour hypothesis' was validated. We therefore propose a new safe patient powered device that can access either conventional 'Arteriovenous Fistula Grafts' or a slight modification of the popular 'Direct Arteriovenous Fistula'– the 'In Situ DeBranched Vein Fistula Graft' or Vein Fistula Graft (VFG). Applying alternating (to avoid necrosis) compressions over either 'graft' exposes the A/V pressure differential, which is utilized to drive precisely regulated flows of blood through the dialyzer. It also adds proportional anticoagulant to the extracorporeal blood flow and drives commensurate dialysate, countercurrent, around its circuit. Small cannulae, sufficient for generous 20–30 ml/min blood flows, promise a plenitude of dialysance. These small cannulae, as well as preservation of adventitial vasa vasorum, lymphatics and any indigenous nerves, promise relative freedom from leaks, infection, clotting and embolization. Irritants that stimulate anastomotic scarring and narrowing are also reduced. The device consists of a twice weekly replaceable radiofrequency sealed blood contacting disposable wrapped around the forearm with VELCRO, disposable adsorbent cartridges easily exchangeable under the shirt cuff, a rechargeable 9V battery principally for timing and valving and a cigarette pack sized blood regulating and dialysate pumping and anticoagulant and CaMg infusing mechanism, all located on the dorsum of the wrist and forearm. Either the battery or a small CO_2 cylinder (or the A/V differential) may be utilized to power the volar graft compressors. A glucose-insulin feedback loop can exquisitely and renewably provide control of blood sugar. Membrane limited cross circulation with a canine might provide economical chronic liver support. **Conclusion Reached:** We propose a practical VFG blood access system and wearable artificial kidney, pancreas and liver etc. that could benefit millions of patients.

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The Use of Xigris in Prolongation of Continuous Renal Replacement Therapy (CRRT) Filter Life

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The use of anticoagulation in CRRT has always encountered many obstacles, each dependent on the technique utilized. Heparinization can lead to bleeding diathesis while regional anticoagulation can result in acid – base disorders and electrolyte imbalances. Thus, limiting the availabilty of this practice in certain patient populations. One of these populations at high risk for complications is that of the severe sepsis patient, especially those with coagulopathies. In our Intensive Care Unit (ICU) we studied twenty-two (22) severe sepsis patients receiving Xigris and initiated on CRRT. Our hypothesis stated that there was no need for implementation of anticoagulation as Xigris would allow prolongation of filter life without the complications of heparin or regional anticoagulation. Patients were followed for the duration of Xigris therapy or up to 96 h. Xigris was continued until markers of severe sepsis corrected or 96 h. Laboratory results; including lactate, c-reactive protein and platelet count, as well as clinical indications for abnormal bleeding were recorded on all patients. Seventeen of the twenty-two patients survived their episode of severe sepsis, and there were no complications from the use of Xigris. All CRRT filters endured for the Xigris duration. There were no abnormalities in coagulation, acid – base or electrolyte measurements. Based on this observation, it is felt that patients with severe sepsis, treated with Xigris and in need of CRRT can be safely treated without anticoagulation and the need for repeated filter changes.

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Blood Purification

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ASN's 39th Annual Renal Week Meeting

Filename: 553356

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Abstract Category: 708.ESRD Treatment Comparison: Clinical Outcomes And Trials

Entities that provided funding for this abstract:
Pharmaceutical Company Support
Clinical Revenue Support

Keywords:
Heparin; Anticoagulation; Beta-2 Microglobulin

Title: Fifty-five Percent Heparin Reduction is Safe with Citrate Dialysate in Chronic Dialysis Patients

Robert J Kossmann, MD[1], Robin Callan, LLM[2] and Suhail Ahmad, MD[3]. [1]Nephrology, Nephrophiles, Santa Fe, New Mexico, United States; [2]Renal, Advanced Renal Technologies, Bellevue, WA, United States and [3]Nephrology/Medicine, University of Washington, Seattle, WA, United States.

Citrate containing dialysate (CD) has been reported to have anticoagulation effect (Tu et

al, D T, 29:620, 2000). Systemic heperinizaton during hemodialysis (HD) is associated with multiple risks including bleeding complications. The purpose of the study was to determine whether heparin can be safely reduced in chronic HD patients using CD. Thirty-one patients from 3 New Mexico FMC dialysis units were identified as having prolonged (>15 minutes) bleeding from needle sites at the end of dialysis when using regular dialysate. These patients were switched to CD and 2 months later their

heparin dose was reduced from an average of 4758 ± 2179 (mean ± SD) units to 3165 ± 1352 units, a 33.5% reduction for a 2 month period (1st reduction). After 2 months the heparin dose was further reduced to 2158 ± 1362 units, another 32% reduction (2nd reduction), a total 55% reduction from the baseline. After the 2nd reduction patients were followed for another 3 months. Single use dialyzers (Optiflux NR160 or NR180) were used and the duration of dialysis, blood and dialysate flow remained unchanged.

After switching the patients to CD and reducing their heparin dose, prolonged bleeding reduced with no reported instances of bleeding.

Throughout the heparin reduction periods the dialyzer and blood tubing remained free of clots. After a total 55% reduction in heparin the Kt/V did not decrease, in fact it increased, as shown in the Table.

