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02/001-Continuous Renal Replacement Therapy in Pediatric Patients Weighing 10 kg or Less


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We describe 86 pts weighing d“10 kg who received at least 24 h of continuous renal replacement therapy (CRRT) at 5 US children’s hospitals between 1993 and 2001. Pts weighed 1.5–10 kg (mean 5.3 B 2.8 kg; 16 pts <3 kg); 69% required pressors at CRRT initiation. BM-11 (58%), AK-10 (8%) BM-25 (11%) and PRISMA (23%) CRRT machines were used. Most circuits were primed with blood/albumin mix. 88% of pts received heparin; others received citrate or no anticoagulation. Mean blood flow rate was 48 B 24 ml/min (range 15–106 ml/min) with mean blood flow rate of 9.5 B 4.2 ml/min/kg body weight. 655 patient-days of therapy were studied (mean 7.6 B 8.6 days/pt, range 1–46 days/pt). 32 pts (38%) survived to leave the ICU; only 4/17 (24%) pts <3 kg survived. The smallest survivor weighed 2.3 kg. Overall, survivors (S) and non-survivors (NS) showed no significant difference in mean weight, days on CRRT or pressor number. However, for pts 13 kg, 28/68 (41%) survived and mean pressor number was lower for S versus NS (0.96 B 1.1 vs. 1.6 B 1.0, p <0.03). We conclude that CRRT is feasible and useful in children weighing d“10 kg. In these small children, significant hemodynamic instability requiring pressor support neither precludes successful CRRT nor adversely affects survival. Following CRRT, the survival rate in children who weigh between 3 and 10 kg is comparable to that seen in older children and adolescents.
02/002-Continuous Renal Replacement Therapy: The Roman Trial Results

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The mortality of critically ill patients affected with Multiple Organ System Failure (MOSF), Systemic Inflammatory Response Syndrome (SIRS) and sepsis remains high despite advances in renal supportive therapy and intensive care. In the acute Intensive Care Unit (ICU) setting, traditional hemodialysis leads to several disadvantages because of hemodynamic instability and hypotension, while Continuous Renal Replacement Therapy (CRRT) is a more adequate treatment in such patients. Aim of the Study: We performed an epidemiological polycentric study in order to assess the incidence and mortality rate of different severe syndromes (SIRS, MODS, SIRS + MODS, MODS + sepsis) and the effect of CRRT on their clinical course. Patients and Methods: We studied 256 critically ill patients hospitalized within the intensive care units of seven Roman Hospitals (S. Filippo Neri Hospital, S. Giovanni Hospital, Cristo Re Hospital, Alatri Hospital, European Hospital, Aurelia Hospital, A. Gemelli Hospital). Two evaluation forms were used to collect the following data: patient’s age and sex, diagnosis at ICU admission, Apache II score, systemic syndrome developed, number of organs affected, kind of CRRT, dialytic protocol, length of treatment, kind of vascular access, daily biochemical and haematological parameters. Results: Patients’ mean age ranged between 65 and 74 yrs and we had 173 male patients (68% of the total population) and 83 females (32%). They resulted to be affected with MODS (36%), SIRS + MODS (34%), MODS + sepsis (16%), and SIRS (14%). The total mortality rate was 59%, with 75% of dead patients in the first 7 days of treatment, while mortality rates for pathology were: SIRS + MODS 66%, MODS + sepsis 65%, MODS 57% and SIRS 43%. The number of affected organs was: 1 organ in 1% of investigated patients (mortality rate: 30%), 2 organs in 74% of pts (mortality rate: 50%), 3 organs in 23% of pts (mortality rate: 83%) and 4 organs in 2% of pts (mortality rate: 100%). Total treatment length ranged between 4.9 and 7.7 days and different kinds of CRRT modalities were used: CVVHDF in 53% of patients (mortality rate: 58%), CVVHD in 27% (mortality rate: 51%) and CVVH in 20% (mortality rate: 73%). The Apache II score in recovered patients averaged 25.6 (27.1 in SIRS patients, 27.2 in SIRS + MODS pts, 25.8 in MODS and 23.7 in MODS + sepsis), while it was 29.9 in dead patients (24.2 in SIRS patients, 29.7 in SIRS + MODS, 30.6 in MODS and 29.4 in MODS + sepsis). Conclusions: It is important to start CRRT immediately when patients affected with MOSF show renal function damage, even if at an initial stage, in order to improve patients’ survival. In fact, in spite of its expensiveness and the great caring engagement, CRRT in Roman ICUs has led to a survival rate of 41%, much higher than the one reached by traditional dialytic methods (25%) or without any dialytic treatment at all (almost 0%). As regards the prognostic score, we were not able to single out patients with a certaily bad outcome in which the uselessness of every treatment could be predicted.
02/003-Continuous High-Volume Hemofiltration on C-Reactive Protein in Severe Acute Pancreatitis

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Objective: The acute-phase reactant C-reactive protein (CRP) is a marker of inflammatory response, it is currently the serum variable of choice for an early, accurate severity assessment of acute pancreatitis in the treatment of severe acute pancreatitis (SAP). The purpose of this study was to evaluate the influence of continuous high-volume hemofiltration (CHVHF) on CRP in SAP patients. Method: Nine SAP patient (7 males and 2 females) with a mean age of 54.67 ± 15.26 (35–73) years were included. CHVHF was started 3.67 ± 1.66 days after onset of disease, the APACHE II score before the treatment was 12.56 ± 4.50 (8–23), the SAPS II score was 33.67 ± 10.11 (13–43) and the CT score was 9.33 ± 1 (8–10). Seven of them were diagnosed as ARDS and treated with mechanical ventilation. CHVHF was sustained for at least 72 h, AN69 hemofilters (1.2 m2) were used and changed every 24 h. The ultrafiltration rate was 4,044.4 ± 341.1 ml/h. The anti-coagulant was low-molecular-weight heparin in 7 patients and citrate in 2 patients. Result: Clinical symptoms of SAP were relieved quickly on CHVHF, including decreased body temperature and tachycardia and increased arterial oxygen concentration. All the patients survived in ICU, but one of them died of septic shock before discharge. The APACHE II, SAPS II and CRP levels were significantly decreased (table 1), and APACHE II scores increased markedly 24 h after suspending CHVHF, while the SAPS II score and CRP maintained the level. Conclusion: CHVHF was effective in alleviating symptoms of SAP and decreasing the acute phase reactant CRP level.

<table>
<thead>
<tr>
<th>Table 1. Change of the APACHE II, SAPS II and CRP in severe acute pancreatitis patients treated with CHVHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before CHVHF</td>
</tr>
<tr>
<td>APACHE II</td>
</tr>
<tr>
<td>SAPS II</td>
</tr>
<tr>
<td>CRP, mg/l</td>
</tr>
</tbody>
</table>

*p < 0.05 vs before CHVHF, **p < 0.01 vs before CHVHF, *p < 0.05 vs 72 h after CHVHF.
02/004-Change of CRP Levels during High-Volume Hemofiltration in Patients with Systemic Inflammatory Response Syndrome

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Objective: Application of high-volume hemofiltration (HVHF) in patients with systemic inflammatory response syndrome (SIRS) is now widespread, and partial remissions were observed in some patients. However, there were no reliable parameters to imply the initiation and indicate the effect of treatments. C-reactive protein (CRP), one of indicators related to SIRS severity, was selected as a parameter during HVHF in patients with SIRS in this study. Methods: Thirty-six patients diagnosed as SIRS, due to sepsis, trauma, burn, and severe acute pancreatitis, were treated by HVHF for 72 h in addition to other therapies. Four liters substitution fluid per hour was used in these patients, and serum CRP levels were evaluated at the start and every 12-hour intervals during HVHF. According to the initial CRP (iCRP) levels, the patients were divided into three groups as I (iCRP < 100 mg/l), II (100 mg/l < iCRP < 200 mg/l), III (iCRP ≥ 200 mg/l). Results: In group I (n = 12), a slight increment of CRP level was observed during 72 h HVHF treatment (0 h: 43.16 ± 28.65; 72 h: 55.72 ± 37.48 mg/l, p < 0.05). In group II (n = 7), no obvious change was found during treatments. In group III (n = 15), a great reduction appeared at 36 h of HVHF, and with a sustaining slight decline during the following time. CRP levels at every 12 h of HVHF from 0 to 72 h in group III were (mg/l): 360.7 ± 127.9, 340.5 ± 124.8, 313.7 ± 130.5, 269.5 ± 118.1 (p < 0.05, vs. point 0), 232.3 ± 117.0 (p < 0.001, vs. 0 h), 183.5 ± 109.9 (p < 0.001, vs. 0 h), 172.0 ± 119.3 (p < 0.001, vs. 0 h). Conclusion: HVHF may be in favor for the reduction of CRP levels in patients with more than 200 mg/l, and this effect may be reverse in patients with CRP levels <100 mg/l.
02/005-Adjusting the Intensity of Renal Support to the Patients’ Need: The R.I.O.S. Experience

Elizabeth Maccariello, Carla Valente, Ricardo Valença, Andrea Martins, Lina Nogueira, Marise Godinho, Eduardo Rocha

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Choosing the best dialysis method for an individual patient may be a difficult task in the management of acute renal failure (ARF) at the ICU. Shorter, daily dialysis procedures (IHD, EDD, SLEDD) are being progressively adopted by numerous centers, although no firm recommendations for patient selection have been overall accepted (grade E evidence). In order to standardize care and improve the quality of renal support, we established stratification criteria based on patients’ characteristics at onset of ARF, followed by daily evaluations. Renal intensity of support (R.I.O.S.) was determined according to each patient’s hemodynamic status, ranging from 0 (no support needed) to 3 (maximal need), with dialysis methods chosen accordingly (Table).

<table>
<thead>
<tr>
<th>Level of support</th>
<th>Procedure</th>
<th>Hemodynamic status</th>
<th>Duration h</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>none</td>
<td>stable</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>every other day HD</td>
<td>stable</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>SLEDD</td>
<td>unstable</td>
<td>up to 12</td>
</tr>
<tr>
<td>3</td>
<td>CVVHDF</td>
<td></td>
<td>24</td>
</tr>
</tbody>
</table>

389 ARF adult ICU patients from 3 affiliated hospitals were followed from Jan 98 to Oct 01. Dialysis need was indicated based on Bellomo and Ronco’s criteria [1]. Procedures were performed in automated devices (Gambro AK95 for daily dialysis; Braun FAD100 for CRRT), using biocompatible membranes (polysulfone and PAN, respectively) and customized bicarbonate-buffered solutions. Prospective utilization of R.I.O.S. in 120 patients (age 65.6 ± 1.8 years, APACHE II 10–24) showed that 75.8% needed maximal level (L) of support at onset [10 (8.3%) L1; 19 (15.8%) L2; 91 (75.8%) L3]. Change in R.I.O.S. status was required in 43 (35.8%) patients, with 77 (64.2%) patients requiring a single level of support throughout hospitalization. Mortality at discharge was observed in 10, 57.9 and 84.6% patients, L1, L2 and L3, respectively. Survival was followed by complete renal function recovery in 70 (L1), 63 (L2) and 100% (L3) of patients. Our preliminary data show that patient stratification according to individual needs may become a necessary first step to the establishment of evidence-based practice guidelines and add to the improvement and optimization of care in ARF patients.

