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1 Energy Expenditure Pediatric Rhabdomyolysis with ARF

A. Katz, T.E. Bunchman

Pediatric Nephrology and Transplantation University of Alabama at Birmingham, USA

Energy expenditure and providing adequate calories during critical illness has continued to be a focus during ICU admissions. Acute critical illness and the underlying processes play a significant role in the degree of basal metabolism during the ICU period. Known hypermetabolic states; sepsis, multiple trauma/burns are well known to represent high energy basal requirements. Little is known of heat stroke/rhabdomyolysis requirements, but the common perception is that due to the skeletal muscle turnover, higher catabolism and probably metabolism is present. Yu FC, et al, have reported a lower RQ (respiratory quotient) in patients with exertional heat stroke associated with ARF (acute renal failure) as well as hypermetabolism. Although none of these patients were critically ill on artificial support at the time of the indirect calorimetry measurements. Acute renal failure by itself represents a hypercatabolic/metabolic state, with UNA of 170–180mg/kg/d in children and REE of 2,562kcal/d in adults. We report our REE by IDCM (indirect calorimetry measurement) of two patients with exertional heat stroke, rhabdomyolysis and ARF requiring artificial support for respiratory and renal failure. Energy needs estimated by the predicted basal metabolic rate (PBMR) using the Harris-Benedict equation correlated poorly with the measured resting energy expenditure by indirect calorimetry. In both patients, REE were 40% greater than the PBMR values. In patients with rhabdomyolysis and ARF, undernourishment may impede their recovery, and providing adequate nutrition a great challenge to the caregivers. Indirect calorimetry to measure REE appears more helpful is guiding nutritional support for these patients, who are hypermetabolic and very catabolic.

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Wt (kg)</th>
<th>PICU (day)</th>
<th>Mechanical Ventilation (day)</th>
<th>CRRT (day)</th>
<th>Intake (kcal/d)</th>
<th>PBMR (kcal/d)</th>
<th>REE (kcal/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>93</td>
<td>14</td>
<td>14</td>
<td>12</td>
<td>5,518</td>
<td>2,084</td>
<td>3,430</td>
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<tr>
<td>15.9</td>
<td>133</td>
<td>15</td>
<td>15</td>
<td>14</td>
<td>2,378</td>
<td>2,597</td>
<td>4,220</td>
</tr>
</tbody>
</table>
Outcome after Continuous Renal Replacement Therapy (CRRT) in a General ICU. A Seven Year Follow Up

M. Bell\textsuperscript{a}, C.-R. Martling\textsuperscript{a}, E. Liljestam\textsuperscript{a}, J. Fryckstedt\textsuperscript{b}, F. Granath\textsuperscript{c}, A. Ekbom\textsuperscript{c}

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Approximately 1,100 patients per year are treated at the multidisciplinary ICU at the Karolinska Hospital, Sweden. Admitting units are the departments of internal medicine and surgery; including urology, otorhinolaryngology, gynaecology and obstetrics. Karolinska Hospital is also the trauma referral centre of the greater Stockholm area (approximately $1.8 \times 10^6$ inhabitants). 8,151 patients were admitted to the ICU between 1995 and 2001. Two hundred thirty-four of these patients (2.9%) were treated with continuous renal replacement therapy (CRRT). The purpose of the study was to characterise the epidemiology of Acute Renal Failure (ARF) requiring CRRT. We sought to assess the ICU-, 28 day- and in-hospital mortality, as well as mortality six months after the start of treatment. Signs and patterns of acute and chronic disturbances of health were used in an attempt to quantify their impact on the course of ARF. Methods: This is a retrospective cohort study in which all patients admitted to our ICU between 1995 and 2001 were monitored. All CRRT patients were included in the study. Since 1994 we have used continuous veno-venous therapy (PRISMA, Hospal, France), as dialysis method. The modality used has been almost exclusively CVVHDF but in recent years the use of CVVH has become more frequent. The ICU database, designed mainly for internal auditing purposes, was used to document the indication for ICU admission, APACHE II score and major ICU interventions. In addition to this, a retrospective review of the patients’ files were carried out if they were subjected to haemodiafiltration. In these cases we investigated previous health status and the indication for dialysis. Criteria for failure of renal, cardiovascular, pulmonary, neurological, haematological, hepatic and gastrointestinal systems were originally described by Knaus and Wagner. Number of failing organs (OSF) was determined at the start of dialysis. By using the hospital database and the unique ten digit national registration number we were able to calculate the hospital mortality and also the mortality after six months. Results and Conclusions: Demographic data, indication for ICU admission, severity score and organ system failure at the start of CRRT were set against mortality. The ICU mortality was 32.9% and the mortality after 28 days was 42.7%. In-hospital mortality was 49.6%. Patients leaving the hospital had a lower mortality; 6 months after inclusion in the cohort the mortality was 57.7%. General measures of severity did not predict mortality of ARF requiring CRRT. Neither APACHE II nor the number of failing organs significantly differed between survivors and non-survivors. A seemingly protective effect was seen in the patients having hypertension. The reason for this is not known at the moment. Diabetes was overrepresented in non-survivors. When the group was stratified into early (0–14 days) and late (15–28 days) mortalities, significance was reached in the latter group. A Kaplan-Meier plot shows that the largest number of mortalities occurred during the very first days. Furthermore, patients surviving the hospital stay cannot be said to be without risk, but after 18 months the mortality is close to that of the general population. Kidney function of the survivors is currently being investigated.

<table>
<thead>
<tr>
<th>Non Survivors (28d)</th>
<th>Survivors (28d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean) 57.9 years</td>
<td>58.3 years</td>
</tr>
<tr>
<td>Sex (M/F) 63/37 (%)</td>
<td>70.9/29.1 (%)</td>
</tr>
<tr>
<td>Diabetes (N/Y) 81/19 (%)</td>
<td>87.3/12.7 (%)</td>
</tr>
<tr>
<td>Heart Failure (N/Y) 65/35 (%)</td>
<td>67.9/32.1 (%)</td>
</tr>
<tr>
<td>Hypertension (N/Y) 84/16 (%)</td>
<td>73.9/26.1 (%)</td>
</tr>
<tr>
<td>APACHE II (Mean) 24.3</td>
<td>21.7</td>
</tr>
<tr>
<td>OSF (Mean) 2.62</td>
<td>2.36</td>
</tr>
</tbody>
</table>

Product-Limit Survival Fit
Survival Plot

Time to event:
Time (months)
Censored by

Summary
Group N, Failed N, Censored Mean Std Dev
Combined 152 82 30.6968 Biased 2.62419

Quantiles
Group Median Lower Upper 25% 75% Failures Failures
Combined 1.4333 1.0333 4.7667 0.2667 0.2667
CRRT in Children Less than 10kg: A Report of the ppCRRT Registry Group

M.A. Baum, M.J.G. Somers, J.M. Symons, P.D. Brophy,
T.E. Bunchman, S.L. Goldstein
The ppCRRT Registry Group, USA