Despite a 55% reduction in heparin pre-dialysis Beta-2 microglobulin levels were lower during the CD, Pre CD 26.1 Vs 2nd reduction 24.0, p=0.08.

The use of citrate dialysate along with a 55% reduction in heparin was successful in decreasing the episodes of prolonged bleeding, was not associated with clotting of the system and an adequate dose of dialysis was maintained.

Kt/V values, mean (SD), during regular and citrate dialysate before and during heparin reductions

Pre CD	1.51 (0.21)
Baseline CD	1.55 (0.18)
1st Reduction	1.59 (0.18)
2nd Reduction	1.60 (0.16)*

*p=0.05 Pre CD Vs 2nd Reduction

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Member Number: 008260
Abstract Category: 708.ESRD Treatment Comparison: Clinical Outcomes And Trials
Entities that provided funding for this abstract:
Pharmaceutical Company Support
Clinical Revenue Support
Keywords:
Dialysis Adequacy; Beta-2 Microglobulin; Dialysate
Title: Increased Dialysis Dose and Decreased Concentration of Beta-2 Microglobulin with Citrate Dialysate

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Increase in Kt/V was earlier reported with citrate dialysate in 22 patients using reprocessed dialyzers (Ahmad et al, AJKD, 35:493, 2000). The purpose of the present prospective study was to evaluate the effect of citrate dialysate (CD) on Kt/V in a larger number of patients (n=142), on single use dialyzers (Optiflux 180NR and 160NR) and over a longer period (6 months). The Kt/V was compared on regular

non-citrate (NCD) dialysate for 6 months (Naturalyte and Granuflo) with

CD (Citrasate) for following 6 months. During the study the dialyzers and dialysis treatment remained unchanged. Patients, 60 F and 82 M, were 63 +/- 14 years old (mean $\pm$ SD) and had been on dialysis for 35 $\pm$ 29 months.

As shown in Figure 1 the Kt/V increased significantly during the CD use compared to NCD (1.57 $\pm$ .20 Vs 1.51 $\pm$ .20, Mean $\pm$ SD, CD Vs NCD respectively, $p < 0.0001$). Over the 6 months of CD use there was a decline in predialysis beta-2 microglobulin concentration (28.1 to 25.9, $p=0.0001$). Kt/V in 19 patients was one SD below the population average on NCD. The Kt/V in this group was 1.19 $\pm$ 0.12 on NCD and on CD it increased to 1.34 $\pm$ 0.16 ($p<0.0001$). The remaining 123 patients the Kt/V values were 1.55 and 1.60 on NCD and CD respectively ($p<0.0001$).

The Kt/V remained unchanged during the 6 months on NCD. The switch to CD was associated with increase in Kt/V, apparent in the first 3 month of CD. The increase in the dose was larger in those patients who had lower Kt/V before the switch.

This study suggests that the anticoagulation effect of citrate keeps the dialyzer fibers and pores open and is responsible for the increased removal of urea and beta-2 microglobulin.

Heparin free citrate dialysis in end stage liver disease (esld) patients is well tolerated.

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Background: Heparin cannot be used for hemodialysis (HD) in patients at high risk of bleeding, but heparin free dialysis is often associated with clotting, leading to early termination. Citrate- containing dialysate (CD) (Citrasate®, Advanced Renal Technologies, Bellevue, WA, USA) has been successfully used for dialysis without heparin in many acutely ill patients. CD differs from standard dialysate only in containing 2.4 mEq/l citrate and 0.4 mEq/l acetate in the final dialysate. Since citrate is mainly metabolized in liver, the use of citrate is generally considered inadvisable in the presence of liver failure. At our institution, acutely ill ESLD patients with renal failure require dialysis either in the intensive care unit or in the operating room during liver transplantation surgery. CD has routinely been used in these acutely ill patients in both settings.

Objectives: To study the safety and efficacy of CD in acutely ill patients with fulminant liver failure

Methods: We retrospectively analyzed the data in our five most recent patients with ESLD who used CD for their heparin-free HD. Three males and 2 females with average age of 57.8 years (range 32-68) used CD for 22 HD sessions (mean 4.4 treatments/patient), blood bilirubin 12.2 +/- 10.8 mg/dl. The length of dialysis ranged 3 to 6 hours (mean 4.12 hrs). Blood and dialysate flow ranged 200-400 (mean 288) and 300-500 (mean 468) ml/min, respectively.

Results: All treatments were well tolerated without any dialysis related complications including one 6hr session conducted during liver transplant surgery in the OR. No treatment was terminated due to clotting or increased bleeding. The pre- and post–dialysis blood values are given below:

Values	Mean (SD)	
IonizedCa		mmol/l
Mg		mEq/l
Na		mEq/l
Bicarb		mEq/l
Anion Gap		mEq/l
BUN		mg/dl

Predialysis	Postdialysis	p Value
1.12 (0.09)	1.12 (0.05)	0.8
1.93 (0.34)	1.83 (0.25)	0.8
133.7 (3.3)	133.7 (2.8)	0.4
23.5 (2.8)	25.4 (1.9)	0.02
13.3 (4)	12.4 (3)	0.04
50.5 (24)	32.4 (18)	0.0000

Ionized Ca and magnesium declined but remained in the normal range. CD was not associated with hypernatremia or increase in anion gap. Thus there was no evidence of accumulation of citrate in these patients, probably because of the low citrate concentration coupled with citrate metabolism in the muscles. Significant increase in bicarbonate and decrease in blood urea nitrogen (BUN) was as expected with HD. In our experience CD is well tolerated in patients with advanced liver failure and bleeding risk and resolves the dilemma of anticoagulation in these patients.