Reference
02/006-The Effect of Hemofiltration on Adult Respiratory Distress Syndrome

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Objective: To analyze the effect of hemofiltration on acute respiratory distress syndrome. Method: Six acute respiratory distress syndrome (ARDS) patients were involved, including 4 males and 2 females with an average age of 56.8 ± 12.7 years. ARDS was associated with severe acute pancreatitis in 1, acute necrotic pancreatitis in 2, 2 patients were after ruptured abdominal aortic aneurysm repairment surgery and 1 was after artificial vessel transplantation. Hemofiltration was performed by using the Baxter BM25 system. The substitute fluid was infused by a pre-dilution route, the ultrafiltration rate was 4–7 l/h, blood flow rate was 250–350 ml/min. F60 hemofilter (1.2 m²), HF1200 hemofiltor (1.25 m²) and FILTRAL16 hemofilter (1.7 m²) were applied without reuse. Low-molecular-weight heparin was used for anticoagulation.

Results: The total number of sessions was 36. The therapy time was 8.2 ± 1.8 h/day. The substitute volume was 47.2 ± 15.9 l/day (0.67 ± 0.21 l/kg/day). The removed fluid was 1,443 ± 1,212 ml each session and its rate was 2.8 ± 2.6 ml/kg/h. Half of the patients got better after hemofiltration, but the other three died although having intensive bloodpurification therapy. Hemodynamic changes showed that the vital signs trend to be more stable and tachycardia stopped automatically (p < 0.05). Both diastolic and systolic pressure raised without any drug adjustment (p < 0.05). Central vessel pressure had no significant change during the therapy. Parameters such as SaO2, SpO2/FiO2 were better than those before therapy (91.4 ± 6.2 vs. 95.2 ± 4.7, 135.0 ± 57.8 vs. 163.1 ± 63.5, p < 0.01). The requirement of FiO2 was lowered (76.8 ± 22.6 vs. 71.8 ± 22.8, p < 0.01). Blood gas analysis showed that PaO2 was higher after therapy, though it had no significance (p > 0.05). Conclusion: Hemofiltration can ameliorate the pulmonary gas exchange function and improve SaO2, so it contribute to the therapy of ARDS.

### Table 1. Effect of Hemofiltration on respiratory parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>n = 36</th>
<th>Therapy duration (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR/min</td>
<td>22.4±5.7</td>
<td>19.7±4.3</td>
</tr>
<tr>
<td>SpO2, %</td>
<td>91.4±6.2</td>
<td>94.3±4.9</td>
</tr>
<tr>
<td>FiO2, %</td>
<td>76.8±22.6</td>
<td>73.2±21.7</td>
</tr>
<tr>
<td>SpO2/FiO2</td>
<td>135.0±57.8</td>
<td>148.1±56.8</td>
</tr>
<tr>
<td>PEEP, cm H2O</td>
<td>8.2±3.7</td>
<td>7.7±3.8</td>
</tr>
</tbody>
</table>

* p < 0.05 vs. pre-hemofiltration, *p < 0.01 vs. pre-hemofiltration.
02/007-Cocaine-Induced Thrombotic Microangiopathy: Outcome of Therapy with Plasmapheresis

C.M. Nzerue, K. Hewan-Lowe

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Aim of study: Presentation of the outcome of plasma exchange therapy for two cases of cocaine-associated TTP (case #1: female, 41 years; case #2: female, 42 years). We have previously described the outcome of plasma infusion in a case of cocaine-associated TTP (Volcy et al, Am J Kidney Dis 35:E3, 2000).

Material and Methods: Plasmapheresis was performed in 3 hourly sessions daily for 7 consecutive days in one patient and for 12 consecutive days in the second patient. We used Spectra cell separator pumps and Baxter blood filters in both patients. We exchanged 1 plasma volume (3–5 liters) using cryopoor fresh frozen plasma for replacement in both patients with a Cobe spectra machine.

Summary: We compare 2 patients with cocaine-induced TTP treated by plasmapheresis. Both patients presented with hemolytic anemia, ARF, progressive thrombocytopenia, and seizures after using crack cocaine. Outcomes: Patient survival was 100% and renal survival was 50%. Patient #1 became dialysis dependent, while patient #2 recovered renal function completely. Patient 1 received 6 units of blood, while case #2 received 3 units of blood. There was total resolution of hemolysis, thrombocytopenia, and neurologic dysfunction.

Conclusions: Cocaine is an uncommon cause of secondary TTP. Plasmapheresis improves survival with cocaine-induced TTP. The outcome of renal function in cocaine-associated TTP is variable. There was 50% total recovery of renal function in our series. Plasmapheresis should be offered to
patients with cocaine induced TTP. In our experience the outcome of renal function with plasma exchange for cocaine-induced TTP appears better than plasma infusion.
02/008-Septic Shock Treatment by Using a Coupled Plasmafiltration-Adsorption (CPFA) Extracorporeal System

M. Formica, G. Cesano, S. Livigni, A. Vallero, M. Pozzato, E. Visetti, C. Tetta, F. Quarello

aDialysis Unit and b Intensive Care Unit, Torino Nord Emergenza San Giovanni Bosco Hospital, Torino; cClinical and Laboratory Research Department, Bellco, Mirandola, Italy

Sepsis is the leading cause of acute renal failure and mortality in intensive care units. The negative results in terms of survival derived from clinical trials focused on specific molecules, such as LPS or TNF, modified the concept of sepsis as a simple pro-inflammatory event and moved the pathogenesis towards a more complex unbalance between pro- and anti-inflammatory substances. The biological correlate of the establishment of the clinical setting of septic shock is the picture of monocytes’ hyporesponsiveness (deactivation-immunoparalysis) to inflammatory stimuli. Continuous renal replacement therapies have made extracorporeal treatment possible in septic patients, with the aim to better control the hemodynamic state and prevent volemic disturbances and hypercatabolic states. Limitations of techniques derived from chronic or acute renal failure treatment, lie upon the convective volumes applied and/or to mediators sieving coefficients, both difficult to overcome with the technology today available. In order to improve the efficiency of a blood purification system in critically ill septic patients, unselective adsorption was added to conventional diffusion and convection in a newly designed device named as coupled plasmafiltration-adsorption (CPFA). CPFA is a two-step, modular system made of plasma separation and adsorption on a hydrophobic resin, with final reinfusion of the plasmafiltrate into the patient’s line before the hemofilter. Five patients, 3 males and 2 females (mean age 52 ± 19.9), all on mechanical ventilation, with a clinical picture of septic shock underwent a mean of 9.8 ± 1.7 CPFA treatments (range 7–12). The Apache II score before treatments was 26 ± 5.6, thereafter 14 ± 3.5. Three patients had quite normal renal function. Statistically significant improvements were recorded about the differences pre/post treatments concerning mean arterial pressure 78 ± 14.9 vs 86 ± 18.3 mm Hg (p < 0.001), cardiac index 3.88 ± 1.03 vs 3.24 ± 0.86 l/m2/min (p < 0.001), systemic vascular resistances 1,423 ± 552 vs 1,862 ± 657 dyn < s/cm5 (p < 0.001), PaO2/FiO2 ratio 199 ± 70 vs. 244 ± 81 (p < 0.001), need for norepinephrine 0.065 ± 0.085 vs. 0.053 ± 0.082 ìg/kg/min (p < 0.01). All patients but one were discharged alive from ICU after a mean of 36.8 ± 14.1 days (range 18–57). Laboratory data showed a sharp decline of C-reactive proteine along the treatment time from 29.7 ± 11.4 to 6.9 ± 4.8 (–77%); data concerning IL-6, IL-10 and sICAM-1 showed, respectively, a reduction to 2.8%, 36.6% and 69.2% in respect of starting values. CPFA is a safe and feasible treatment and seems to allow good results in terms of hemodynamics, pulmonary function and survival in septic shock patients. The procedure provides the removal of the cytokines involved in the development of the sepsis scenario and induces a sort of immunomodulation process with the target of avoiding peak concentration of immunoactive mediators, thus creating a non-specific cytokine ‘magic shield’. The treatment fits the requirements of critically ill septic patients unrelated to the presence of concomitant renal insufficiency.
02/009-Successful Treatment of Severe Hepatic Encephalopathy by Continuous Albumin Dialysis in Patients with Hyperacute or Acute Liver Failure but Failure of MARS System

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Albumin dialysis is a new method for the treatment of hepatic encephalopathy. We have previously shown successful treatment of hepatic encephalopathy in patients with acute-on-chronic liver failure and in a patient with Wilson’s disease. We now report the result of our pilot study in patients with hyperacute and acute liver failure and hepatic encephalopathy. The method is similar to continuous hemodialysis except that the dialysate has an albumin concentration of 4.4 g/dl. Technical details: bedside monitor: bm 25 (Edwards, Germany); dialyzer HdF 100 (Fresenius, Germany); albumin dialysate: addition of 1.3 l of 20% human albumin solution to a 4.5-liter bag bicarbonate-buffered hemofiltration solution (Fresenius, Germany), resulting in 44 g/l albumin; dialysate flow: 1–2 l/h; prädilution: 1 l/h; blood flow: 150–200 ml/min; ultrafiltration rate according to the patients condition; venous access: double-lumen jugularis dialysis catheter; anticoagulation: low dose heparin or heparin free. Patients: 5 female patients with hyperacute or acute liver failure due to intoxication with potassium dichromate, ecstasy, Kava Kava extract, galerina marginata or occlusion of the hepatic artery. Our indication to start treatment was hepatic encephalopathy grade III. Treatment time ranged from 1 to 3 days. In all patients hepatic encephalopathy could be stabilized or improved. They were all successfully bridged for transplantation. In 3 of them intracranial pressure was monitored and decreased during the treatment. In 2 patients with hemodialysis requiring acute renal failure albumin dialysis was a sufficient replacement therapy for renal failure. One patient was treated crossover with the MARS system. During the first 24 h treated by albumin dialysis her encephalopathy improved from grade III to I. After initiation of the treatment with the MARS system she had within 5 h grade IV encephalopathy despite a decrease of bilirubin from 22.5 to 15.4 mg/dl as a marker for a technically successful treatment. Ventilation had to be started. After placement of an intracranial catheter albumin dialysis was reintroduced and the intracranial pressure decreased from 38 to 24 mm Hg. This severe deterioration could be due to the recycling of the albumin solution which may not remove all pathogenetic factors involved in the pathogenesis of hepatic encephalopathy in hyperacute or acute liver failure. Our method of albumin dialysis and the MARS system have therefore to be studied separately. The promising results warrant further studies to explore the effect of albumin dialysis in patients with hyperacute or acute liver failure and severe encephalopathy. Patients who deteriorate with the MARS system could profit from a trial of albumin dialysis.
02/010-Development of New Dialysate Solutions Containing Bicarbonate