Little data has been reported on the outcome of infants and very small children receiving CRRT. Using the ppCRRT Registry of 77 patients from 5 centers from 1/1/01–10/31/02, we analyzed demographics and survival of the 12 children <10kg who received CRRT. Median age was 17 days (range 3 days to 35 months) with a median weight of 4.7kg (1.3–9.5kg). Primary diagnoses included cardiogenic shock (4), metabolic disorder (2), ATN (1), hypovolemic shock (1), hepatorenal syndrome (1), sepsis (1), renal vein thrombosis (1), and nephrotoxic drugs (1). Fluid overload with electrolyte imbalance was the indication for CRRT in 75% of the children with a median percent fluid overload (%FO) of 16% (range 0–220%). Access for CRRT was via dual or triple lumen catheter with all catheters between 7–12.5 F. 58% of accesses were placed in the femoral vein, 25% in the internal jugular, and 17% in the subclavian. 11 of the children received CVVHD and 1 received CVVH only. Median blood flow was 6ml/kg/min (general range 3–22ml/kg/min with one outlier at 46ml/kg/min). Median dialysate or replacement fluid rates were 2,315ml/hr/1.73m². CRRT duration ranged from 0–12 days (median 4 days). 67% of the children <10kg were non-survivors (NS) and 33% survivors (S). Of the children less than 5kg, however, 85% were NS. When we compared NS to S, we found that NS had higher PRISM 2 scores at ICU admit (23 vs. 10; p=0.008) and at CRRT initiation (27 vs. 13; p=0.01) and had higher mean airway pressures at CRRT initiation (12 vs. 7; p<0.05). There were no differences between S and NS in number of pressors prescribed at CRRT initiation, urine output or GFR prior to CRRT, %FO at CRRT initiation, dialysate or replacement fluid rates or in duration of CRRT treatment. Comparing all other children in the ppCRRT Registry to children <10kg, we found no statistically significant differences in PRISM 2 scores at ICU admission or overall survival between the two groups. PRISM 2 scores at CRRT initiation were higher, however, in children <10kg than in the larger children (22 vs. 14; p=0.006). There were no statistically significant differences in %FO, pressor number, or GFR at CRRT initiation between the two groups. We conclude: 1) NS children <10kg were more critically ill than S children as manifested by higher PRISM 2 scores and MAP at CRRT initiation. 2) Children <5kg had the worst survival. 3) Compared to the larger children in the registry, children <10kg were more critically ill by PRISM 2 scores at CRRT initiation.
CRRT for Non-Renal Indications: A Report from the ppCRRT Registry Group

M.J.G. Somers, M.A. Baum, J.M. Symons, P.D. Brophy, T.E. Bunchman, S.L. Goldstein
The ppCRRT Registry Group, USA

Little data exists as to the utilization of CRRT in critically ill children with a clinical indication for solute clearance other than acute renal failure. To better understand this population, we identified all children in the ppCRRT Registry whose primary indication for CRRT was not directly related to impaired renal function (n=11; median age 10.4yr; median weight 32kg). Underlying diagnoses included malignancy and tumor lysis in 6 children, inborn error of metabolism in 3, isolated electrolyte anomaly in 1, and hepatic failure in 1. Median PRISM 2 score on both ICU admission and CRRT initiation was 11 (range 3–21 and 3–26 respectively). At CRRT initiation, median urine output was 3ml/kg/h (range 0.2–8) and median calculated GFR was 60ml/min/1.73M2 (range 28–134). Median calculated fluid overload from ICU admission to CRRT initiation was 4.1% (range 0–15%). 9 children were placed on CVVHD and 2 on CVVH with median dialysate or replacement fluid rates of 2,400ml/h/1.73M2. 8/11 (73%) children survived their illness after a median CRRT duration of 3 days (range 1–11 days). Children who died had higher PRISM 2 scores than survivors both on ICU admission (17 vs. 12, p=0.02) and on CRRT initiation (22 vs. 9, p<0.01), required more pressor support to maintain hemodynamic stability (2.3 vs. 0 pressors, p=0.02), and all eventually developed multisystem organ failure. Survival was not related to age, gender, urine output or GFR prior to CRRT, degree of fluid overload, days in ICU prior to CRRT, or dialysate or replacement fluid rate. When compared to all other children in the ppCRRT Registry (n=66), the children with a non-renal indication for CRRT were placed on CRRT sooner in their ICU stay (1.4 vs. 8.5 days, p<0.002), became less fluid overloaded in the ICU prior to CRRT (5 vs. 23%, p<0.001), had higher GFR upon CRRT initiation (60 vs. 35ml/min/1.73M2, p<0.04), were less likely to be oliguric (27% vs. 68%, p=0.01), required fewer pressor agents (0.6 vs. 1.7, p<0.02), and had shorter duration of CRRT (3.5 vs. 7.2 days, p<0.004). Moreover, although there was no difference in PRISM 2 scores between the 2 groups at ICU admission or CRRT initiation, survival was more likely in the children who received CRRT for a non-renal indication (73% vs. 47%). We conclude that children who receive CRRT for a non-renal indication are: 1) Initiated on CRRT earlier in their ICU admission than children undergoing CRRT for primary renal dysfunction; 2) Maintain hemodynamic stability with fewer pressors; 3) Become less volume overloaded in their ICU course, potentially related to preserved GFR and urine flow; and 4) Require shorter duration of CRRT. We speculate that the increased survival rates seen in these critically ill children may be related to these factors.
Efficient Clearance of Sustained Low Efficient Dialysis for Gentamicin and Vancomycin

Y.M. Ku, K.N. Gibson, N.G. Guirguis
University of Nebraska Medical Center, USA

Purpose: To report the efficient clearance of gentamicin and vancomycin during sustained low efficient dialysis (SLED) obtained from a case with extensive pharmacokinetic monitoring. Methods: Case report: A 26-year-old, Caucasian female with a dry weight of 111 kg was admitted and treated for necrotizing pancreatitis and pseudocyst. The organisms identified from the pseudocyst drainage included Enterococcus faecalis, Pseudomonas aeruginosa, and Coagulase-negative Staphylococcus. Gentamicin, vancomycin, and cefepime were initiated according to antimicrobial sensitivity results. The patient underwent pseudo-drainage and debridement procedures but progressed to septic shock. Because of her cardiac instability and impaired renal function, SLED was started on August 16, 2002 and continued through September 18, 2002. The patient was treated with cefepime 2,000 mg every 12 hours. A series of plasma concentrations for gentamicin and vancomycin were determined prior to and at the completion of every SLED therapy session. The concentrations were used to estimate pharmacokinetic (PK) parameters, including elimination rate constant (Ke), half-life (T1/2), and volume of distribution. The dosage and dosing frequency of gentamicin and vancomycin were then determined based on PK calculation results. Results: The patient received 20 sessions of SLED therapy during this period. The duration of SLED therapy ranged from 8 to 27.83 hours. There were 23 and 18 drug concentration levels available for gentamicin and vancomycin, respectively. Eleven doses of gentamicin ranging from 150–400 mg were administered from 8/18–9/16. Six doses of vancomycin ranging from 1,000–1,500 mg were administered from 8/18–8/27. The estimated Ke, T1/2 and dosage during SLED therapy are summarized and compared to reported literature values with normal kidney function and with various dialysis strategies (please see Table). Through the use of SLED therapy and extensive antimicrobial PK monitoring, desirable antimicrobial concentrations were able to be achieved. The patient responded to antimicrobial treatment and recovered from septic shock. The patient’s kidney function also recovered and dialysis was discontinued. Conclusion: It is apparent that SLED more efficiently eliminates gentamicin and vancomycin when compared to CA VH or CA VHD. We conclude that gentamicin and vancomycin are extensively eliminated during SLED and thus the drug concentrations must be closely monitored during this therapy.