Keywords: haemodialysis: anticoagulation, haemodialysis: adequacy, haemodialysis: complications, haemodialysis: technique

Title: HEPARIN REDUCTION WITH CITRATE DIALYSATE

Suhail Ahmad[1], Robin Callan[2] and Robert Kossmann[3]. [1]Nephrology, Medicine, University of Washington, Seattle, WA, United States; [2]Advanced Renal Technologies, Bellevue, Washington, United States and [3]Nephrophiles, LLC, Santa Fe, New Mexico, United States.

INTRODUCTION AND AIMS: Systemic heparinization during hemodialysis (HD) is associated with significant clinical problems. Some patients despite receiving relatively small dose of heparin have constant oozing around the needles during the treatment and/or continue to bleed for a long time after the needles are removed. Citrate containing bicarbonate dialysate (Citrasate®, Advanced Renal Technologies, Bellevue, WA, USA) has been reported to have some anticoagulation properties. Regular bicarbonate dialysate contains acetic acid as acidifying agent (AD) whereas Citrasate contains citric acid with known anticoagulant properties. The Aim of the study was to determine whether the use of citrate dialysate (CD) would permit a 30% reduction in heparin dose without increasing the risk of clotting of the dialyzer and dialysis set up and a decrease in the dialysis dose.

METHODS: Twenty chronic HD patients (11 females) from Fresenius Medical Care Santa Fe Dialysis Center, Santa Fe, NM, USA were identified to have excessive bleeding problems. These patients took more than 15 minutes to stop bleeding after the needles were removed and two patients also developed sub-conjunctival hemorrhage in addition to prolonged bleeding. They were switched from AD to CD and their heparin dose was reduced by an average of 30%. The AD contained either 4 mEq/l acetate (19 patients) or 8 mEq/l acetate (1 patient). CD contains 2.4 mEq/l citrate and 0.3 mEq/l acetate. The clotting assessed by the examination of the dialyzer and the set up. The dialyzer clotting was further measured by the urea reduction during the treatment and is expressed as Kt/Vurea. The data for two months on AD is compared with data for two months on CD.

RESULTS: The reduction in the heparin dose averaged 30% from 4275 $\pm$ 1758 (mean $\pm$ SD) during AD to 2970 $\pm$ 1322 units/treatment during CD. No clotting of dialysis set up was noted on reduced heparin and CD treatments. The Kt/V for the two months on AD and usual heparin were 1.61 $\pm$ .15 and 1.62 $\pm$ .15, this remained unchanged during the two months on 30% less heparin on CD, 1.62 $\pm$ .19 and 1.59 $\pm$ .17, all p values ns. With a 30% reduction in the heparin dose bleeding episodes decreased.

CONCLUSIONS: The use of CD permitted a significant reduction in heparin without any increase in clotting during the treatment, and without any decrease in the dose of dialysis as determined by Kt/Vurea. Based on these results a larger reduction in heparin dose will be studied.

Acknowledgement: The study was supported by Fresenius Medical Care, NA.

Slow, Low, Efficient, Daily Dialysis (SLEDD) in the Critically Ill Patient

By Pat Isaacs, MSN, CS, CNN, NP

April 24, 2006

Slow, low, efficient, daily dialysis (SLEDD) is a form of renal replacement therapy for the critical care setting.

The slow continuous removal of solute and water tends to offer greater hemodynamic stability than a conventional hemodialysis treatment. SLEDD is a newer technique of renal replacement therapy that utilizes conventional hemodialysis equipment, but with similar therapeutic goals as Continuous Renal Replacement Therapy (CRRT).

SLEDD techniques combine the advantages of CRRT and Intermittent Hemodialysis (IHD) by using conventional hemodialysis machines with blood flow rated (BFR) between 50-200 and dialysate flow rates (DSF) of 200-400. Dialysis time varies anywhere from 6 to 12 hours or can be done continuously. The possible variations and adaptations of blood flow, hemofiltration rate and duration of dialysis time as a function of needs of the patient are practically unlimited, which makes SLEDD applicable to the critically ill patient. Clinical trials comparing SLEDD to CRRT have failed to demonstrate a survival difference when adjusting for disease severity. The benefit is in being able to use one type of machine for any renal replacement therapy, instead of one machine for hemodialysis and a different machine for CRRT.

Several economic evaluations have shown SLEDD to be less expensive than CRRT. The main source of savings is in conventional dialysis supplies, versus CRRT equipment supplies, i.e. bloodlines, kidneys and dialysate, versus industrially produced sterile substitution fluid. A hospital did a cost analysis of a CRRT treatment for an episode of acute renal failure, lasting an average of 9.3 days with a replacement of the extracorporeal circuit every 2.5 days. The cost of consumables (hemofilter, blood and fluid lines and replacement fluid) per episode (9.3 days) of acute renal failure was $1,614. The replacement fluid alone cost $880.00. The equivalent cost for treatment with conventional dialysis machines was $672.00, assuming 10 daily treatments.