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In patients with multiple organ failure, the physiologic buffer – bicarbonate – is preferred for the treatment of acute renal failure (ARF) by continuous renal replacement therapies (CRRT) because it does not need metabolic conversion and does not cause any undesired side effects. Therefore, a family of bicarbonate-based solutions have been developed. Three ready-to-use formulations are available to allow treatment flexibility. The solutions present a physiological pH (F7.4) and contain the typical standard concentration of buffer (35 mmol/l), sodium (140 mmol/l), calcium (1.75 mmol/l) and magnesium (0.50 mmol/l) but differ by the content of potassium (0, 2 or 4 mmol/l) and dextrose (0 or 1 g/l). The ready-for-mixing solution is packaged in a two-chamber bag in order to keep separated active substances (such as calcium and bicarbonate) to avoid calcium carbonate precipitation during sterilisation and storage. The top chamber contains the electrolytes and the lower chamber contains the bicarbonate solution. The reconstituted solution is easily obtained: the interchamber frangible is broken and the content of the upper chamber is transferred by gravity into the lower chamber. This process takes less than 5 min. During the development phase, these bicarbonate-based solutions were presented to several physicians and nurses in France. Due to its ease-of-use and the improved safety associated (e.g. no need to spike bicarbonate or potassium into the solutions as they are already present in the ready-to-mix configuration), this new product was very well accepted by hospital staff.
02/011-Potential Use of Mesoporous Activated Carbons In CRRT


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The developments of continuous renal replacement therapies such as haemofiltration and haemodialysis have allowed patients experiencing acute renal failure to be adequately managed on the intensive care unit. Although these techniques have made a significant contribution to the way critically ill patients are managed, they are not without drawbacks. For example achieving adequate removal of solutes often requires very high ultrafiltration and/or dialysis rates to be employed which, in turn, creates an additional cost burden. Adsorbent-based techniques, either on their own, or on-line with other extracorporeal methods, could offer clinical and cost benefits, as they do not depend on convective or diffusive forces to deliver effective solute clearance. In this study adsorption properties of mesoporous polymer pyrolysed activated carbons (AC) produced from crosslinked polyvinylpyridine or polystyrene have been investigated towards middle molecule sized uraemic toxins from ultrafiltrate of patients with acute renal failure (n = 6) at early stage in haemofiltration. The samples were passed through a column containing spherical granules of AC, and fractions were analysed by SDS-polyacrylamide gel electrophoresis and liquid chromatography. Complete or partial adsorption of all proteins in the middle molecular range of 1.5–30 kD was observed up to 360 min, with most efficient adsorption within the first hour. Although detailed identification of the removed proteins was not attempted, it is likely that the adsorbed proteins include β2-microglobulin. Ability of the studied AC to remove middle molecules could be attributed to their unique pore size distribution. They contain mesopores with diameter within 2–50 nm range, and the size of ‘middle molecules’ fits within such pores. Presence of micropores (diameter less than 2 nm) ensures high adsorption capacity of these AC towards small molecules – indicators of renal failure such as creatinine. In fact, 95–100% removal of creatinine was achieved throughout duration of all experiments, i.e., for at least 360 min, and no breakthrough was observed. With initial creatinine concentration of 376 Îmol/l in the ultrafiltrate, the adsorption capacity of AC was no less than 23 Îmol/g of adsorbent. Adsorption of urea is a weak point in the use of AC, as activated carbons do not possess high affinity towards urea. Nevertheless, at least 0.29 mmol of urea/gram of adsorbent was removed, but the breakthrough occurred within the first hour. These results demonstrate the ability of mesoporous activated carbons to adsorb substances within the middle molecule range, which cannot be achieved using conventional AC with predominantly microporous structure. Their use in ultrafiltrate and/or dialysate regeneration could significantly reduce costs and improve efficiency of extracorporeal treatment. Being made from materials precursors with tightly controlled chemical purity and having high mechanical strength, these AC could have biocompatibility sufficient for direct contact with blood, thus creating opportunities for new applications in other areas of intensive care medicine.
02/012-The Use of Resin Based Adsorbents for the Removal of Lipopolysaccharide

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Sepsis is a major cause of morbidity and mortality in intensive care units throughout the world with a particularly high fatality rate for patients developing multi-organ dysfunction syndrome (MODS). Human sepsis is often initiated by the presence of lipopolysaccharide (LPS), a constituent of the outer cell membrane of Gram-negative bacteria. Via a series of events the LPS stimulates the systemic release of inflammatory mediators including cytokines and complement activation products. The release of these inflammatory species evokes a systemic response that may result in septic shock, MODS and death. The use of adsorbents may provide a rational way forward to counteract the process of sepsis by reducing the systemic level of both LPS and circulating cytokines that mediate the inflammatory process. This study compared the adsorption capacity of the Purolite ResinsTM (MN500 and MN250 (table 1) by measuring the response of murine bone-marrow macrophages to LPS. Briefly, batch experiments were prepared using 1 ml aliquots of Dulbecco's minimal essential medium (DMEM), DMEM + Resin (0.1 g), DMEM + LPS (10 Î¼g/ml), DMEM + Resin + LPS (10 Î¼g/ml). The samples were agitated overnight at 4°C to limit microbial contamination growth prior to centrifugation at 2,000 rpm for 5 min to pellet the adsorbent. The old medium was removed and the supernatant was added to the RAW 264.7 cells that were then cultured for a further 24 h. The measurement of nitrite accumulation in the culture medium serves as an indirect measurement of nitric oxide (NO) production. Nitrite (NO2 –) is a stable product of the reaction between NO and molecular oxygen and can be measured spectrophotometrically at 540 nm, following the addition of Greiss reagent. The total protein content of the cells was determined using a modification of the Bradford method. The reduction in nitrite concentration, expressed as pmol/lg protein, is related to the concentration of LPS in the DMEM. The RAW 264.7 assay has been fully validated and preliminary results suggest that both the Purolite ResinsTM tested have the ability to adsorb LPS. It has also been shown that the MN250 resin has a greater ability to remove LPS from DMEM than the MN500 (fig. 1). These differences may be a result of the altered functionality and pore-size distribution of the two resins (table 1).
Table 1. Characteristics of Purolite adsorbents

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MN-500</th>
<th>MN-250</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface area, m²/g</td>
<td>800–1,000</td>
<td>800–1,000</td>
</tr>
<tr>
<td>Pore volume, ml/g</td>
<td>1–1.1</td>
<td>0.6–0.8</td>
</tr>
<tr>
<td>Meso-/macropore radius, nm</td>
<td>85–95</td>
<td>30–40</td>
</tr>
<tr>
<td>Micropore radius, nm</td>
<td>1.5</td>
<td>1.4</td>
</tr>
<tr>
<td>Functionality</td>
<td>Strong acidic cationic</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1
It can be seen from the results presented here that Purolite Resins™ have the ability to remove LPS from solution and that by manipulation of the pore size and surface chemistry of these adsorbents it may be possible to increase their efficiency still further. To this end further studies are currently being undertaken on a range of resins of varying pore size and surface chemistry. These results support the hypothesis that resin-based adsorbents may provide a rational therapy for sepsis by reducing the circulating LPS titres.
02/013-Convective Solute Clearances during Continuous Venovenous Hemofiltration at Various Ultrafiltration Flow Rates using Multiflow-100 and HF-1000 Filters

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Clearances (K) of solutes were measured during continuous venovenous hemofiltration at various ultrafiltration rates (Quf: 1–4.5 l/h) using two different filters. Preset Multiflow-100 (M-100) and HF-1000 hollow-fiber filters (Gambro, St-Leonard, Canada) were compared (5 patients for each type); they are respectively made of 0.9 m² AN69 membrane and 1.1 m² polysulfone membrane. For small solutes (urea, creatinine, phosphate, and urate), the effluent to plasma ratio (E/P or sieving coefficient) remained near 1.0 at all ultrafiltration rates; clearances for those small molecules were thus equal to Quf for both filters. All rates combined however, E/P was slightly but statistically lower for urea and phosphate for the M-100 compared to the HF-1000 (urea: 0.94 ± 0.05 vs. 0.97 ± 0.05, p = 0.03 and phosphate: 1.00 ± 0.05 vs. 1.02 ± 0.03, p = 0.04, respectively). Increasing Quf from 1.0 to 4.5 l/h did not significantly modify E/P.

Convective clearance was lower for β2-M compared to small solutes. For the M-100, average E/P was 0.62 ± 1.10 and did not significantly change from Quf 1.0 to 4.5 l/h. Hence, M-100 clearance of β2-M increased linearly with Quf at roughly 60% the small solutes rate. For the HF-1000, average E/P were significantly lower compared to the M-100 (0.42 ± 0.09 at 1.0 l/h and decreased progressively to 0.26 ± 0.06 while increasing Quf to 4.5 l/h. With predilution, a progressive decrease in patient clearance was observed, reaching a maximum of 34%, 39%, 40% for urea, creatinine, and urate on average for both filters, with a Quf rate of 4.5 l/h in predilution. We were not able to estimate the impact of predilution on phosphate clearance since phosphate was routinely added to reinjection solutions (* in table). There were no significant differences between the two filters for small solutes. Predilution decreased patient clearance of β2-M by 39% for the M-100 and 44% for the HF-1000 (p = 0.04). For the HF-1000, by combining the progressive fall of E/P with the impact of predilution, patient clearance of β2-M reached a plateau of 10 ml/min at Quf of 2.5 l/h and above. Conclusions: Small solute clearances equaled Quf at evaluated rates. Urea and phosphate clearances were marginally better with the HF-1000, whereas β2-M clearance was higher with the M-100.
<table>
<thead>
<tr>
<th>Substance</th>
<th>M-100 filter K (ml/min)</th>
<th>M-100 patient K (% by predilution)</th>
<th>HF-1000 filter K (ml/min)</th>
<th>HF-1000 Patient K (% by predilution)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea</td>
<td>71.6 ± 2.8</td>
<td>47.5 ± 2.8 (34)</td>
<td>72.5 ± 4.8</td>
<td>47.4 ± 2.5 (35)</td>
</tr>
<tr>
<td>Creatinine</td>
<td>75.8 ± 5.4</td>
<td>47.2 ± 3.1 (38)</td>
<td>74.2 ± 3.9</td>
<td>44.9 ± 1.9 (40)</td>
</tr>
<tr>
<td>Urate</td>
<td>75.3 ± 7.0</td>
<td>46.0 ± 4.1 (39)</td>
<td>77.9 ± 6.6</td>
<td>45.7 ± 5.1 (41)</td>
</tr>
<tr>
<td>Phosphate</td>
<td>73.5 ± 3.5</td>
<td>*</td>
<td>73.8 ± 1.3</td>
<td>*</td>
</tr>
<tr>
<td>β₂-M</td>
<td>47.0 ± 5.0</td>
<td>28.6 ± 2.3 (39)</td>
<td>19.6 ± 4.4</td>
<td>10.9 ± 2.3 (44)</td>
</tr>
</tbody>
</table>
02/014-Citrate Anticoagulation Monitoring: Post-Filter Act or Ionized Calcium?