<table>
<thead>
<tr>
<th></th>
<th>Normal function</th>
<th>SLED</th>
<th>CAVHD</th>
<th>CAVH</th>
<th>IHD</th>
</tr>
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<tbody>
<tr>
<td>Gentamicin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kel (1/hour)</td>
<td>0.173–0.462</td>
<td>0.029–0.09</td>
<td>0.026</td>
<td>0.02</td>
<td>0.231</td>
</tr>
<tr>
<td>T1/2 (hours)</td>
<td>1.5–4</td>
<td>7.7–24</td>
<td>27</td>
<td>34.6</td>
<td>3</td>
</tr>
<tr>
<td>Dose recommended</td>
<td>1.7 mg/kgq</td>
<td>Average of 1.5 mg/kg with PK monitoring</td>
<td>NA</td>
<td>1.7 mg/kgq</td>
<td>0.85 mg/kg</td>
</tr>
<tr>
<td></td>
<td>8 hours</td>
<td></td>
<td></td>
<td>24–48 hours</td>
<td>post-IHD</td>
</tr>
<tr>
<td>Vancomycin</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Kel (1/hour)</td>
<td>0.087</td>
<td>0.033–0.08</td>
<td>0.01–0.05</td>
<td>0.02–0.04</td>
<td>0.02</td>
</tr>
<tr>
<td>T1/2 (hours)</td>
<td>8</td>
<td>8.6–21</td>
<td>14–58</td>
<td>18–36</td>
<td>36</td>
</tr>
<tr>
<td>Dose recommended</td>
<td>1,000 mgq</td>
<td>1,000–1,500 mgq</td>
<td>NA</td>
<td>1,000 mgq</td>
<td>1,000 mgq</td>
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<tr>
<td></td>
<td>12 hours</td>
<td></td>
<td></td>
<td>24–96 hours</td>
<td>4 days</td>
</tr>
</tbody>
</table>
Serum Haptoglobin Concentration in Patients on Peritoneal Dialysis Treatment

M. Sucharzewska-Tomczak\textsuperscript{a}, A.E. Grzegorzewska\textsuperscript{b}

\textsuperscript{a}Nephrology Word and Dialysis Unit of Medical Care Center, \textsuperscript{b}Department of Nephrology, University of Medical Sciences, Poland

One of the markers of inflammation in the human organism is the increment of serum haptoglobin (HTG) concentration. In peritoneal dialysis (PD) patients inflammation is closely associated with poor nutrition, atherosclerosis and, frequently, with high peritoneal permeability. Elderly patients usually show more pronounced atherosclerosis than younger individuals. The aim of this investigation was to find a relationship between HTG concentration, parameters of nutrition, serum cholesterol and peritoneal permeability in PD patients below or over 65 years old. The concentration of HTG was determined by immunonephelometry in serum of 60 patients (53 ± 14 years) treated with continuous ambulatory PD (54 patients) and automated PD (14 patients). The mean time of dialysis duration was 16 months (median 10.2, range 0.4–66 months). HTG measurements were performed simultaneously with examinations of dietary intake, nutritional status, serum cholesterol level and peritoneal permeability estimated using standard peritoneal equilibration test (PET). The mean concentration of HTG (2.4 ± 1.2g/l) was elevated as compared to the normal range (0.3–2.0g/l) and was not dependent on duration of dialysis treatment. There was a significant relationship between HTG concentration and patient's age ($r=-0.455$, $p<0.001$). In a subgroup of 17 patients in the age over 65 there was the significant statistical dependence of HTG concentration on daily saccharose intake ($r=-0.512$, $p<0.020$), lean/total body mass ratio ($r=-0.598$, $p<0.020$), plasma albumin concentration ($r=-0.532$, $p<0.030$), mean corpuscular volume ($r=-0.493$, $p<0.050$), mean corpuscular hemoglobin ($r=-0.637$, $p<0.010$) and permeability of the peritoneum expressed by $D_4/D_0$ of glucose ($r=-0.542$, $p<0.030$). Such relationships were not noticed in a subgroup of 43 patients in the age below 65 years. In the whole group and both subgroups there was no dependence of HTG concentration on weekly $K_t/V$, total weekly clearance of creatinine and serum cholesterol concentration. Increased serum HTG concentration reflects the chronic inflammation in PD patients. In older individuals inflammation expressed by HTG levels is more closely related to nutritional parameters and peritoneal permeability than it is observed in younger persons.
Myoglobin Removal by CVVH (D):
Effect of Dialyzer Size, Convection and Diffusion

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Myoglobin removal was assessed in a 16 YO male presenting with oligoanuric renal failure due to sepsis, diabetic ketoacidosis (serum glucose 1,225mg/dl), hypernatremia (serum Na=165meq/l) and rhabdomyolysis. CRRT was performed using the PRISMA system (Gambro, Lakewood, Colo., USA) with ACD-A (Baxter, Deerfield, Ill., USA) anticoagulation. Normocarb™ (Dialysis Solution, Richmond Hills, Ontario, Canada) was used both as dialysate and predilution fluid. Multiflow-60 and 100 hemofilter (AN69, 0.6m² and 0.9m², respectively) were studied. For the initial 48hrs, NaCl was added to the Normocarb™ in order to achieve a gradual decrease in the patient’s serum osmolality. Myoglobin removal was calculated for isolated diffusive clearance as well as combined diffusive and convective clearances. Serum myoglobin dropped from 278,000 to 72,200mcg/l over 48hrs despite oliguria. Myoglobin diffusive clearance was similar for both membranes sizes (5 and 4ml/min – Table). The addition of predilution Normocarb™ at a rate of 1,000 and 2,000ml/hr fluid resulted in enhanced myoglobin clearance –7.8 and 11ml/min respectively (Table). The latter was equal to 20% of the urea clearance. Serum osmols normalized over 72hrs. Thus, CVVHDF, but not CVVHD, is efficient in removing considerable amounts of myoglobin. Myoglobin clearance can be improved by increasing the convective component and perhaps, due to potential myoglobin binding to the membrane, replacement of hemofilter may improve myoglobin clearance adsorption. Furthermore, CRRT is an easy to use, safe modality, for the management of severe hyperosmolar syndromes in patients with reduced urine output. It remains unknown whether myoglobin removal would affect the length of myoglobin associated acute renal failure.

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<th>Dialysate flow rate (mls/hr)</th>
<th>Predilution flow rate (mls/hr)</th>
<th>Net fluid removal (mls)</th>
<th>Cr clearance (ml/min)</th>
<th>BUN clearance (ml/min)</th>
<th>Myoglobin clearance (ml/min)</th>
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Table to abstract 7
CVVHD: An Adjunct to Normal Renal Function for Solute Clearance in Tumor Lysis

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Children with B or T cell malignancies are at risk for developing complications from hyperkalemia, hyperphosphatemia, hypocalcemia or hyperuricosemia due to break down of the tumor burden at the time of initiation of therapy for the malignancy. The use of forced diuresis, alkalization of the urine with bicarbonate containing intravenous fluids and Elitek\textsuperscript{TM} (Sanofi-Synthelabo Inc., NY, NY) have been effective for uric acid management but less effective for calcium, phosphorous and potassium clearance. The balance of the rate of tumor break down (and solute clearance) must not exceed solute clearance by native renal function in order to avoid complications yet this rate of break down is not predictable. In those patients with large tumor loads (high WBC, organomegaly from tumor invasion) CRRT can be used to increase the total clearance of solute. From February 2001 to October 2002, 7 children (age range 7–15 years, weight range 23–67kgs) were placed on CVVHD to increase their solute clearance at the time of induction of treatment. The average WBC was 157,000 (range 123,000–220,000) and all had evidence on exam or CT of organomegaly. All underwent CVVHD with use of the PRISMA (Gambro Healthcare, Lakewood, CO) and 5/7 was on the M-60 while 2/7 was on the M-100. Blood flow rates ranged from 100–180mls/min via a dual or triple lumen femoral vascular access in all, Normocarb\textsuperscript{TM} (Dialysis Solutions Inc, Richmond Hills, Ont.) dialysate with no additives flow rates ranged from 1,000–2,500mls/hr, no net ultrafiltration was needed due to native urine output, and citrate anticoagulation was used in all children. All patients had a Foley urinary drainage catheter placed and urine output ranged from 5–13 liters/day due to the forced diuresis. Average length of CVVHD treatment was 3.7 days (range 2–5 days). An example of phosphorous clearance is seen in a 57kg teen whose urine output was 7,000mls/day and the CVVHD was 48 liters/day. Her urine phosphorous excretion was 720mg/day while here CVVHD phosphorous excretion was 1,776mg/day; her plasma phosphorous never exceeded 6.1mg/dl. Citrate anticoagulation allowed for continuous infusion of calcium chloride to the child avoiding any complications of hypocalcemia. No complications occurred but metabolic alkalosis was present in all by day 3 due to the bicarbonate based diuresis fluids (stopped in all), as well as the citrate conversion to bicarbonate. This was easily treated by the addition of normal saline (pH 5) to the replacement fluid of the PRISMA in the CVVHDF mode. We conclude that CRRT should be considered safe and effective to use as an adjunct to normal renal function when the rate of tissue breakdown and need for solute clearance may not be sufficient with forced native urine out put.
Effect of High-Volume Hemofiltration on Pulmonary Infection in Renal Transplantation Patients