In CRRT, when unable to use heparin, regional citrate (RC) used to be the anticoagulant of choice. Citrate acts as an anticoagulant by binding the calcium. RC anticoagulation requires the infusion of citrate into the arterial line. RC is costly, the set-up is complex and it requires additional staff involvement. Calcium needs to be replaced via the venous line and ionized calciums need to be closely followed. With prolonged RC infusion, metabolic alkalosis and hypocalcaemia have been reposted.

Citrasate®, a new acid bath/concentrate, matches very well with SLEDD as the renal replacement therapy of choice for the critically ill patient. Citrasate® contains a small amount of citrate, which anti-coagulates the extracorporeal circuit. Citrasate® causes no significant decline in calcium or magnesium. The half-life of citrate is very short, which allows it to be quickly metabolized by the liver. Citrasate® has also been successfully used on liver transplant patients with no metabolization problems. Citrasate® can provide a better dialysis treatment, reduced blood loss and a reduction in acidosis.

The use of Citrasate® in SLEDD or conventional hemodialysis treatments is an excellent alternative for an anticoagulant when heparin cannot be utilized; i.e. heparin-induced thrombocytopenia (HIT), bleeding risks, trauma and impending/post surgery procedures.

In summary, SLEDD is an increasingly utilized renal replacement therapy that facilitates efficient detoxification and has a favorable cardio-vascular tolerability profile for the critically ill patient. The technically simple, conventional, hemodialysis equipment is easier to operate, supplies are less expensive and one has more flexibility in planning patient therapies.

ALTERNATIVES TO HEPARIN ANTICOAGULATION DURING SLOW EXTENDED DAILY DIALYSIS IN THE ICU

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Renal Services Program, University of California Davis Medical Center, Sacramento, CA, U.S.A.

BACKGROUND

- Slow Extended Daily Dialysis (SLEDD) is a well tolerated method of Renal Replacement Therapy in ICU patients
- Concern exists about the amount of heparin that is used to maintain the dialysis circuit in most critically ill patients. This is particularly true when a patient has antibodies to heparin.
- Alternative methods utilized to perform dialysis in these situations include, frequent saline flushes, citrate based dialysate (Citrasate®), and regional citrate anticoagulation
- *In this report, we review our experience with alternatives to heparin-based anticoagulation during SLEDD treatments among the critically ill admitted to UC Davis Medical Center*

METHODS

- Patients receiving SLEDD in the Intensive Care Units, 2005-2006.
- For inclusion, patients were = 18 years, on no systemic anticoagulation, and on SLEDD without heparin use.
- Alternatives to heparin included:
  1. ***Saline flushes*** with 200 cc at least every hour
  2. ***Citrasate®:*** (2.5meq/L) citrate-based dialysate
  3. ***Regional citrate: ACD-A*** (0.113 mol/L) & Calcium gluconate (40mg/ml)
- Clotting was defined as early discontinuation of dialysis, greater than 30 minutes prior to prescribed time because of circuit clotting in lines, chambers, or dialyzer.
- Data was abstracted by chart review and groups were compared using Chi-Square, T-test and ANOVA

Slow Extended Daily Dialysis Technique

SLEDD Prescription: 6-8 hours, Qb=200 ml/min, Qd=400 ml/min, with either standard acid dialysate or Citrasate® 30 brand dialysate.

ACD-A Protocol: Goals - pt's $_{i}Ca^{2+}$ [1.11-1.31], Circuit $_{i}Ca^{2+}$ [0.35-0.50]. ACD-A (citrate) infused proximally in the circuit, calcium gluconate in separate central venous access.

Data collected: Record any dialysis related adverse event, continuous cardiac monitoring, mean arterial pressure, ionized Ca^{2+} when indicated, and any chamber, circuit or dialyzer clotting.

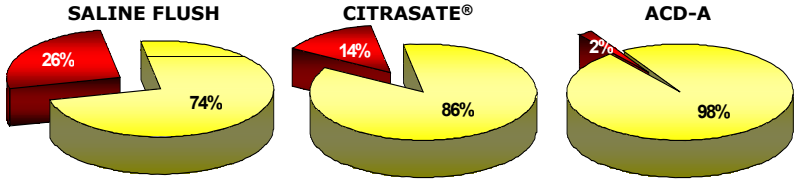
RESULTS

Baseline Characteristics

	Saline Flush (n=97 pts) 336 treatments	Citrasate® (n=19 pts) 72 treatments	ACD-A (n=16 pts) 87 treatments	P value
Age (yrs)*	58 (± 16)	50 (± 14)	57 (± 14)	<0.01
Women (%)	36	81	23	<0.01
Pressors (%)	16	28	34	<0.01
SLEDD treatment per pt†	3.5 (1-28)	3.8 (1-14)	5.4 (1-34)	0.01
Actual treatment time (hr)*	5.8 (± 1.34)	5.9 (± 1.22)	6.1 (± 1.1)	0.11 NS
Average Starting BP (mmHg)	130/60	126/62	122/58	0.35 NS

*Values expressed as means (±SD), or † expressed as means (ranges)