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Purpose: Interest in regional citrate anticoagulation for CRRT is growing. Several protocols have been proposed. However, controversy still exists as to which parameter should be preferably monitored, and as to what target should be aimed for. Proposed target values for whole blood activated clotting time (ACT) in the literature range from 180 to 300 s. Based on expert opinion, the target ionized calcium (iCa) within the extracorporeal circuit during citrate regional anticoagulation has also been proposed as being between 0.25 and 0.35 mmol/l. We studied the relationship between ACT and iCa observed during a phase II trial evaluating a novel citrate anticoagulation regimen for CVVH/CVVHDF. Methods: We used a citrated replacement fluid solution adapted to the predilution PRISMA system. Details of our protocol have been presented previously. We monitored ACT and iCa at different sites of the extracorporeal circuit: systemic pre-citrate (Syst), post-citrate/pre-filter (Pre-F), postfilter (Post-F) and post-neutralizing calcium 1% + magnesium solution (Post-Ca). The following results were obtained from 15 critically ill patients over an 840-hour observation period.

Results:

<table>
<thead>
<tr>
<th>Site</th>
<th>System</th>
<th>Pre-F</th>
<th>Post-F</th>
<th>Post-Ca</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>120</td>
<td>31</td>
<td>105</td>
<td>31</td>
</tr>
<tr>
<td>iCa, mmol/l</td>
<td>1.06 ± 0.14</td>
<td>0.3 ± 0.07</td>
<td>0.3 ± 0.1</td>
<td>0.4 ± 0.1</td>
</tr>
<tr>
<td>ACT, s</td>
<td>124 ± 23</td>
<td>242 ± 67</td>
<td>227 ± 92</td>
<td>171 ± 71</td>
</tr>
</tbody>
</table>

Sixteen (6%) ACT values above 300 s were noted concomitantly to iCa values below 0.3 mmol/l.

Conclusion: Reliance on post-filter ACT with target values between 200 and 250 s and/or a post-filter iCa value between 0.3 and 0.4 mmol/l appears appropriate based on a subjective risk/benefit ratio. Both measures are associated with considerable variance that may represent ill-defined interactions with citrate. Hence, neither shows obvious superiority over the other. But monitoring remains warranted for patient safety in order to prevent citrate intoxication.
02/015-Citrate Pharmacokinetics and Metabolism in Cirrhotic and Noncirrhotic Critically Ill Patients

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Background: Regional anticoagulation with sodium citrate minimizes bleeding risk and improves biocompatibility of extracorporeal blood detoxification. Critically ill patients are at increased risk of bleeding and could benefit from citrate anticoagulation. However, citrate is primarily metabolized by the liver and its accumulation can cause life-threatening ionized hypocalcemia. Aims: To investigate citrate pharmacokinetics and metabolism in critical illness. Patients: Critically ill cirrhotic (n = 12) and noncirrhotic patients (n = 10). Methods: Serial analysis of blood samples obtained during and after a 2-hour infusion of trisodium citrate (0.5 mol/kg/h) and calcium chloride replacement (0.17 mol/kg/h). Results: Cirrhotic and noncirrhotic patients had similar baseline citrate levels (0.10 vs. 0.09 mmol/l, mean, p = 0.92) and similar steady state volumes of distribution (25 vs. 23 l, p = 0.72). In cirrhotic patients, AUC (citrate) was increased (211 vs. 129 mmol*min/l, p = 0.008) and clearance was reduced (378 vs. 710 ml/min, p = 0.04). Changes in pH were not different. Citrate clearance was correlated with renal function only in cirrhotic patients suggesting that the kidney significantly contributes to citrate elimination in cirrhosis. Marginally lower ionized calcium levels in cirrhotic patients were not associated with clinical complications. A total/ionized calcium ratio 12.5 was not able to predict increased citrate levels. Conclusions: Relative to noncirrhotic patients, citrate clearance in critically ill cirrhotic patients was reduced to 54%. Metabolic effects, however, were not different between groups and no complications occurred. Provided dose adaptation and monitoring of ionized calcium, citrate anticoagulation seems feasible even in advanced cirrhosis.
02/016-Trisodium Citrate Combined with Low Dosage of Low-Molecular-Weight Heparin Anticoagulation in Continuous Venovenous Hemofiltration

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Objective: Although regional citrate anticoagulation may be effective in maintaining patency of extracorporeal circuit during continuous venovenous hemofiltration (CVVH), clotting events are inevitable in sometimes and life span of hemofilters is not as long as expected. A new protocol of regional citrate combined with low dosage of low molecule weights heparin (LMWH) for anticoagulation was proposed and the effectiveness and safety was evaluated in this study. Methods: Forty patients who received CVVH treatment and at high risk of bleeding were subgrouped as A (n = 20) and B (n = 20) according to anticoagulation regime. Patients in group A were anticoagulated with only citrate at a rate of 0.4 mmol/min and with i.v. supplement of calcium and magnesium, patients in Group B were anticoagulated with a loading dose of 2,000 IU and sustaining infusion of 200 IU/h LMWH in addition to citrate anticoagulation. Systemic and post-filter whole blood activated clotting time (WBACT), serum ionized calcium and arterial blood gas analysis were performed at the start, 4 h and the end of CVVH in each patient group. Every filter's life span was recorded. Results: There were no complains with the application of citrate anticoagulation in all patients. No worsened bleeding tendency was observed in each group. Blood gas analysis showed a slight increase in PH and BE values during CVVH (pH from start 7.35 B 0.04 to end 7.41 B 0.05; base excess from start –4.32 B 0.97 to end –0.53 B 0.45, p < 0.01). Serum ionized calcium levels were kept beyond 1.0 mmol/l in all patients (from start 1.21 B 0.45 to end 1.09 B 0.78, p 1 0.05). Systemic WBACT varied little in group A during CVVH (from start 105.6 B 53.0 s to end 107.8 B 68.7 s, p 1 0.05), and prolonged a little in group B (from start 110.3 B 62.3 s to end 135.4 B 70.1 s, p < 0.01). A great prolongation of post filter WBACT was found in group A (190.9 B 50.9 s, p < 0.01), and it was greater in group B (520.5 B 105.8 s, p < 0.001). Mean life span of filters in group B was 55.3 B 12.5 h and is much longer than that in group A (32.3 B 7.1 h, p < 0.01). Conclusion: A slight prolonged systemic WBACT may not lessen the attractiveness of the applying of the present new anticoagulation protocol because of its satisfactory anticoagulation effect.
02/017-Anticoagulation Efficacy and Safety with a Low-Molecular-Weight Heparin – Tinzaparin in Continuous Renal Replacement Therapies

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One of the most drawbacks of CRRT is anticoagulation. Excessive anticoagulation determines bleeding complications, whole circuit clotting decreases dialysis effectiveness, increases blood loss and transfusion necessity. The aim of the study was to evaluate efficacy and safety of tinzaparin as anticoagulant for extracorporeal circuit in CRRT. The optimal necessary dose of tinzaparin was examined in 8 CRRT sessions, 5 CVVHDF (Qb = 134 ± 15.7 ml/min, Qd = 35 ± 7 ml/min, minimal UF = 500 ml/h, total time = 120.5 h) and 3 CVVH (Qb = 150 ± 13 ml/min, minimal UF = 500 ml/h, total time = 72.5 h) in 5 patients (M = 4, F = 1, mean age = 51.78 ± 8.9 years, BW = 60 ± 15.3 kg) with ARF and associated comorbidities. Anticoagulant efficiency was measured by absence or presence of clinical and pressure signs of clotting in dialyzer or extracorporeal circuit. Mean dose of tinzaparin was 540.3 ± 114.2 iuAXa/h (range 400– 800). Overall, tinzaparin proved a satisfactory anticoagulation regime for all patients. In all patients clinical signs of clotting in dialyzer or lines during the CRRT sessions were absent. In 3 patients it was necessary to change the dose of tinzaparin in the first 5 h of CRRT sessions to prevent clotting, using pressure values. In 1 patient minor hemorrhages (hemoptysis) appeared during CRRT session. No major hemorrhages appeared. Other adverse events due to tinzaparin (thrombocytopenia) did not occur during the study. In conclusion, tinzaparin in CRRT has an excellent anticoagulant effect, preventing clotting in dialyzer and extracorporeal circuit, without major adverse events, in spite the long-time utilization of the drug during the procedure.
02/018-Argatroban Anticoagulation during Renal Replacement Therapy

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*University of Chicago, Chicago, Ill., USA*