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Objective: High-volume hemofiltration (HVHF) has been reported to be beneficial in sepsis shock and systemic inflammatory response syndrome (SIRS). This study was performed to evaluate the effect of HVHF on critical pulmonary infection in renal transplantation patients. Methods: 9 renal allograft recipients with critical pulmonary infection were involved, including 8 males and 1 female, averagely aged 42.9 (28~54) years. All the infections occurred 2–4 months after renal transplantation. HVHF was started when patient presented with acute respiratory distress syndrome (ARDS) or acute pulmonary injury (API), or respiratory failure index (RFI) below 300. HVHF was carried out continuously for 72 hours with AN69 hemofilter (1.2m²) and the ultrafiltration (UF) flow of 6L/h. A new hemofilter was changed every 24 hours. Clinical data were recorded including blood pressure, blood gas analysis, blood routine, C-reactive protein (CRP) and APACHE II scores, and filtration parameters were detected before and every 12 after the initiation of HVHF. Results: In every of the nine patients, pulmonary symptoms were found recovered and inflammatory parameters improved during HVHF treatment. APACHE II scores and RFI were found better improved in the survived patients than died, and the APACHE II scores at the initiation of HVHF found associated with the later patient survival. None of these patients died in the following week after HVHF treatment, although the overall mortality was 67%. The decrement of serum level of C-reactive protein (CRP) was more sensitive in the evaluation of treatment efficacy than that of peripheral white blood cell counts. Conclusion: This study showed that HVHF was beneficial in renal allograft recipients present with severe early pulmonary infection, with respect to the improvement of pulmonary symptoms, inflammatory response parameters and short term amelioration of general conditions. Early initiation of HVHF in these patients might afford a better chance for the control of inflammatory response and the amelioration of acute lung injury.
Creatinine Index as an Indication of Nutritional Status and as a Prognosis Factor in Acute Renal Failure

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Normalized creatinine production (creatinine index: CI) has been shown to reflect protein nutritional status and outcome in chronically hemodialysis patients but such has not yet been established in acute renal failure (ARF). We therefore investigated CI as an indicative parameter of protein denutrition and outcome in ARF requiring extrarenal replacement therapy (ERRT). **Methods:** 24 patients (APACHE II score 29.6±5.7) with ARF treated by intermittent hemodialysis or continuous veno-venous hemofiltration (CVVHF) have been studied along 7 days from the first ERRT session (D1–D7). Weight, diuresis, BUN, creatinemia, urinary urea nitrogen and creatinine were collected daily, before and after each ERRT. During CVVHF, fractional ultrafiltrat urea nitrogen and creatinine collections were also collected. Normalized Protein Catabolism Rate (nPCR) and nitrogen supply were estimated daily and an average of 7 days (D1–D7) was calculated. CI was calculated at D1 and D7 according to the formula and CI changing rate from D1 to D7 according to cCI = (D7CI – D1CI)*100/D1CI. From ICU survival, two groups were individualized and compared. **Results:** Mean CI was 28.3±9.6 at D1 and 22.2±7.9mg/kg/day at D7 (p=0.05); mean cCI was 21.5±26.6%. Average nPCR was 1.87±0.77g/kg/day whereas average nitrogen supply was 0.14±0.06g/kg/day. ICU survival rate was 50%.

<table>
<thead>
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<th>Deceased (12)</th>
<th>Survived (12)</th>
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<tr>
<td>CI D1 (mg/kg/24h)</td>
<td>24.0±9.6</td>
<td>32.7±7.9</td>
</tr>
<tr>
<td>CI D7 (mg/kg/24h)</td>
<td>16.8±6.6</td>
<td>27.5±8.8</td>
</tr>
<tr>
<td>cCI %</td>
<td>-29.7±11.8</td>
<td>-13.3±27.9</td>
</tr>
<tr>
<td>nPCR (g/kg/24h)</td>
<td>2.0±0.9</td>
<td>1.7±0.6</td>
</tr>
<tr>
<td>Nitrogen supply (g/kg/24h)</td>
<td>0.16±0.06</td>
<td>0.13±0.07</td>
</tr>
</tbody>
</table>

No correlation was found between nPCR and CI neither between nPCR and nitrogen supply. **Conclusion:** We conclude that CI before and seven days after initiation of ERRT is a predictive factor of outcome in ARF and that a dramatic decrease of CI after the first week of ERRT worsens significantly the outcome. These results would also suggest that in ARF patients, CI and CI changes are better indicative of protein denutrition than nPCR. (a) CI (md/kg/24h) = \( \frac{[(C_b \cdot T_2 - C_b \cdot T_1) \times \text{weight} \times 0.6]/T + (C_u \times V_u)/T + (C_{uf} \times V_{uf})/T \times 0.113 \times 1.440/\text{weight} + [(C_b \cdot T_1 + C_b \cdot T_2)/2] \times 0.0429, \) where C = Creatinine in blood (b.), urine (u.) and ultrafiltrat (uf.), V = Volume of urine (u) and ultrafiltrat (uf), and T = time in minute from T1 to T2.