Clotting Episodes

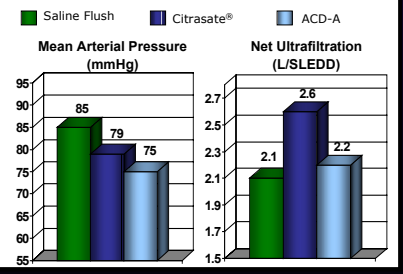


Clotting Event Rate

Saline Flush (26%) vs. Citrasate® (14%) P=0.005
Saline Flush (26%) vs. ACD-A (2%) P<0.001
Citrasate® (14%) vs. ACD-A (2%) P=0.026

Treatment Observations

Values are based on end of treatment results



Regional Citrate Management

Initial ACD-A Infusion
176 (±40) cc/hr
47% required adjustments, only 3% required 3 or more

Achieved mean sys-iCa
0.42 (±0.07) mmol/L

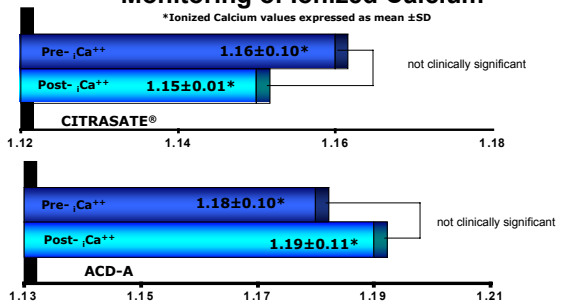
Initial Calcium gluconate Infusion
112 (±31) cc/hr
55% required adjustments, only 16% required 3 or more

Achieved Pt-iCa, Post- SLEDD
1.19 (±0.11) mmol/L

RESULTS - CONTINUED

Monitoring of Ionized Calcium

*Ionized Calcium values expressed as mean ±SD



DISCUSSION

- SLEDD was a safe, effective and well-tolerated method of renal replacement therapy in all ICU patients in this study
- Saline flushes, the most commonly employed alternative to heparin, was least effective at preventing circuit clotting
- Citrasate® was more effective in maintaining the circuit than saline flushes, and appears to safe for use in SLEDD
- We observed no clinically significant hypocalcemia events using either Citrasate® or regional citrate
- Regional citrate, using our protocol, was the superior method to keep the dialysis circuit from clotting.
- Our regional citrate protocol was safe and required limited adjustments in about half of all treatments
- It appears that regional citrate and Citrasate® can safely be used for SLEDD treatments in critically ill patients

LIMITATIONS

- Retrospective, observational, single center Review
- Small cohorts, non-randomized

405 Stars

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Source: DGNews | Posted 5 years ago

Citrate-containing Dialysate an Option for Chronic Dialysis Patients Unable to Receive Anticoagulants

Tags:

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By Maria Bishop

PHILADELPHIA, PA -- November 11, 2005 -- Citrasate, a dialysate containing sodium citrate, may provide an option for patients undergoing extended daily dialysis (EDD) who cannot take systemic anticoagulants, researchers reported here at the 38[th] Annual Meeting and Scientific Exposition of the American Society of Nephrologists (ASN).

Chronic dialysis patients sometimes have contradindications to anticoagulants, such as an allergy to heparin, noted James R. Madison, DO, MS, Division of Nephrology, Renal Services Program, University of California Davis Medical Center, Sacramento, California, United States. Citrasate offers these patients an effective alternative, he added during his presentation on November 10[th].

In their retrospective cohort study, Dr. Madison and colleagues examined 59 EDD treatments using Citrasate without systemic anticoagulation in 14 intensive-care-unit patients. Treatments were ordered for 6 to 8 hours, and saline line flushes were performed at 1-hour intervals in 92% of cases.

Cases were compared to a group of matched control patients who received saline flushes alone during anticoagulant-free EDD treatments in the ICU.

Results show that patients on Citrasate with hourly saline flush every 30 to 60 minutes had significantly less clotting compared to those on saline flush alone (16% vs. 30%).

The results also show that use of Citrasate also required less frequent flushing of dialysis circuits, thus reducing nursing time.

Median ionized calcium levels in Citrasate patients remained stable at the end of dialysis. Mean arterial pressure in these patients decreased by 5 mm Hg (P = .008), with a median ultrafiltration of 2.1L (1.4 to 3.0 interquartile range). The ultrafiltration goal was not reached due to system clots in five of 59 treatments.

Treatments were terminated early in 15% of cases (9 of 59 cases were cut short by a mean of 2.0 hours), venous chamber clots were seen in all cases, and dialyzer clotting was noted in 67%.

No adverse events were noted in this study.

Dialysis access was via non-cuffed catheter in 39 cases (internal jugular location in 35) and in the remaining via tunneled catheter or arteriovenous graft.

The researchers concluded that use of a citrate-containing dialysis may be an option in the management of renal replacement therapy in the complicated, acute-care setting.

[Presentation title: Citrate-Containing Dialysate Is Well Tolerated by Patients on Extended Daily Dialysis (EDD) in the Acute-Care Setting. Abstract 621]

405 Stars Star This? Yes / No

Comments

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Display Settings: Abstract

Am J Kidney Dis. 2000 Mar;35(3):493-9.

Dialysate made from dry chemicals using citric acid increases dialysis dose.