Background: Argatroban is a synthetic direct thrombin inhibitor, FDA-approved for anticoagulation in patients with heparin induced-thrombocytopenia and thrombosis. The recommended initial dose is 2 lg/kg min, reduced to 0.5 lg/kg/min in the presence of hepatic impairment. No dose reduction has been recommended in patients with renal impairment. Aim: 1. To determine the Argatroban dose requirements in patients with severe renal failure. 2. To determine the efficacy of Argatroban as an anticoagulant during renal replacement therapy (RRT). Methods: We conducted an IRB approved retrospective study of 7 hospitalized patients with renal failure requiring RRT (6 ESRD and 1 ARF). The 6 ESRD patients received a total of 47 intermittent hemodialysis treatments (IHD) while anticoagulated with Argatroban. The ARF patient received 1 IHD and 11 days of continuous venovenous hemofiltration (CVVH) on Argatroban. We compared the initial and maintenance Argatroban dose requirements for these patients. We also reviewed the dialysis and clinical records of these patients to discern the efficacy of anticoagulation during RRT, and any overt bleeding complications. Results: In this study we found that the mean starting dose of Argatroban was 0.9 ± 0.3 (SD) mcg/kg/min. The mean maintenance Argatroban dose was 0.70 ± 0.43 lg/kg/min, attaining a mean PTT of 56.4 ± 8.5 s and a mean PT of 19.3 ± 1.7 s, values 1.8-fold and 1.2-fold increased from baseline, respectively. These patients received a total of 48 IHD treatments while receiving Argatroban with only 4 episodes of circuit clotting (8%). During CVVH the mean filter time was 44 ± 33 h. Conclusions: 1. Argatroban appears to be a safe and effective anticoagulant during renal replacement therapy. 2. Patients with severe renal failure receiving renal replacement therapy may require Argatroban doses significantly below 2 lg/kg/min for therapeautic anticoagulation (PTT of 1.5- to 2.0-fold above the baseline value). Prospective studies should be conducted to establish the optimal dose of Argatroban for anticoagulation during IHD and CRRT.
Dialysis solutions used for CVVHD can be bicarbonate based (Normocarb®; Dialysis Solution Inc [DSI], Richmond Hills, Ont., USA) or pharmacy produced or lactate based (Hemofiltration Solution, Deerfield, Ill., USA). Data has shown that bicarbonate based solutions result in improved hemodynamics and less clinical lactic acidosis. Pharmacy produced solutions have been used as a substitute for lactate based solutions but are at risk of being more costly due to personnel cost of production and have a relative risk of human error with immediate patient effect and additive (unknown) physician and hospital liability. Historically this program used lactate based solutions but transitioned to pharmacy made bicarbonate based solutions initially produced by pharmacy but since December 2000 has used Normocarb® exclusively for CVVHD in 1200 patient days on pediatric CVVHD. Patient cost comparison of each find the cost of Baxter Hemofiltration Solution (USD 30.45/bag) vs. pharmacy produced (USD 29.38/bag) vs. DSI Normocarb® (27.06/bag). Pharmacy time to prepare each is Baxter Hemofiltration Solution (3 min/bag) vs. pharmacy produced (45 min/bag) vs. DSI Normocarb® (5 min/bag). Whereas DSI Normocarb® and Baxter Hemofiltration Solution have industry standard quality control, the pharmacy made solution lacks quality control and adds in an unknown but true liability cost to both physicians and hospital. Comparison of the two industry produced solutions identifies the difference is that DSI Normocarb® is bicarbonate based and calcium free whereas the Baxter Hemofiltration Solution is lactate based. Normocarb® allows for ease of use with citrate anticoagulation or calcium can be added if needed when heparin or no anticoagulation is preferred. In conclusion, with the availability of DSI Normocarb®, one can use a physiologic bicarbonate based solution with either citrate or heparin anticoagulation that has industry quality assurance maximizing the physiologic benefit to the patient and minimizing physician and hospital liability. Further cost of DSI Normocarb® is marginally better then the Baxter Hemofiltration Solution and certainly better as compared to pharmacy produced.
02/020-Efficacy and Safety of Nadroparine as Anticoagulant Therapy in Continuous Venovenous Hemofiltration

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Purpose: Nadroparine is a low-molecular-weight heparin (LMWH) we recently use instead of unfractionated heparin (UH) as anticoagulant therapy during continuous venovenous hemofiltration (CVVH). Laboratory monitoring of LMWH is not possible, there is accumulation in renal failure and no antidote is available. We looked at the used dose of nadroparine in terms of efficacy and safety. Methods: 15 patients receiving CVVH were retrospectively analysed. CVVH was only started in haemodynamic unstable patients. The standard procedure for anticoagulation was a fixed dose of 0.6 ml nadroparine (15,000 U. Axa.I.C.) at the start of CVVH via the arterial line followed by a bolus of 0.3 ml (75,000 U. Axa.I.C.) every 4 h. The method used for CVVH was standardized in all patients. The hemofilter was changed every 48 h. The hemorrhagic risk before starting CVVH was estimated as high, intermediate and low by defining the concomitant medication, recent surgery or trauma, PT, aPTT and platelets. The primary endpoints were time before filter clotting (efficacy) and the hemorrhagic events (safety) defined as none, trivial (bruising, secretions, ecchymoses) and significant (need for transfusion, intervention or change of dose of nadroparine or death caused by bleeding). Results: The hemorrhagic risk was estimated as low in 4 patients, intermediate in 7 and high in 4 patients. Filter clotting occurred in 8 patients. The mean clotting time was 17 h (range 4–35 h). In 4 patients there was a combination of clotting and bleeding. In 10 patients no hemorrhagic event occurred; 2 of them had a high and 3 an intermediate hemorrhagic risk. In 2 patients the bleeding was trivial. In 3 patients treatment resulted in a significant bleeding with death as result. Conclusion: Nadroparine couldn’t prevent clotting or bleeding in more than half of our patients. In a fourth of the patients there was even clotting and bleeding in the same patient. In half of the patients there was clotting of the hemofilter after a variable short time. In a third of the patients there was a trivial or significant bleeding. All patients with a significant bleeding died. They all had an intermediate or high hemorrhagic risk. In patients with trivial and high hemorrhagic risk at the start of CVVH a lower dose of nadroparine or even other anticoagulant therapy (UH, citrate) should be considered. A lower risk for bleeding is preferred to a higher risk for clotting by using a lower dose of nadroparine.
02/021-Establishing a Continuous Renal Replacement Therapy (CRRT) Program in a Small Hospital Setting

Wendy E. Yemec, Maureen M. Flenard, Dale P. Smith, Janae M. Riddle, Holly H. Hall, Jon H. Mobley, Mariah T. Lowry, Deb Kerr, Lori J. Otterstrom, Nicholas R. Loon

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CRRT is used to treat unstable patients with acute renal failure (ARF) almost exclusively in large tertiary care facilities. Patients with a similar diagnosis in smaller hospitals are often too unstable to transfer or be treated with standard hemodialysis (HD). Thus there is a need to make available CRRT in small hospitals. We studied the feasibility of establishing such a program in our hospital that has a capacity of 93 total and 12 intensive care unit (ICU) beds. The hospital is 1 h driving distance from the nearest tertiary care facility. In the first eleven months of 2001, 98 inpatients received a discharge diagnosis of acute renal failure (ARF). 46 patients received HD for a total of 184 individual treatments during this time. In January 2001 we established a core of 8 ICU staff nurses led by a clinical nurse specialist and a solo private practice nephrologist. We modeled our program after a well-established CRRT program in a large tertiary care hospital. Only continuous veno-venous hemofiltration (CVVH) was used with a Baxter BM-25 machine. The replacement fluid contained citrate given pre-filter with regional anticoagulation, adding calcium gluconate post-filter. A femoral vein dual-lumen hemodialysis catheter was the preferred method of access. Standard orders were developed and training done on-site by a nurse specialist provided by Baxter. This nurse specialist was present at the initiation of our first CVVH treatment and available for telephone consultation on subsequent therapies until competence and confidence were attained. In the first eleven months of the program, we have performed CVVH on five patients with established ARF. Three patients were hemodynamically unstable due to sepsis (n = 2) and cardiogenic shock (n = 1), and two were hemodynamically stable but oligo-anuric, requiring a large daily fluid removal. The range of CVVH duration was 1–8 days, mean 3.5 days, and three patients received preceding and/or subsequent HD. No major complications were seen as a result of the CVVH, but a 24-hour delay initiating therapy in two patients was due to staffing problems. Four patients recovered renal function sufficient to discontinue dialysis therapy and were discharged home from hospital. The fifth patient withdrew from subsequent HD treatments due to a terminal malignancy and died in hospital. In conclusion, we believe there is a need and it is feasible to establish a successful CRRT program at less than 100-bed hospitals in rural communities, this despite a relatively small number of suitable patients. Advance planning, training and a dedicated nursing and medical staff are imperative. Gradual progression to more complicated patients and support from highly trained off-site specialists assures success. CRRT as an alternative therapy to hemodialysis in selected patients in this setting may provide improved outcomes.
02/022-Enhanced Clearance of Fluconazole during Sustained Low-Efficiency Dialysis

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Purpose: To report a case with increased clearance of fluconazole during sustained low-efficiency dialysis (SLED). Methods: Case report: A 41-year-old African American male was previously a chronic peritoneal dialysis (PD) recipient due to end stage renal disease secondary to hypertension. The clinical picture was indicative of peritonitis. All cultures were negative. Thus, fungal peritonitis was suspected. Fluconazole was started at an oral dose of 100 mg daily. During this time, the patient was no longer on PD, but was started on SLED therapy with dialysate flow rate of 500 ml/min for 8 h. After one week of fluconazole treatment, fluconazole was changed to intravenous 200 mg daily due to patient's vomiting problem and no clinical improvement. Adequacy of fluconazole therapy was evaluated at this point. Fluconazole blood levels were obtained 2 h before dialysis and two-and-half hours after dialysis to assess fluconazole pharmacokinetics during SLED. Results: The level drawn before SLED was 2.7 ìg/ml, and post-dialysis level was 1.3 ìg/ml. The clearance of fluconazole from SLED in this patient was 103.7 ml/min. The clearance due to SLED is almost three-fold the clearance estimated in non-renally impaired patients (36.7 ml/min, based on population pharmacokinetics estimation) and is about five-fold the clearance during continuous arteriovenous hemofiltration (22 ml/min, literature report value). Conclusion: It is apparent that SLED increases the clearance of fluconazole. We conclude that a dose of at least 200 mg daily of fluconazole should be given after SLED therapy.
02/023-Pharmacokinetics and Pharmacodynamics of Pipericillin/Tazobactam during Continuous Veno-Venous Hemodiafiltration in Critically Ill Patients

Patrick R. Mayo, Irvin Mayers, Patrick S. Robertson, R.T. Noel Gibney, W.Dat Chin, Barb Litwinowich, Concetta Carbonaro, Margo Miller

University of Alberta, Edmonton, Alta., Canada

Introduction: A paucity of data exists on the pharmacokinetics and pharmacodynamics of antimicrobial drugs during CVVHDF. Methods: Patients requiring both CVVHDF and pipericillin/tazobactam were recruited for the study. The dose of pipericillin/tazobactam was 2.25 g i.v. q6h and the patient had to have received 3 doses prior to pharmacokinetic sampling. A total of 12 pre- and post-filter blood samples were drawn over the 6 h dosing interval to determine the drug pharmacokinetics. In addition, 6 dialysate samples were also drawn to determine drug clearance. The samples were assayed for pipericillin using a previously published HPLC assay. Tazobactam analysis is pending. To date, 8 patients have completed the study. Mean age, weight, height and APACHE II scores were 65.8 ± 14.0 years, 74.9 ± 13.2 kg, 173.7 ± 11.2 cm and 22.8 ± 3.9 respectively.

Results: Pharmacokinetics

<table>
<thead>
<tr>
<th>$t_{1/2}$, h</th>
<th>$\lambda$, h$^{-1}$</th>
<th>AUC mg·h/l</th>
<th>CL ml/min</th>
<th>$C_{max}$ mg/l</th>
<th>Vss, l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>4.4</td>
<td>0.1642</td>
<td>497.30</td>
<td>54.023</td>
<td>126.3</td>
</tr>
<tr>
<td>SD</td>
<td>1.1</td>
<td>0.0348</td>
<td>262.74</td>
<td>31.65</td>
<td>65.9</td>
</tr>
</tbody>
</table>

Pharmacodynamics: Time > MIC: *Pseudomonas aeruginosa* = 12.6 h. Time > MIC: Enterobacter spp = 8 h.