Continuous Renal Replacement Therapy after Cardiac Surgery: Review of 85 Cases


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Objective: To evaluate survival, renal outcome and renal support characteristics of patients who require continuous renal replacement therapy (CRRT) following cardiac surgery. Method: Review of all patients who underwent CRRT in the postoperative period among 5,564 consecutive patients who received cardiac surgery between September 1997 and March 2002 at the Montreal Heart Institute. Results: During this time, CRRT were performed for 85 patients after cardiac surgery. Mean age was 64±13 years and 35 were females. Diabetes (32%), hypertension (39%) and recent contrast exposure (17%) were the preoperative risk factors identified. Preoperative renal dysfunction (defined as a serum creatinine≥130μmol/L) was found in 49.4% of cases and CRF with dialysis-dependency in 2 patients. Although diabetes, hypertension and preoperative renal dysfunction were more frequent among survivors, there was no statistically significant difference with non-survivors. Seventy-nine percent of survivors and 86% of non-survivors had been on cardiopulmonary bypass (CPB) for an average of 119±54 and 134±65min, respectively (p=NS). SAPS II score at ICU admission and intraortic ballon pump (IABP) requirement were significantly higher in non-survivors (p<0.05). Renal support in all cases was provided using the Prisma System (Gambro, St-Leonard, Quebec, Canada) with Multiflow 60 or Multiflow-100 hemofilters (AN69 of 0.6 and 0.9m²). For dialysate and replacement solution (always in pre-dilution) Hemosol LG2 or Hemosol B0 were used. Heparin was used in 89.5% of patients whereas danaparoid in 3.5%. Seven percent of patients did not receive any anticoagulation because of bleeding or thrombocytopenia. The mean number of filters spent per patient was 3.3±2.6 (range 1–15). Delay between surgery and CRRT initiation was 5 days (range from immediate to 61 days) and mean duration of CRRT was 9 days (range 0.5–47 days), without difference between survivors and non-survivors. Types of CRRT were distributed as follows: CVVHDF (n=69), CVVH (n=15) and CVVHD (n=1). Five patients were initially treated with CVVH and transferred to CVVHDF. Delivered clearances with CRRT were estimated at 25–28ml/min (~40L/day), 29–32ml/min (~46L/day) and 17ml/min (~25L/day) for CVVH, CVVHDF and CVVHD, respectively. Among 48 survivors, 45 recovered, 2 patients did not recover renal function before hospital discharge, and 1 CRF patient returned to PD. In this subgroup, 30 patients received an average of 4 sessions of intermittent hemodialysis (IHD) after CRRT. Among 37 non-survivors, 5 received an average number of 12 IHD sessions. In-hospital mortality was 43.5% for the entire group; when excluding from the analysis 3 patients who had non-renal indication for CRRT and 2 patients with chronic renal failure already on dialysis, the mortality of patients with ARF fell to 42.5% (34/80). No difference in mortality was observed between patients who presented normal renal function at baseline and those with preoperative renal dysfunction. Mortality was 33.3% post-coronary revascularisation (CABG), 57.1% post-CABG and valve surgery, 60% post-valve and 72.7% for redo-CABG or redo-valve. The mean length of hospital stay was 34.2 and 22.3 days for survivors and non-survivors, respectively (p<0.05). Conclusions: In our review, survival rate was 56%; most of survivors recovered renal function at hospital discharge and we did not find different mortality between patients with normal renal function and those with mild renal dysfunction at baseline. Mortality appears associated with high SAPS II score, type of surgery and IABP requirement. We consider CRRT an adequate therapeutic option for critically ill patients suffering ARF after cardiac surgery.
CRRT – An Indian Experience
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Introduction: Continuous Renal Replacement Therapy is fast becoming a preferred modality of treatment for Acute renal failure in the ICU settings even in developing countries. The outcome and mortality rates are very similar to the data available from developed countries. Objective: To share and discuss our experience of CRRT on critically sick and post Cardio-thoracic surgery patients. Methods: This is a retrospective analysis of 57 patients subjected to CRRT between January 2002 and 30th November 2002 at our center (CARE Hospitals, Hyderabad, India). Discussion: 57 patients were subjected to CRRT at our Centre between January 2002 and November 2002. 77% were subjected to CRRT following Cardio-thoracic surgery and 23% were subjected to CRRT in ICU settings as they were haemodynamically unstable with a diagnosis of Acute renal failure secondary to Septicaemia, Multi organ failure, burns (a single patient), severe cardiac failure. Mean age of treated patients was 56.4 yrs. Mortality was very different between those subjected to CRRT following Cardio-thoracic surgery compared to those subjected to CRRT following a diagnosis of ARF due to other causes. All were subjected to CRRT, CVVHD using a Braun CRRT machine. Results: The mortality of patients subjected to CRRT in Cardio-thoracic unit was very different from those subjected to CRRT in ICU. The procedure and staff involved being the same it was the underlying cause of ARF that determined the outcome of CRRT. Mortality in the CT-ICU group was 24% as against 82% in ICU group.
Functional Alteration of Monocyte in Patients with Acute Pancreatitis during CVVH

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Objective: The aim of this study was to investigate the change of monocyte function in patients with acute pancreatitis during continuous venovenous hemofiltration (CVVH). Methods: Seven acute pancreatitis patients underwent CVVH for 72 hours in a pre-dilution mode using a polyacrylonitrile filter (AN69, Prisma). Ultrafiltration flow were 4,000 ml/h. Blood were taken from the patients at 0, 2, 6, 12, 24, 48 and 72h during CVVH. Monocytes were isolated and were cultured with LPS 10 μg/mL for 12 hours at 37°C. IL-10 (and other cytokines) in supernatants were tested by ELISA to determine the secretion function of monocyte. The expression of monocyte HLA-DR were tested by flow cytometry to determine the antigen presentation function. Results: Four of the seven patients were accompanied with MODS, one died. After CVVH treatment, in other six patients who recovered, the monocyte HLA-DR was gradually elevated (nearly 2–10 times than pre-treatment) and the IL-10 secretion was decreased (see figure). It means the function of monocyte was improved after CVVH. In the died patient (the case 7), the IL-10 level rapidly increased in the course of the disease (more than 2 times than pre-treatment). The HLA-DR level was very low persistently.

Conclusion: 1. The monocyte function of the patients with acute pancreatitis were improved during CVVH. 2. The level of IL-10 and HLA-DR as an indicator to estimate the curative effect of CVVH treatment and to estimate the severity of the disease may be useful in clinics.
Withdrawal from Care in Acute Renal Failure Requiring Renal Replacement Therapy

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\textbf{Introduction:} Acute renal failure (ARF) severe enough to require renal replacement therapy (RRT) is an ominous complication of acute medical or surgical illness and generally carries a mortality rate near 50%. Mortality in this setting is related largely to underlying co-morbidity rather than to the type of RRT. Some patients with unrelenting illness in this setting are withdrawn from aggressive intervention and life support, usually after discussion between family and care givers. In ESRD, we know that 10–20\% of deaths are related to voluntary withdrawal from dialysis, but the frequency and circumstances of similar decisions in the acute setting have not been described.\textbf{Methods:} As part of the ongoing surveillance for outcomes in ARF requiring RRT at our center during the calendar years 2000 and 2001, we find that among the 203 deaths (52\% of 389 total cases), 57\% (115/203) follow an active decision to withdraw support. The presence of such discussion and decisions was noted during record review.\textbf{Results:} Patients for whom support is withdrawn, compared to patients who died without such decisions being made, have more total hospital days (19.7\textpm1.1 vs. 18.2\pm1.1) and ICU days (14.5\textpm0.9 vs. 9.9\textpm1.5), are more often medical than surgical cases (69 vs. 47\%), and have elevated but somewhat lower APACHE III related scores (93\textpm2.4 vs. 102\textpm2.8). However, patients for whom support is withdrawn were not statistically distinct for age, gender, number of pre-RRT hospital days, underlying primary diagnosis (cardiac, hematologic, infectious, pulmonary, liver or vascular), number of identifiable complications, or initial RRT modality (hemodialysis vs. continuous RRT). The elapsed time from withdrawal of support to demise was <24h in 70\% of deaths and did not correlate with APACHE III related score, number of complications, specific demographic factors, or type of RRT. It is of some interest that the need for CRRT predicts a higher mortality but does not correlate with withdrawal from treatment, suggesting that some unidentified factors, distinct from those ordinarily used to predict mortality, impact withdrawal decisions. Analysis of the relation between withdrawal of support and prior advance directives or recent DNR orders is under review with complete data not yet available.\textbf{Conclusion:} The recognition of impending demise is common and frequently results in a decision to withdraw support that generally leads directly to death in a very short time. Sensitivity by families and care givers to the futility of continuing intervention, as marked by the high frequency of this phenomenon in the setting of severe ARF. Such decisions to withdraw support are noted particularly in cases with prospectively high mortality risk and prolonged intensive care with the additional burden of severe ARF. Specific predictors for withdrawal are not identical to those for mortality itself and remain to be characterized definitively. Even so, our experience suggests that such decisions are frequently accepted by family and staff and increase the possibility of reconciled deaths after intensive efforts have failed to reverse complications.
Prevalence of Adrenal Insufficiency in Critically Ill Patients on Continuous Renal Replacement Therapy