Ahmad S, Callan R, Cole JJ, Blagg CR.

Department of Medicine, Division of Nephrology, University of Washington, Seattle, WA, USA. sahmad@u.washington.edu

Abstract

A new dry dialysate concentrate acidified with citric acid (citrate dialysate) has been used in two separate clinical studies of hemodialysis patients. The first compared a single treatment using this dialysate, with one dialysis using regular standard dialysate acidified with acetic acid (regular dialysate) in a prospective, randomized, crossover study of 74 dialyses. Changes in blood levels of electrolytes and other blood constituents during dialysis were calculated by subtracting postdialysis from predialysis blood concentrations. Compared with acetic acid dialysate, citrate dialysate was associated with significantly greater decreases in total and ionized calcium, magnesium, and chloride levels. Citrate dialysate was also associated with greater increases in serum sodium and citrate concentrations, although their postdialysis concentrations remained within or just outside normal ranges. Changes in other blood constituents were similar with both dialysates. The second study used citrate dialysate exclusively for all dialyses over a 12-week period in 25 patients. Predialysis blood samples were drawn at the start of the study and at 4-week intervals thereafter, and postdialysis blood samples were obtained after the first and last dialysis. Repeated-measure analysis showed that although predialysis blood concentrations of magnesium, potassium, and citrate remained within the normal range, there was a significant declining trend over the course of the study. At the same time, predialysis serum bicarbonate levels increased, and significantly more patients had a predialysis bicarbonate concentration within the normal range at the end of the study than at the start (15 versus 8 patients; P = 0.001, chi-square). In 19 patients (excluding 3 patients for whom the type of dialyzer was changed during the study), the dose of dialysis for the first and last dialysis was calculated by urea reduction ratio and Kt/V. There was a significant increase in both measurements without changes in dialysis time, blood and dialysate flows, or dialyzer used. The urea reduction ratio increased from 68% +/- 5.9% to 73% +/- 5.3% (P < 0. 03), and the Kt/V from 1.23 +/- 0.19 to 1.34 +/- 0.20 (P = 0.01) from the first to last dialysis, respectively. In conclusion, this citric acid dialysate was well tolerated, and intradialytic changes in blood chemistries were similar to those seen with regular dialysate. Using dialysate containing citric instead of acetic acid increases the delivered dialysis dose.

PMID:10692276[PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

LinkOut - more resources

Heparin Free Acute Dialysis Using Citrate Dialysate

Annie Tu MS, ARNP, CNN, Suhail Ahmad MD. Scribner Kidney Center, Division of Nephrology, University of Washington, Seattle, WA, USA

Background:

Heparin Antibody

A hospital patient, with an antibody to heparin, received acute dialysis using regional citrate anticoagulation. Outpatient dialysis with regional citrate was unavailable. A newly approved citrate dialysate (DRYalysate, Advanced Renal Technologies, Kirkland, WA) was successfully used for heparin free dialysis. Subsequently, eleven acutely ill patients with bleeding risk, who generally clotted when using regular dialysate without heparin, were switched to citrate dialysate. Data is presented here comparing the treatment results.

Anticoagulation In Acute Hemodialysis

Acute dialysis patients with

- active bleeding,
- a high risk of bleeding, or
- with a heparin antibody

present a major treatment challenge because heparin free dialysis is frequently complicated by clotting.

The most prevalent alternative methods in clinical practice when heparin is contraindicated include;

1) Regional citrate anticoagulation is effective and well tolerated. It is expensive and complex, requiring close monitoring by the dialysis staff. This method is not compared here.
2) Periodic rinsing of the extra-corporeal system with saline has limited efficacy, generally increases the patients fluid load and extends the time required for dialysis.

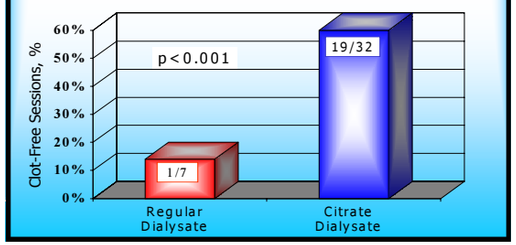
Since DRYalysate contains citric acid, an anticoagulant, we wanted to assess its effectiveness in conducting heparin free dialysis.

Subjects & Methods:

- N = 11, Acutely ill ICU patients:
  - Heparin Antibody 3
  - Risk of /Active Bleeding 8

Regular Dialysate, N = 7
Citrate Dialysate, N = 32

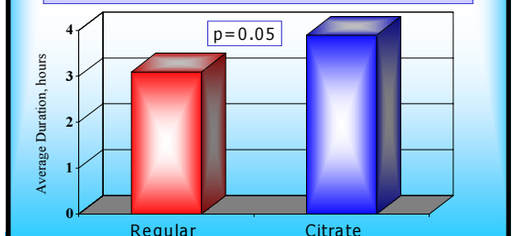
Clot-Free Treatments



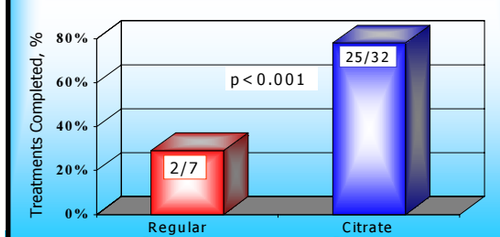
Composition of Two Dialysates
(Differences Highlighted)