Conclusions: The half-life of pipericillin is four times normal during CVVHDF. Total body clearance is 54 ml/min suggesting a dose of 3.375 g i.v. q8h or 2.25 g i.v. q6h should achieve acceptable bactericidal concentrations in susceptible organisms. Tazobactam concentrations are pending to determine if the drugs remain in an 8:1 synergistic ratio.
02/024-Pharmacokinetics and Pharmacodynamics of Ciprofloxacin during Continuous Veno-Venous Hemodiafiltration in Critically Ill Patients

Patrick R. Mayo, Irvin Mayers, Patrick S. Robertson, R.T. Noel Gibney, W.Dat Chin, Barb Litwinowich, Concetta Carbonaro, Margo Miller

University of Alberta, Edmonton, Alta., Canada

Introduction: A paucity of data exists on the pharmacokinetics of antimicrobial drugs during CVVHDF.

Methods: Patients requiring both CVVHDF and ciprofloxacin were recruited for the study. The dose of ciprofloxacin was 400 mg i.v. q24h and the patient had to have received 3 doses prior to pharmacokinetic sampling. A total of 12 pre- and post-filter blood samples were drawn over the 6 h dosing interval to determine the drug pharmacokinetics. In addition, 6 dialysate samples were also drawn to determine drug clearance. The samples were assayed for ciprofloxacin using a previously published HPLC assay. To date, 4 patients have completed the study. Mean age, weight, height and APACHE II scores were 55.3 ± 12.3 years, 81.5 ± 3.0 kg, 174.3 ± 17.2 cm and 21.0 ± 1.8 respectively. Serum creatinine before and after CVVHDF was 353.8 ± 110.1 and 167.7 ± 116.3 ìmol/l (p < 0.05, paired t test).

Results: Pharmacokinetics

![Pharmacokinetics Chart]

Conclusions: The half-life of ciprofloxacin is three times normal during CVVHDF. Total body clearance is 53.7 ml/min. The Cmax/MIC ratio for pseudomonas is lower than the suggested ideal of 8. Therefore if an elevated volume of distribution is suspected a dose of 600 mg i.v. q24h may be required.
02/025-Adequacy of Renal Failure Support by Retrospective Analysis of Circuit ‘Off Time’ in Patients Treated with CRRT in the Intensive Care Unit

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Introduction: Continuous renal replacement therapy suggests a treatment without interruption. In turn it may be expected that urea and creatinine levels would reduce and or stabilise in the critically ill. Interruptions to treatment occur as a result of filter clotting and or other procedures in the ICU. Furthermore this filter off time can be a measure of nursing expertise and staffing patterns providing CRRT in the ICU setting. Patients: Critically ill adults, tertiary referral ICU. Objectives: To ascertain the actual percentage of possible operative time for CRRT and to assess for any correlation between this and adequacy of renal failure support evidenced by delta urea and creatinine. Methods: All patients were treated with continuous venovenous hemofiltration, at 2 l/h of ultrafiltration. Coagulation was generally achieved with heparin administered prefiltet. Filter functional life was documented for each CRRT circuit as progressive cumulative hours of operation. This meant that the time off treatment could be calculated for each 24-hour period. These data were then correlated with the delta urea and creatinine over this time. Results: 85 days of CRRT treatment was assessed in 3 female and 1 male patients, average age 51 years. The filter off time for this period was 20% or 4.8 h without treatment per day. There was a strong correlation between filter off time and delta urea (p < 0.0001) and creatinine (p < 0.0066). Conclusion: There is a strong correlation between time without treatment with CRRT and solute control. A comparison for this percentage of off time between facilities may be useful in determining what is optimal operative time for CRRT.
02/026-A Comparative Analysis of Regional Citrate Anticoagulation Techniques in Continuous Renal Replacement Therapy (CRRT)

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Introduction: Regional citrate anticoagulation (RCA) is increasingly utilized as the preferred method of anticoagulation for CRRT as it avoids systemic anticoagulation and prolongs filter lifespan. However, the use of RCA may be complex and lead to metabolic alkalosis, hypocalcemia, or hypernatremia. Following the initial description of this technique over a decade ago, new protocols for RCA have been published recently. We performed a comparative analysis of these methods to determine what modifications have been used, and their efficacy in maintaining patency of the extracorporeal circuit and the incidence of complications. Methods: The published literature and all abstracts from previous sessions of the International Continuous Renal Replacement Therapies Conference over the last 6 years were reviewed for any reports of citrate anticoagulation in adults on CRRT. Abstracts containing data that had previously or subsequently been published were excluded. When available, we recorded the modality of CRRT and its operational characteristics, the method of administering and titrating citrate anticoagulation, mean filter lifespan, dialyzer clearance, and incidence of side effects. Results: 18 studies were identified and 12 were selected for this review. Studies were classified based on the operational characteristics of CRRT. As shown in the table, 275 patients representing over 36,000 h of experience with RCA were identified. A review of protocols revealed 10 different protocols have been described for all CRRT techniques.

Acid citrate dextrose solution A (ACD-A) has been studied only with CVVHDF and represents 3 of the studies and 79 of the patients in the table. An accurate assessment of the rate of complications between the different protocols was not feasible due to the various definitions employed for the occurrence of hypocalcemia and metabolic alkalosis. Conclusions: Regional citrate anticoagulation for CRRT is now
widely available and is used for hemofiltration, hemodialysis and hemodiafiltration techniques. Modifications include: a) site of citrate delivery (separate prefilter infusion or replacement fluid) b) concentration of citrate solution used c) form of citrate employed (TSC or ACD-A) d) method of titrating citrate dose (postfilter ACT or ionized calcium) e) dialysate and replacement fluid composition. Despite variations in the methodology, all techniques avoid systemic anticoagulation and the majority report an improved filter lifespan compared to heparin. Disadvantages include various levels of complexity, risk of hypocalcemia and metabolic alkalosis. There has been no direct comparison of these methods and it is difficult to compare the efficacy of these techniques since there is no standard method of reporting filter performance or complications. It would be helpful to establish a registry of citrate anticoagulation for CRRT to prospectively evaluate the effectiveness of this technique.
02/027-Metabolic Parameters in 30 Patients Treated with CRRT using Regional Citrate Anticoagulation

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Background: A large number of patients in the intensive care unit who require continuous renal replacement therapy have absolute or relative contraindications to systemic anticoagulation. Citrate regional anticoagulation is now commonly used in many centers as the preferred method of dialysis circuit anticoagulation. Hypernatremia, metabolic alkalosis, and citrate accumulation have been reported metabolic complications associated with this therapy. We present a single center experience with a citrate anticoagulation protocol. Methods: An observational study of all patients admitted to a medical/surgical ICU at a single tertiary care hospital over a sixmonth period who were treated with CRRT using regional anticoagulation with 4% trisodium citrate (TSC). All patients had demographic and dialysis data collected prospectively. Chart reviews were done to retrieve the blood work that was not initially monitored. All patients were followed until death or discharge. The patients were analyzed as a whole group and then divided into subgroups of survivors, non-survivors and those with hepatic dysfunction as an admitting diagnosis. All patients except one, treated with CVVH, received CVVHDF. Gambro Prisma machines with M100 AN 69 filters were used in pre-dilution mode. The regional citrate anticoagulation protocol used at this institution has been previously published and will not be described in detail here. Anticoagulation was monitored using circuit and serum ionized calcium levels. Citrate accumulation was measured by monitoring the difference between serum total calcium and serum ionized calcium levels (calcium gap). Results: Sepsis was the admitting diagnosis in 80% of the patients, the remainder were admitted with pancreatitis (2/30), hepatic failure (2/30), and respiratory failure (2/30). 37% of patients were intubated when CRRT was initiated. All patients were vasopressor dependent. Demographic information and results are displayed in chart form. The average highest and lowest values for serum sodium, calcium, and bicarbonate levels during CRRT treatment are recorded.
Conclusion: Despite the significant base and sodium load associated with citrate based regional anticoagulation, no significant sodium or acid/base disturbances were observed in the patients who received CRRT. The calcium gap was moderately increased in patients with liver disease, however clinically significant ionized hypocalcemia was not observed.
02/028-Development of a Profitable Continuous Renal Replacement Program That Improves Patient Care and Outcomes

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Introduction: Critically ill patients encounter many obstacles, such as acute renal failure, that will increase their length of stay as well as their hospital cost. Since many of these patients develop multi-system organ failure and will succumb to their disease, significant medical resources are exhausted while tremendous costs are incurred for both the patient and the hospital. Dialysis in these patients is often ineffective thereby prolonging the inevitable and significantly increasing the cost of care. A dialysis program that could improve patient care and outcome while improving revenue capture would be ideal.

Methods: An in-house continuous renal replacement therapy (CRRT) program was developed. The goal of this program was to have a significant impact on the medical care of critically ill burn, trauma and surgical patients. Using the latest technology in CRRT equipment, along with an innovative hands-on CRRT training program for nurses and physicians, a specialized CRRT team was created. Working in conjunction with the hospital business office, new revenue charge codes were created and existing codes were updated. All patients that underwent CRRT had their financial records reviewed for the following elements: hospital cost to perform CRRT including nursing time, total hospital units billed to the payer source, CRRT revenue 881 (billing units) charged to the payer source, total account charges, total reimbursement for the account, percentage of reimbursement, collected CRRT revenue, and payer source.

Results: In the past 13 months, CRRT has been performed on 30 critically ill patients including 20 burn, 4 surgical, 3 trauma, 1 cardiology, 1 pediatric, and 1 neonatal patient. Overall patient care improved as evidenced by a survival rate of 43.3% (13/30). The cost of CRRT for all patients was USD 147,002, which included all CRRT disposables, hospital and pharmaceutical supplies and nursing time. The revenue of 881 billable units was USD 295,395, overall collections were USD 152,604, with an average reimbursement percentage of 40.1%. Interestingly, the burn patients had a significantly higher average reimbursement percentage of 62.1%, which produced a net profit of USD 46,453. Payer sources that demonstrated the highest reimbursement included workman's compensation and private insurance companies.