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**Purpose:** The purpose of this study is to examine the incidence of adrenal insufficiency (AI) in critically ill patients who required continuous renal replacement therapy (CRRT). **Methods:** A retrospective study was performed on patients who required CRRT after being admitted to the medical or surgical ICU in St. Mary Hospital of Mayo Clinic from August 2000 to July 2002. AI is diagnosed when either adrenal dysfunction (AD) or functional hypoadrenalism (FH) is present. AD is defined as a serum cortisol level less than 20 μg/dL at any time point. FH is defined as either a cortisol level between 20 μg/dL and 30 μg/dL at any time point, or a less than 9 μg/dL increase in cortisol level 60 minutes after ACTH stimulation in patients with cortisol levels above 30 μg/dL at all time points. **Summary of the Results:** During the two-year period, 317 patients required CRRT after being admitted to either medical or surgical ICU. Among the 116 patients tested, 96 (82.8%) patients, including 48 (41.4%) with AD and 48 (41.4%) with FH, were diagnosed with AI, and 20 (17.2%) patients had cortisol levels above 30 μg/dL at all time points with 2 having normal adrenal function by ACTH stimulation test and 18 indeterminate due to the lack of ACTH stimulation testing. Overall, the incidence of AI is at least 30.3% in this patient population. **Conclusion:** The incidence of AI in the ICU patients who required CRRT is significantly higher than the reported incidence of 0.1–28% in the general ICU patients. The significance of screening for AI in this patient population on survival is under investigation.
Loss of Body Heat during Continuous Veno-Venous Hemodialysis (CVVH-D) in Critically Ill Patients

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CVVH-D has solved many of the complications previously seen with acute intermittent hemodialysis (AIH), but has introduced the potential problem of hypothermia. Unlike AIH, which exposes the patient’s blood to warmed dialysate for short periods of time, CVVH-D continuously circulates blood past room-temperature dialysate. Loss of body heat poses a potential threat to critically ill patients by taxing cardiovascular reserves, initially raising metabolic rate, and stimulating shivering. Little research has been done concerning the problem of heat loss during CVVH-D, although commercial manufacturers of dialysis equipment are developing warming devices. Even less is known about how patient characteristics and dialysis conditions influence body heat loss. **Problem Statement:** The problem addressed by this study was to determine how patient blood volume (measured by body surface area [BSA], and estimated to be approximately 7–10% of body weight), duration of blood/extracorporeal interface exposure, and dialysate temperature, influence heat loss during CVVH-D. **Study Purpose:** To determine at intervals throughout CVVH-D: 1) the association between BSA and body temperatures; 2) the effects of blood flow and dialysate flow rates on body temperature. **Study Variables:** Blood volume was estimated by calculating BSA by Moesteller’s formula. Body temperatures included by Diatek 9000 Instatemp tympanic membrane temperature (TMT) and blood temperatures (BT1 and BT2) measured by TEGAM 871A (Geneva, OH) at access and return lumen of the venous access. Dialysate temperature gradient (DT1 and DT2) measured before and after blood interface estimated patient-to-dialysate temperature gradient (PTDG) calculated by DT2 minus DT1. Dialysate flow rates (DFR) in ml/hr and blood flow rates (BFR) in ml/min were measured from the dialysis machine (Prisma, Gambro, Lakewood CO). **Design and Sample:** This descriptive correlational study used a convenience sample of 11 adult critically ill patients from a large midwestern medical center. None of the sample received other extracorporeal therapy within 24 hours. **Procedures:** After informed consent, all study variables were measured at baseline, 30 minutes, 2, 4, 8, and 12 hours after CVVHD initiation. **Data Analyses:** To determine associations between BSA and TMT, BSA and BT2, DFR and TMT, BFR and TMT, and BFR and PTDG, Kendall’s tau correlation procedures were performed at all time intervals. Mean blood temperature changes were examined for all BSAs at each time interval. **Results:** Ten of eleven (91%) patients became hypothermic during therapy; additionally 64% began to shiver. DFR had a greater impact on the development of hypothermia than did BFR. A BSA <2m² correlated with the development of hypothermia. **Conclusions:** Patients undergoing CVVH-D are likely to become hypothermic during therapy, especially those <2m² BSA and those with DFR >1,000 ml/hr. This has implications beyond patient comfort and alterations in metabolic demands of patients who are cold, but also impacts the nutritional needs of individual patients.
24-hr Creatinine Clearance as a Guide for CRRT Withdrawal: A Retrospective Study

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University of Alabama at Birmingham, USA

**Introduction:** Continuous renal replacement therapy (CRRT) has emerged as an alternative form of renal replacement therapy in the critical care setting. Its advantages include slow continuous fluid removal, steady acid-base correction, and hemodynamic stability. Disadvantages of CRRT include cost, ICU space and time, possible metabolic complications from CRRT and vascular access complications. There are no published criteria on the timing for terminating CRRT, and the decision is based on the clinical improvement of the patient. Usually CRRT is stopped when the urine output has increased, and the patient’s urine output and electrolytes are followed to reassess the need for restarting therapy. We evaluated the usefulness of a 24-hour urine creatinine clearance (CrCl) obtained while on CRRT as a tool to guide discontinuation of therapy.

**Methods:** We retrospectively evaluated patients over the last year who had 24-hour urine creatinine clearances performed when they became non-oliguric while on CRRT. We included patients from adult medical, surgical and cardiac intensive care units. CRRT was performed as CVVHDF using a COBE Prisma device. Oliguria was defined as urine output <400ml/24hrs. A successful discontinuation of CRRT was defined as not restarting CRRT for at least two weeks. A total of 10 patients were identified with clinical characteristics as follows: 7 males and 3 females, mean age of 49±17 years, and mean APACHE II score of 27 at initiation of CRRT. All patients had normal pre-morbid kidney function (creatinine of <1.4mg/dL) and were oliguric or anuric during CRRT.

**Results:** The median creatinine clearance on the day of CRRT discontinuation was 17.1ml/min, with a median urine volume of 1300ml/24hrs. The median serum creatinine was 2.4mg/dL. The median CRRT ultrafiltration rate was 26ml/min. Three patients out of 10 required resumption of CRRT; all had a CrCl <15ml/min. Six of the seven patients who successfully remained off CRRT had a CrCl ≥15ml/min. The median CrCl in the failure group was 12ml/min. The median CrCl in the group that remained off CRRT was 25ml/min.

**Discussion:** Much attention has been given to the optimal time to start CRRT, while there is relatively little information on when to stop this expensive therapy. These data suggest that the use of a collected CrCl while on CRRT may be helpful as a guide to when to terminate therapy, with a CrCl of >15ml/min being predictive of renal recovery. Patients who did not have a CrCl of >15ml/min, despite increasing urine output, required resumption of CRRT. Larger, prospective, randomized trials are needed to confirm these findings.
Explicit Computerized Protocols for Hemofiltration in Congestive Heart Failure

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- Heart failure (CHF) is a major problem in the USA.
- Progressive heart failure (CHF) is associated with diuretic resistance. Hemofiltration can reverse diuretic resistance and modify the natural history of CHF.
- Isolated intermittent hemofiltration has been used to treat CHF.
- Hemofiltration differs from both drug induced diuresis and intermittent hemodialysis.
- A definitive clinical trial of hemofiltration is needed and may open a large CHF opportunity for extracorporeal renal support.