Chemicals	Regular	DRYalysate
Na (mEq/l)	137	137
K	0-4	0-4
Ca	2.5/3.0	2.5/3.0
Mg	0.75	1.0
Cl	~105	~105
Dextrose	200	200
Citrate	0	2.4
Acetate	4	0.3
HCO3	37	37

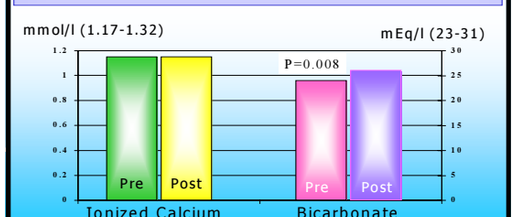
Duration of Treatments



Completed Treatments



Pre- & Post-dialysis Serum Concentrations When Using Citrate Dialysate



Summary:

Most heparin free dialyses with regular dialysate could not be completed.

In the same patients, dialyses with citrate dialysate were significantly more successful (p=0.001).

Citrate dialysate was associated with less clotting.

Dialyses with citrate dialysate were of longer duration than with regular dialysate.

No complications were noted with citrate dialysate, even in patients with poor liver function (transplantation).

There was no decline in serum calcium.

Conclusions:

Citrate dialysate was significantly better than regular dialysate for heparin free hemodialysis in acute patients.

Citrate dialysate was well tolerated and no side effects were noted.

The presence of citrate in dialysate may help prevent the clotting of dialyzer fibers.

Citrate dialysate appears to be a safe and effective alternative when heparin cannot be used in high-risk acute patients.

Presented at the American Society of Nephrology meeting in Toronto, Ontario October 2000

INCREASED DIALYZER EFFICIENCY USING A DIALYSATE CONTAINING CITRIC ACID IN PLACE OF ACETIC ACID

Suhail Ahmad, Robin Callan, James J. Cole, Christopher R. Blagg
University of Washington, Seattle and Advanced Renal Technologies, Kirkland, Washington

Hemodialysate

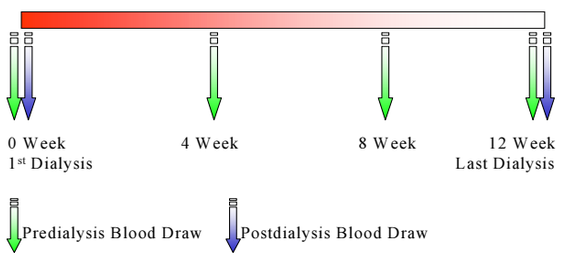
- Dialysate: Last Major Modification In 1970s – Bicarbonate Dialysate
- Bicarbonate Dialysate: Two Concentrates
  - Acid Concentrate – All Electrolytes
  - Bicarbonate Concentrate – Sodium Bicarbonate
- Acid Concentrate Contains Acidifying Agent To Control Dialysate pH

Acid Concentrate

- Current Acid Concentrate Contains **Acetic Acid** to Lower pH of Final Dialysate
- New Acid Concentrate (DRYalysate™) Contains **Citric Acid** As Acidifying Agent
- **Citric Acid** Allows Acid Concentrate To Be Dry Powder

Study Design

Twenty two stable hemodialysis patients used DRYalysate exclusively for 12 weeks.



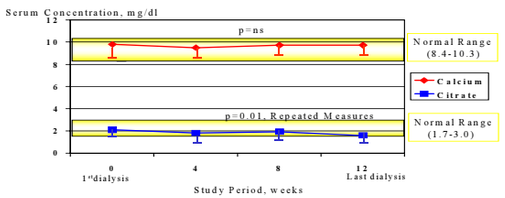
12-Week Study

RESULTS

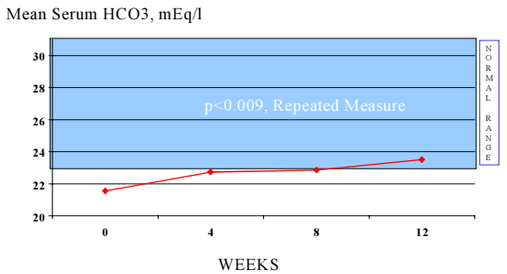
DRYalysate Treatment Well Tolerated, No Unexpected Symptoms Observed

- No Bleeding Problems Observed, ACT In 4 Patients Checked & Unchanged From Usual
- Staff Noted Increase In Number of Reuses
- Several Positive Effects Noted

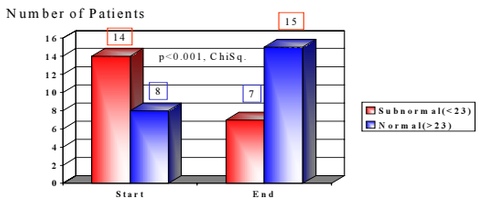
Predialysis Serum Calcium & Citrate Concentrations, mg/dl