Conclusions: An in-house CRRT program provided for improved patient care and outcomes and was extremely cost-effective. Hospitals that provide intensive care to a large population base should consider the development of their own CRRT program.
02/029-Continuous Venovenous Hemofiltration as a Bridge to Liver Transplantation

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Purpose of the Study: To study the efficacy of CVVH as a bridge to liver transplantation among critically ill patients with combined hepatic and renal failure. Methods: We cross-matched the list of patients who received CVVH with the list of patients awaiting liver transplant at the MGH between 1997 and 2001. Records of all patients that were simultaneously on both lists were reviewed for: days on CVVH; anticoagulation method and patency of the CVVH circuit; control of extracellular fluid volume and metabolic parameters; successful bridging to transplant; renal recovery and survival. Results: Thirteen patients received CVVH for acute renal failure (ATN or hepatorenal syndrome) while actively awaiting liver transplant. Additional patients received CVVH in the hope of subsequent listing or relisting for liver transplant, but were not considered suitable liver transplant candidates at the time they received CVVH and therefore were not included in the study. CVVH was performed for an average of 3.24 days per patient. Eleven patients received a bicarbonate-based replacement fluid (RF) without the use of anticoagulant and one patient received bicarbonate with heparin. Two patients received regional citrate anticoagulation using a citrate-based RF, one due to clotting without the use of heparin and one due to thrombocytopenia associated with heparin. The average filter life was 17.8 ± 12.9 h. An average of 13.7 liters of fluid per patient was removed allowing for unlimited amounts of blood products, nutrition support and medications. Patients received a mean of 6 units of PRBCs, 30 units of platelets and 16 units of FFP while on CVVH. Table 1. Effect of CVVH on metabolic parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Onset of CVVH</th>
<th>End of CVVH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine, mg/dL</td>
<td>5.2</td>
<td>2.8</td>
</tr>
<tr>
<td>Urea, mg/dL</td>
<td>80</td>
<td>38</td>
</tr>
<tr>
<td>Potassium, mg/L</td>
<td>4.2</td>
<td>3.5</td>
</tr>
<tr>
<td>Bicarbonate, mmol/L</td>
<td>19.3</td>
<td>24.5</td>
</tr>
<tr>
<td>Anion gap, mmol/L</td>
<td>18.0</td>
<td>13.5</td>
</tr>
<tr>
<td>Total Ca**, mg/dL</td>
<td>8.8</td>
<td>9.9</td>
</tr>
<tr>
<td>Ionized Ca** mmol/L</td>
<td>1.03</td>
<td>1.08</td>
</tr>
<tr>
<td>Phosphorus, mg/dL</td>
<td>6.4</td>
<td>3.6</td>
</tr>
<tr>
<td>Ammonia, μmol/L</td>
<td>97</td>
<td>34</td>
</tr>
<tr>
<td>Total bilirubin, mg/dL</td>
<td>17.9</td>
<td>20.3</td>
</tr>
<tr>
<td>PT, s</td>
<td>19.7</td>
<td>18.8</td>
</tr>
</tbody>
</table>
Eleven of the 13 patients (85%) underwent liver transplantation of whom 8 (72.7%) were alive at the end of 1 year. All 8 patients recovered renal function. Two patients did not undergo liver transplantation. One of the two developed systemic infection and was taken off the transplant list and subsequently died, while the other (acetaminophen overdose) recovered liver and kidney function and survived. Conclusion: CVVH provides effective control of fluid balance and metabolic parameters and appears to be an effective bridge to liver transplant among critically ill patients with combined hepatic and renal failure.
02/030-Does Length Matter? Survival Rates in Pediatric Patients Requiring Prolonged Continuous Renal Replacement Therapy (CRRT)

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Survival rates of patients receiving CRRT have been reported as being between 40 and 45% in both children and adults. Factors reported to affect patient survival include primary disease, need for pressor support, and degree of volume overload prior to initiation of therapy. The length of time on CRRT has not been reported as a prognostic factor, although available data is limited. Objective: To determine if the survival rate of pediatric patients receiving CVVH 614 days is similar to that of pediatric patients receiving fewer days of therapy. Methods: A retrospective analysis of all pediatric patients receiving CVVH at the University of Michigan Medical Center was performed using a previously established database of all patients receiving renal replacement therapy at our center. Data collected included sex, age, year of treatment, primary diagnosis, indication for dialysis, type of replacement therapy (RRT), duration of therapy, use of anticoagulation, use of pressors, survival, and recovery of renal function. Complications were also noted. Inclusion criteria was an available complete data set. Statistics performed using routine descriptive methods. Results: From 1990 to 1998, 380 pediatric patients received some form of RRT, with 118 patients receiving CRRT. 116 patients had a complete data set and were included for the purpose of the study. Of these, 20 (17%) patients were on CRRT for 14 or more days. The demographics of this subset of patients compared to the overall patient population are seen in the table.
There was no difference in the survival rate of patients requiring therapy for 614 days compared to those with a shorter length of treatment. There was also no difference in renal survival between these patient subsets, with 23% of patients requiring CRRT for 114 days recovering renal function prior to hospital discharge v. 26% of patients having shorter length of treatment. Conclusion: Length of time on CRRT should not be used as a prognostic indicator for either patient or renal survival in pediatric patients undergoing CRRT.
02/031-Continuous Renal Replacement Therapies – Clinical Experience in an Intensive Care Nephrology Department

M. Voiculescu, C. Ionescu, G. Ismail, D. Micu, M. Rosu
Department of Internal Medicine-Nephrology, Fundeni Institute, Bucharest, Romania

Acute renal failure (ARF) treated by daily or intermittent hemodialysis is, in general, efficient, but the procedure has diverse adverse events due to associated comorbidities and unphysiological way of renal substitution. The aim of the study was to establish the role of CRRT in the treatment of ARF in patients admitted into a Nephrology Department. We performed CRRT in 20 patients with ARF from different etiology in patients with native kidney or renal transplant. In 16 cases (M = 8, F = 8, mean age = 43.2 ± 15.7 years, BW = 49 ± 7.5 kg, mean BP = 107 ± 16.6 mm Hg) we performed CVVHF and in 10 cases (M = 7, F = 3, mean age = 39 ± 9.9 years, BW = 55.5 ± 5.6 kg, mean BP = 104 ± 18.8 mm Hg) CVVHDF. 13 patients (65%) associated severe comorbidities: sepsis in 3 patients, coma in 4 patients, anasarca in 5 patients (1 patient hepatic cirrhosis, 1 patient cardiac failure and 4 patients nephrotic syndrome), CID in 1 patient. Mean period of CVVHF was 21.6 ± 11.3 h with a mean blood flow rate of 116.9 ± 16.4 ml/min and an ultrafiltration rate of 6.42 ± 4.6 ml/min. In CVVHDF mean period of procedure was 24.0 ± 8.5 h, mean blood flow 134 ± 15.2 ml/min and mean ultrafiltration rate 5.6 ± 2.1 ml/min. Vascular approach was by jugular vein in 14 patients, femoral vein in 6 patients. Anticoagulation was performed with UHF in 13 patients (in 2 patients without bolus and in 11 patients bolus with mean 1,666.6 IU at the start followed by continuos infusion with 500–1,500 IU/h in CVVHF and 500–1,200 IU/h in CVVHDF) and LMWH in 5 patients. In 1 patient anticoagulation was performed by repeated washback with saline solution. Renal function was recovered completely in 4 patients (20%), partially in 3 patients (15%) and 9 patients (45%) goes to chronic HD. Survival rate was 80% CRRT (4 patients died). Complications of procedures appear in 6/20 patients (30%) and were represented by cardiac events (hypotension in 2 patients, arrhythmia in 1 patient), bleeding disorders in 3 patients and dyselectrolithemias in 2 patients. In conclusion, continuous renal replacement therapy is efficient and well tolerated with a low frequency of adverse events.
02/032-Continuous Flow Peritoneal Dialysis (CFPD) in the ICU: Case Report

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A 60-year-old male diabetic with ESRD and severe peripheral vascular disease was treated with hemodialysis via a Permcath. He had two peritoneal catheters inserted for ultrafiltration of recurrent dialysis ascites. He was hospitalized for Pseudomonas sepsis and the Permcath was removed. Because of lack of adequate hemodialysis access, and hemodynamic instability, he was treated with CFPD. A Fresenius 2008H, in CRRT mode, was set up with conventional dialysis tubing and an Ultraflux AV400S hemofilter. The system was primed with heparinized saline. External dialysate was prepared online from purified tap water to a final concentration of potassium of 4 mEq/l, and calcium of 2.5 mEq/l. The dialysate flow was set at 300 ml/min. One liter of 1.5% dextrose Fresenius PD fluid was infused into the peritoneal cavity, in addition to an unmeasured amount of ascitic fluid. This fluid was recirculated at 300 ml/min through the external circuit. Ultrafiltration rate averaged 400 cc per hour. The treatment lasted 11.5 h. 3036 cc was the net ultrafiltration. Pre and post treatment blood chemistries were:

Two days later, the patient was still septic and had developed peritonitis. CFPD was resumed using 2 liters of 1.5% PD fluid after draining 2 liters of ascites. Treatment ran 12 h, with an ultrafiltration rate of 40 ml/h. Pre and post chemistries:

Extensive fibrin deposition was noted in the hemofilter after the treatment. The PD catheters were removed because of Gram(−) peritonitis. The patient returned to hemodialysis with a new Permcath and was eventually discharged. CFPD can provide effective solute and volume control in a critically ill patient in the ICU. Urea reduction ratios of 28% over 12 h are clearly superior to conventional acute PD. Additional heparin should prevent fibrin formation and improve clearances.
02/033-High Volume Hemofiltration in Critically Ill Patients: The Mayo Clinic Experience, 2000 to Present

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Over the last several years, there have been intriguing reports supporting utilization of high volume hemofiltration (HVHF) among critically ill patients with and without renal dysfunction. Theorized mechanisms accounting for improved survival include increased cardiac contractility and systemic vascular resistance. Continuous venovenous hemodiafiltration (CVVHDF) has dominated renal replacement therapy for critically ill patients at our institution. However, in cases of septic shock or systemic inflammatory response syndrome, practice patterns have varied. The goal of this study was to investigate our experience with HVHF with attention to patient characteristics, mortality, and renal recovery. In a retrospective fashion, we evaluated 15 patients who underwent HVHF, defined as 72 l/day of predilution substitution fluid, for greater than 24 h, taken from a cohort of 363 continuous renal replacement (CRRT) patients identified in our dialysis database from January 1, 2000 to present. Thirteen patients met criteria and their histories and dialysis records were reviewed. High volume hemofiltration was selected in 4% of cases treated with CRRT. Overall the HVHF cases averaged an APACHE II score of 30 ± 6.7. Clinically, sepsis and volume overload were the major indications for HVHF. All patients had renal dysfunction. Treatment duration averaged 3.6 ± 1.6 days and achieved clearances of approximately 84 ± 13.3 l/day. Overall survival at 30 days post HVHF was 38.4%. However, when treatment was initiated within 2 days of ICU admission, survival was 57% at 30 days post HVHF. Among survivors there was a 60% renal recovery at 30 days post initiation. Currently high volume hemofiltration accounts for a very small percentage of our CRRT program. In selected cases of critically ill patients with sepsis or volume overload, early initiation of high volume hemofiltration may offer a possible advantage for renal recovery and survival.
02/034-Outcomes in Patients Treated with CRRT using Regional Citrate Anticoagulation: A Single Center Experience

Neesh Pannu, Noel Gibney
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Background: A large number of patients in the intensive care unit who require continuous renal replacement therapy have absolute or relative contraindications to systemic anticoagulation. Citrate regional anticoagulation is now commonly used in many centers as the preferred method of dialysis circuit anticoagulation. We present patient outcomes using a citrate protocol developed at this institution.