Much of medical care delivered during clinical trials, including the test intervention, is associated with inter-physician variability and failure to implement evidence-based care, even at academic medical centers [1]. The compliance of nephrologists with recommended dialysis dose (Kt/V) prescription is only about 50% [2]. We are developing an explicit computerized protocol for performing a CHF Hemofiltration clinical trial with less unnecessary variation from study protocols. This will be pivotal for advancing the use of hemofiltration in CHF by leading to more definitive and more credible clinical trial results. Our software tools standardize clinician decisions and enable patient-specific clinical care delivery. We are extending, to the CHF Hemofiltration clinical trial, tools and protocols already developed and currently implemented with partial support from the NIH/NHLBI ARDS Network. These tools will ultimately enable evidence-based, explicit clinical methods to be extended to other clinical centers for research or clinical care purposes. Our explicit methods (bedside computerized protocols) will reduce variation during the CHF clinical trial. They will reduce noise due to unnecessary variation both in the experimental interventions and in non-experimental cointerventions, and increase the signal to noise ratio. This will make outcomes more precise and therefore clearer. This is an extension of the system biology approach in cell biology [3] to the holistic scale of the patient in the clinical environment [4, 5].

References

Pediatric Multi-Organ System Failure: A Report from the ppCRRT Registry Group

S.L. Goldstein, M.J.G. Somers, J.M. Symons, P.D. Brophy, M.A. Baum, T.E. Bunchman

The ppCRRT Registry Group

Most previous pediatric (ped) CRRT studies report a retrospective single-center experience without severity of illness (SOI) assessment. From 1/1/01 to 10/31/02, the ppCRRT Registry has collected data from 78 critically ill pediatric patients (pt) who received 10,274 hours of CRRT at 5 US centers and used Pediatric Risk of Mortality (PRISM 2) score to control for SOI. The current abstract reports demographics and outcome for the 66/78 ppCRRT Registry pt with multi-organ system failure (MOSF). Each center followed local practice for initiation, modification and termination of CRRT. Survival was defined as discharge from the intensive care unit (ICU). Sepsis (31.3%), cardiovascular shock (26.3%) and bone marrow transplant (BMT)/malignancy associated liver dysfunction (12.4%) were the most common primary diseases associated with acute renal failure leading to CRRT. Complete outcome data were available for 65 MOSF pt. 31/65 (47.7%) pt survived to ICU discharge. 12/24 (50%) septic pt and 3/9 (33%) BMT pt survived. Pt age, weight, and PRISM 2 score did not differ between survivors (S) and non-survivors (NS) at time of ICU admission. GFR, pressor number and CVP were also no different for S vs. NS at time of CRRT initiation. Both percent fluid overload (%FO) and PRISM 2 at time of CRRT initiation were significantly lower for S vs. NS (table). %FO was still lower (p<0.01) for S vs. NS when controlled for SOI by PRISM 2 at CRRT initiation using multiple regression analysis. All 3 BMT S had CRRT initiated at <10% FO. Our ppCRRT data show: (1) no difference in clinical variables for S vs. NS at time of ICU admission and (2) only %FO and PRISM 2 at time of CRRT initiation were significantly worse for NS vs. S (table). We suggest that (1) greater degrees of %FO might lead to worse SOI and (2) ‘early’ initiation of CRRT at 10% FO may improve survival in critically ill children with MOSF.

<table>
<thead>
<tr>
<th>Mean values</th>
<th>Survivors</th>
<th>Non-survivors</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRISM at ICU admit</td>
<td>14.3 ± 9.1</td>
<td>17.7 ± 9.1</td>
<td>NS</td>
</tr>
<tr>
<td>PRISM at CRRT init</td>
<td>11.4 ± 5.7</td>
<td>19.1 ± 7.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>9.5 ± 7.1</td>
<td>9.8 ± 8.0</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>34.1 ± 23.5</td>
<td>35.0 ± 24.4</td>
<td>NS</td>
</tr>
<tr>
<td>CVP at CRRT init (mmHg)</td>
<td>16.7 ± 7.0</td>
<td>20.9 ± 7.5</td>
<td>NS</td>
</tr>
<tr>
<td>Pressor number at CRRT init</td>
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<td>1.9 ± 0.8</td>
<td>NS</td>
</tr>
<tr>
<td>GFR at CRRT init</td>
<td>32.7 ± 23.6</td>
<td>43.2 ± 34.4</td>
<td>NS</td>
</tr>
<tr>
<td>%FO at CRRT init</td>
<td>12.0 ± 11.7</td>
<td>20.2 ± 15.2</td>
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</table>
Continuous Venous Hemofiltration in Treatment of Acute Severe Hyponatremia

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Objective: To investigate the effect of continuous venous hemofiltration (CVVH) in treatment of acute severe hyponatremia (ASH). Methodology: Six ASH patients involved, including 5 males and 1 female, with average age of 48.5(25–61) years. Complication of ASH before CVVH included confusion in 6 patients, drowsiness in 3 patients, delirium in 3 patient. CVVH was started 47 (45–48) hours after onset of disease and sustained for at least 45.6h. During CVVH, the replacement solution flow rate was 2,000ml/h, flow rate was 200–250ml/min, and the substitute fluid was infused by a predilution route. Low molecular weight heparin was used for anticoagulation. Results: The average treatment duration of CVVH was 59.7(45.6–86) hours. All the patients survived and tolerated CVVH well, of which 3 patients maintained hemodialysis and 3 patients recovered renal function. A significant decrease in urea nitrogen and creatinine was found. During CVVH, the serum sodium increased significantly (pre-CVVH:101.2±4.2mmol/L, 6th hour during CVVH: 115.0±0.27mmol/L and the correction rate of 2.5±0.4mmol/L-h, 24th hour during CVVH: 129.2±4.1mmol/L and the correction rate of 1.2±0.1mmol/L-h, 48th hour during CVVH: 140.3±1.6mmol/L and the correction rate of 0.82±0.10mmol/L-h). The replacement solution sodium levels was higher than the serum sodium as much as 16.0±6.0mmol/L at 0 hour, and 11.6±4.3mmol/L at 4th hour, 5.5±5.1mmol/L at 24th hour, 0.74±0.96mmol/L at 48th hour of CVVH. After initiating CVVH, the serum osmolality increased significantly (216.7±7.4mOsm/kg-H2O pre-CVVH, 245±5.5mOsm/kg-H2O at 6th hour, with the correction rate of 5.16±0.81mOsm/kg-H2O-h; 272.7±7.1mOsm/kg-H2O at 24th hour, with the correction rate of 2.33±0.28mOsm/kg-H2O-h; 295.0±4.2mOsm/kg-H2O at 48th hour, with the correction rate of 1.63±0.20mOsm/kg-H2O-h). The Glasgow scores and APACHE II scores in these patients got a great improvement than pretreatment. Conclusion: CVVH is effective in treating of ASH, and should be chosen because of its slow and continuous nature. A low-sodium replacement solution should be prepared to minimize its sodium concentration difference from patients’ serum concentration. We recommend the current guideline in SAH patients is that the serum sodium concentration should be corrected at an average rate of 2.5±0.4mmol/L-h (at 6h), 1.2±0.1mmol/L-h (at 24h) and 0.82±0.10mmol/L-h (at 48h).
An Easy Method of Estimating the Metabolic Component of Acid/Base Balance Using the Stewart Approach