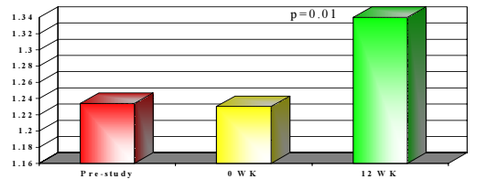
Predialysis Serum Bicarbonate



Predialysis Serum Bicarbonate



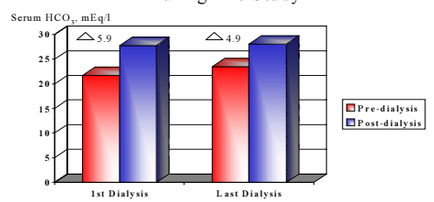
Delivered Kt/V (Daugirdas Formula)



Qb (ml/min)	370 ± 49	368 ± 48	375 ± 42 NS
Time (hrs)	3.9 ± 0.41	3.9 ± 0.39	3.9 ± 0.48 NS

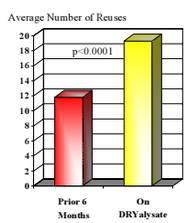
No Changes In Dialyzers

Pre- And Post-dialysis Serum Bicarbonate During The Study

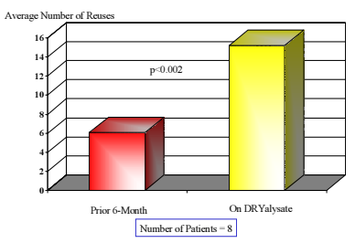


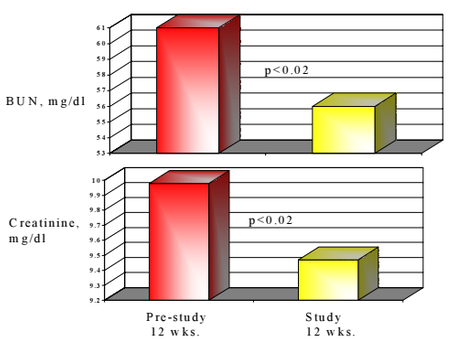
Dialyzer Reuse Comparison

Twenty patients exclusively used DRYalysate >3 months (starting with new dialyzers). Average dialyzer reuse during this period is compared to average reuse during previous 6 months on regular dialysate. (Maximum Reuse = 25)



Patients With <10 Reuse Before DRYalysate





Average Predialysis Values of BUN & Creatinine For 12 Weeks Immediately Before Study Compared with Those During 12 weeks of Study.

Summary & Conclusion

- With DRYalysate Use:
  - No Decline in Serum Calcium was Noted
  - No Increase in Predialysis Serum Citrate Concentration was Observed
- DRYalysate Use Associated with Decreased Acidosis
- DRYalysate Use Increased Dose of Dialysis (Higher Kt/V, Lower BUN & Creatinine)
- DRYalysate Use Increased Dialyzer Reuse

Presented at the American Society of Nephrology meeting in Miami, Florida November 1999

U.S. FOOD AND DRUG ADMINSTRATION
2006 Safety Alerts for Drugs, Biologics, Medical Devices, and Dietary Supplements
Heparin Sodium Injection
Audience: Vascular surgeons, ER personnel, pharmacists, and other healthcare professionals

[Posted 12/08/2006] FDA notified healthcare professionals of revisions to the WARNINGS section of the prescribing information for Heparin to inform clinicians of the possibility of delayed onset of heparin-induced thrombocytopenia (HIT), a serious antibody-mediated reaction resulting from irreversible aggregation of platelets. HIT may progress to the development of venous and arterial thromboses, a condition referred to as heparin-induced thrombocytopenia and thrombosis (HITT). Thrombotic events may be the initial presentation for HITT which can occur up to several weeks after the discontinuation of heparin therapy. Patients presenting with thrombocytopenia or thrombosis after discontinuation of heparin should be evaluated for HIT and HITT.

How Significant is Your Heparin Problem?

Heparin-induced Thrombocytopenia (HIT) occurs in 3% of patients who receive therapeutic intravenous unfractionated heparin and 0.5% - 1% of patients who receive lower doses (subcutaneous or flushes), low- molecular-weight heparin, or even the tiny amounts that leach from heparin-coated catheters. (1-3). HIT can present 5 to 12 days after heparin exposure, with or without arterial or venous thromboemboli. Delayed recognition and treatment of HIT can contribute to poor patient outcomes (4).

Use of heparin can produce:

- Decrease in platelat count
- 30% - 75% of patients with HIT experience venous or arterial thromboemboli (5), causing:
    - Deep venous thromboses and pulmonary emboli
    - Arterial thromboses of the extremities
    - Stroke
    - Myocardial infarction
    - Dyspnea (shortness of breath)

References:

1. Warkentin TE, Levine MN, Hirsh J, Horsewood P, Roberts RS, Gent M, et al. Heparin-induced thrombocytopenia in patients treated with low-molecular-weight heparin or unfractionated heparin. N Engl J Med. 1995;332:1330-5. [PMID: 7715641]

2. Rice L, Huffman DM, Levine ML, Udden MM, Waddell CC, Luper WE. Heparin-induced thrombocytopenia/thrombosis syndrome: clinical manifestation and insights (Astract). Blood. 1986;68(Suppl 1):339a.

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4. Rice L, Attisha WK, Drexler A, Francis, JL. Delayed-onset heparin-induced thrombocytopenia. Ann Intern Med. 2002;136;210-215

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