Methods: An observational study of all patients admitted to a medical/surgical ICU at a single tertiary care hospital over a six month period who were treated with CRRT using regional anticoagulation with trisodium citrate (TSC). All patients had demographic and renal replacement therapy data collected prospectively. Chart reviews were done to retrieve the laboratory results that were not initially recorded. All patients were followed until death or discharge. The patients were analyzed as a whole group and then divided into subgroups of survivors, non-survivors and those with hepatic dysfunction as an admitting diagnosis. All patients except one, treated with CVVH, had CVVHDF. Gambro Prisma machines with M100 AN 69 filters were used in pre-dilution mode. The regional citrate anticoagulation protocol used at this institution has been previously published and will not be described in detail here.

Results: Thirty patients were studied. Sepsis was the admitting diagnosis in 80% of the patients (24/30). The others were admitted for pancreatitis (2/30), hepatic failure (2/30) and respiratory failure (2/30). 27% of the patients had a surgical procedure prior to developing renal failure. The mean age of all patients was 54 years and the patients were 60% male. The average SAPS II score on admission to the ICU was 67. Overall patient survival was 23%. The non-survivors were significantly older than the survivors (mean age 57 vs. 44 years) and had a higher SAPS II score (69 vs. 61). Dialysis dose was similar amongst survivors and non-survivors (31.9 vs. 37.7 ml/kg/h). Survival in the group with an admitting diagnosis of hepatic dysfunction was 30%, however patients with a previous diagnosis of cirrhosis who did not receive a transplant had 100% mortality (8/8). Acute liver failure had a good prognosis with 100% survival (2/2). Similarly, patients with a previous orthotopic liver transplant also had a better prognosis with a 50% survival (1/2). Citrate accumulation measured by a calcium gap was notably higher in the patients with cirrhosis as compared to the other patients (mean Ca gap 1.4 vs. 1.2 mmol/l). Patients with a serum bilirubin levels greater than 100 Î¼mol/l at the time of initiation of CRRT also appear to have a lower survival rate (20 vs. 25%).

Conclusion: Overall patient survival was 23%. Patients with endstage chronic liver disease and patients with serum bilirubin level 1100 Î¼mol/l have a particularly poor prognosis. Monitoring calcium gap for citrate accumulation is valuable in all patients receiving citrate regional anticoagulation for CRRT but mandatory in patients with significant hepatic dysfunction.
Continuous Renal Replacement Therapy for Rhabdomyolysis

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Standard treatment for rhabdomyolysis includes fluid resuscitation and mannitol/bicarbonate infusion. If therapy is delayed, acute renal failure ensues and morbidity is increased. Conventional dialysis may be required, but can be detrimental due to hemodynamic compromise. Continuous veno-venous hemodiafiltration (CVVHDF) utilizes ultrafiltration in order to effectively remove metabolic waste products while maintaining hemodynamic stability. Three patients with rhabdomyolysis that were treated with CVVHDF are discussed.

Case 1: A 60-year-old female developed a compartment syndrome of the left upper extremity. Serum creatinine phosphotase kinase (CPK) was 54,240 U/l and her creatinine (CR) was 3.0 mg/dl. Emergent fasciotomy revealed extensive necrosis and a guillotine amputation was performed. CPK decreased to 11,200 U/l, but the patient became anuric and profoundly septic necessitating CVVHDF. Within 12 h of CVVHDF, the pH had normalized, all vasopressors had been stopped, and CPK was 2,456 U/l. CVVHDF was utilized for 244 h and upon completion of therapy the CR was 1.3 mg/dl and urine output was 50–75 ml/h. At one-year follow-up she has no residual renal impairment and has a functional prosthetic arm.

Case 2: A 69-year-old white female sustained full thickness circumferential alkali burns to her left upper extremity. Physical examination revealed compartment syndrome and rhabdomyolysis. CPK was 15,623 U/l and CR was 0.7 mg/dl. Fluids and mannitol decreased the CPK to 2,252 U/l but her urine output decreased to 10–20 ml/h and CR increased to 2.2 mg/dl. She developed acute pulmonary edema and respiratory failure requiring 100% FiO2. CVVHDF was initiated for a total of 18 h and the CPK decreased to 310 U/l, the CR to 0.9 mg/dl and she was extubated within 3 days. One-year follow-up was unremarkable.

Case 3: A 40-year-old male presented in septic shock with a cold pulseless right lower extremity. White blood cell count was 30,000, lactic acid was 7.2, CR was 4.1 mg/dl, and CPK was 131,000 U/l. An emergent fasciotomy was performed and then a right above knee amputation. CVVHDF was initiated and within 2 days the CPK decreased to 21,000 U/l. CVVHDF was continued for 187 h, the patient was placed on conventional dialysis for 1 week but the CR increased to 8.0 mg/dl. CVVHDF was restarted for 114 h and at the end of therapy the CR was 1.1 mg/dl and the urine output was 150 ml/h. Six weeks later the patient was discharged to a rehabilitation center. In the setting of rhabdomyolysis, CVVHDF allows for rapid correction of acidosis and electrolyte abnormalities, removal of toxic metabolites, and precise control of fluid balance while maintaining hemodynamic stability. CVVHDF should be the mainstay of therapy for rhabdomyolysis when conventional methods fail, or if the patient develops significant acidosis or acute renal insufficiency.
Hantavirus pulmonary syndrome (HPS) is a devastating condition with no specific therapy and a high mortality rate. We report the use of continuous renal replacement therapy and activated recombinant protein C in the successful management of a case of severe HPS. A previously healthy 46-year-old female presented with a seven-day history of progressive fever, dry cough and progressive dyspnea. Her temperature was 39.3°C. Her chest radiograph showed dense bilateral airspace disease. Initial hemoglobin was 17.9 g/dl, white blood cell count 26,400 with 22% band forms. Platelet count was 53,000. INR was 1.2 and PTT 56 s. Serum sodium was 125 mmol/l, serum creatinine 128 Î¼mol/l (1.4 mg/dl) and serum urea 11 mmol/l (30.8 mg/dl). A diagnosis of severe community acquired pneumonia was made and she was commenced on azithromycin and cefotaxime. The findings of hemoconcentration, thrombocytopenia and dense bilateral airspace infiltrates were strongly suggestive of HPS. This suspicion was increased by family members stating the patient had found mouse droppings in her rural home two weeks earlier. She rapidly deteriorated with the development of severe dyspnea and hypoxemia and required endotracheal intubation and mechanical ventilation. Her- PaO2/FiO2 ratio was 69 and she was ventilated with tidal volumes of 6 ml/kg. Within hours, she developed progressive hypotension for which she received fluid resuscitation. This did not result in improvement in hemodynamic status but was followed by worsening hypoxemia. Norepinephrine infusion was then used for hemodynamic support. Invasive hemodynamic monitoring showed depressed cardiac output. An echocardiogram showed global right and left ventricular hypokinesis. EKG and cardiac enzymes did not demonstrate myocardial ischemia. Dobutamine infusion subsequently improved her cardiac output. She became anuric within 24 h of admission with elevation of serum creatinine to 210 Î¼mol/l (2.4 mg/ dl). APACHE II score in the first 24 h was 27. She was commenced on a 96-hour infusion of recombinant activated protein C (rAPC) at 24 Î¼g/kg/h for her severe septic shock and multiple organ failure. As her PCWP had risen to 21 mm Hg and she was anuric, she was treated with CVVH with 3 litres replacement fluid/h (25 ml/kg/h) and net fluid removal of 100 ml/h with no anticoagulant initially. Despite PTT rising to 98 s while receiving rAPC, the hemofilter clotted within 8 h on 2 occasions. Consequently, she was changed to CVVHDF with trisodium citrate anticoagulation. She had no bleeding complications during her therapy. Hantavirus antibody test was positive for IgM and negative for IgG for Hantavirus Sin Nombre strain. She was weaned off vasoactive medications on day 4. CVVHDF was also discontinued on day 4. She had return of urine output on day 6 and no further renal replacement therapy was required. Her gas exchange progressively improved and she was extubated on day 9. She was discharged home on day 13. HPS is a severe respiratory illness characterized by the rapid development of severe noncardiogenic pulmonary edema and shock, with a mortality rate of up to 54%. It is caused by the Sin Nombre species of Hantavirus, and is spread by inhalation of contaminated aerosols from deer mouse excreta. There is no specific therapy, as antiviral use has been disappointing. Supportive therapy involves avoidance of aggressive fluid resuscitation and
hemodynamic support with vasopressors, inotropes and even extracorporeal cardiopulmonary support. This case shows the value of continuous renal replacement therapy in minimizing fluid overload in HPS. It also demonstrates the use of rAPC in the successful management of HPS. While rAPC has significant anticoagulant activity this was not adequate to avoid hemofilter clotting during CRRT. If anticoagulation is required for CRRT during rAPC therapy, heparin is contraindicated and citrate anticoagulation should be considered.
02/037-Continuous Renal Replacement Therapy in Burn Resuscitation

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Introduction: Large volume resuscitation remains the standard for burn patients with extensive injury. Although advances in fluid resuscitation have decreased mortality, some patients will require extra fluids and vasopressors. Significant complications often develop ultimately increasing mortality. Modalities that could limit the need for excessive fluid and vasopressors would be ideal. Methods: Eight patients were reviewed who were initially treated with standard fluid resuscitation. Each patient quickly developed significant complications and demonstrated hemodynamic and/or ventilatory failure. Continuous renal replacement therapy (CRRT) was initiated as an adjunct therapy. Results: Eight patients, 5 females and 3 males, average age of 42 years, were admitted with an average burn size of 60%, and all had a diagnosis of inhalation injury. Within 72 h, all patients were treated using CRRT (table 1).

Patients 1–4 were eventually discharged, while patients 5–8 died, ultimately from complications of their extensive burns (average 85% TBSA). Using CRRT, all the patients maintained adequate arterial blood pressures, pulmonary wedge pressures at 14–18 mm Hg, pH at 7.30–7.45, while fluid infusion rates decreased. Moreover, respiratory status also improved with patients initially requiring 90–100% FiO2, and at the termination of CRRT, all patients were on a maximum of 60% FiO2. In the 4 survivors, urine output increased and creatinine levels decreased over the duration of CRRT, a trend not seen in the patients who died. Conclusions: Burn patients that demonstrate poor resuscitation often succumb to their injuries. In
these patients, CRRT maintains filling pressures, improves acid/base balance, increases urine output, even with decreased fluid intake. Pulmonary and renal function is improved leading to increased survival. In the significantly large burns, CRRT therapy has improved initial management but has not affected overall outcome.