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The Stewart approach defines acid/base abnormalities as resulting from changes in strong ion difference (SID), the pCO\(_2\), and the weak acids (mainly albumin). The standard base excess (SBE) is a measure of the net effect of changes in SID and weak acids, therefore, metabolic acid/base balance can be described as SBE effects of changes from normal of these parameters. We compared our mental estimation of strong ion (SI) effects with a computer calculation of SI effects. Acid/base abnormalities were identified in critically ill patients. The SBE effects of change in SI, change in albumin, and the effect of ‘Other Species’ (unmeasured anions) were calculated. An estimate of the SI effects was determined. The difference between SID (using \([\text{Na}^+] + [\text{K}^+] - ([\text{Cl}^-] + \text{lactate})\)) and normal SID (42mEq/L) estimated the effect of the change in SID. The effect of a change of albumin from normal was estimated as 0.25×(normal albumin − measured albumin). The predicted SBE was defined as estimated change in SID plus albumin effect. The estimated effect of ‘Other species’ was actual SBE minus predicted SBE. The Bland-Altman method was used to test agreement. Calculations were made on 46 data sets from 44 individuals. The bias for calculated and estimated SI effects, calculated and estimated albumin effect, and calculated and estimated ‘Other species’ were −1.26mEq/L, 0.5mEq/L, and 0.76mEq/L respectively. Our estimation of SI effects has a clinically acceptable bias and is a simple method for quantifying acid/base abnormalities with respect to SBE.
Cytokine Elimination with High Permeable Hemofilters. A Feasible Clinical Modality for Septic Patients?
Department of Nephrology, Charité, Humboldt University, Berlin, Germany

Renal replacement therapies with high permeable hemofilters are new approaches in the adjuvant therapy of sepsis. We analyzed the cytokine elimination capacity of a newly developed high permeable polyamide hemofilter. Different renal replacement therapies are compared and tested for their clinical feasibility. Blood from healthy volunteers (n=15) was incubated for 4 hours with 1 mg of endotoxin and then circulated through a closed extracorporeal circuit. A newly developed polyamide membrane (P2SX) was used as hemofilter. Hemofiltration, hemodialysis and albumin dialysis were tested. IL-1ra (17KD), IL-6 (28kD), TNF-α (51kD), albumin (64kD), Creatinkinase (80kD) and IgG (140kD) were measured in blood and filtrates prior to the initiation and after 5 min, 1, 2 and 4 hours. Hemofiltration was superior to hemodialysis in the clearance capacity of all substances when applied in the 1L/hr ultrafiltration mode. Increasing the ultrafiltration rate/dialysate flow from 1L/hr to 3L/hr led to a significant increase in cytokine clearances (p<0.001). At 3L/hr the differences between hemofiltration and hemodialysis vanished and both techniques achieved comparable cytokine clearances. Median clearance values ranged between 25 to 54ml/min for IL-1ra, 23 to 42ml/min for IL-6 and 15 to 28ml/min for TNF-α. Albumin loss was highest in the hemofiltration group with albumin clearances ranging between 7 to 13ml/min. Using diffusion instead of convection significantly reduced the loss of albumin (p<0.01 for 1L/hr, p<0.05 for 3L/hr). Albumin dialysis was able to completely inhibit albumin loss but cytokine clearance capacity was limited. High permeable hemofilters achieve high clearances for inflammatory IL-6 and TNF-α. Due to the high protein loss in hemofiltration, dialysis in combination with balanced protein substitution seems to be a suitable approach for clinical trials.
The Nephro-Intensivist (NI) Teamwork in the Treatment of Acute Renal Failure (ARF)

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SCDU Nefrologia, Dialisi e Trapianto Renale, Ospedale S Giovanni Batti, Italia

In response to the increasing ARF incidence in the 12 Intensive Care Units (ICUs) of our 1300 beds teaching hospital, a multidisciplinary approach has been developed based on: common NI early indications, daily 12hours SHF treatment by an equipment provided of fluid autonomy for the whole interval, weight loss scheduled by Intensivist within a range of 5–7ml/min, minimal use of heparin adopting pre-dilution (30ml/min with 35mEq/L bicarbonate), 0.6m² polyamide filters, dual-lumen venous catheters, blood flow of 150–200ml/min, 50ml/min UF flow, until 30–35liters/12hrs. In severe fluid overload, session was immediately resumed, becoming CVVH. The SHF sessions were opened in sequence by one nephrology nurse and closed during the next shift. A computer connection via modem sent SHF data to Dialysis Center, displaying on line alarms and intradialytic parameters and storing the whole session off-line. In 22 months, 278 patients with ARF were treated by a total number of 1784 SHF (6.41 SHF/patient, 1–7 sessions (average =2.7)×day). SHF treatments showed a high tolerance due to respected refilling rates and biocompatibility. The long daily duration sustained a high depurative efficiency for middle and low weight uremic toxins with an average weekly Kt/V of 5.4; the mean serum creatinine value of 3.98mg/dL at the beginning of the treatment averaged 1.8mg/dL at the 5th day. Sessions prematurely stopped were 12%, mostly for clotting episodes (10.3%); however, pre-dilution and fixed scheduled length of sessions minimized heparin use decreasing the risk of severe bleeding (0.3%). Episodes of severe hypotension were rare (1%). In our experience, SHF was safe and effective, providing a standard quality level in different ICU location, minimizing training and equipment costs and allowing satisfactory flexibility for different clinical situations.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Abstracts</th>
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<td>Congestive heart failure</td>
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<tr>
<td>Sepsis</td>
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<tr>
<td>Hepatic failure</td>
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<tr>
<td>Vascular surgery</td>
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<td>Liver transplantation</td>
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<td>Kidney transplantation</td>
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<td>Heart transplantation</td>
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<tr>
<td>Lung transplantation</td>
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<td>Trauma-rhabdomyolysis</td>
<td>6</td>
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<td>Exogenous toxic</td>
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<tr>
<td>Vasculitis</td>
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<tr>
<td>Cholesterol embolism</td>
<td>3</td>
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<tr>
<td>SLE</td>
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<td>HIVAN</td>
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<td>EBV nephritis</td>
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<td>HELLP syndrome</td>
<td>1</td>
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<tr>
<td>Total number of SHF-treated patients</td>
<td>278</td>
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**Dualing Prismas: Blood Priming in Pediatric CRRT**

University of Michigan, USA

Available circuits for pediatric hemofiltration, result in up to 50% of the pediatric and neonatal patient circulating blood volume being extracorporeal. Due to this fact it has become necessary to blood prime the circuit prior to initiation. With patients requiring long-term hemofiltration, and frequent circuit changes, the risk associated with exposure to blood products and hemodynamic instability has become a concern. In an effort to decrease patient risk associated with the frequent exposure to blood products and improve hemodynamic stability, our program has developed a procedure for initiating subsequent circuits without the use of blood products beyond the initial prime. The procedure utilizes 2 Prisma machines. Prisma 1 refers to the circuit currently on the patient. Prisma 2 refers to the new saline primed circuit. Circuit changes entail: Prisma 2 is set for DFR and/or FRF rates, then Prisma 1 blood pump is stopped, the arterial line is disconnected, a saline line is added to the arterial line, and Prisma 2 arterial line is connected to the red lumen of the patients access. Simultaneously Prisma 1 and Prisma 2 blood pump are restarted at 15ml/minute. Prisma 2 circuit is primed with the patients blood, while Prisma 1 returns the circuit blood to the patient via the venous line at the same rate. When Prisma 1 blood is completely returned and Prisma 2 circuit is primed, both blood pumps are stopped. Prisma 1 venous line is disconnected and Prisma 2 venous line is connected to the blue lumen of the patients access. We report 2 infant patient receiving hemofiltration with Prisma circuits that required blood priming with each circuit change. Patient 1 was 27 months old (12kg) with HLHS. Post-op, the patient developed hypovolemia resulting in acute renal failure and hemofiltration was initiated. Patient 2 was 12 days old (3kg) with significant hypoxia at birth resulting in MOSF. Hemofiltration was initiated. Both patients required frequent circuit changes requiring blood priming. We used this procedure a total of 5 times with these patients with success as evident by hemodynamic stability and no use of further blood products. Although this technique has its limitations, the benefits are significant. The limitations include the availability of 2 Prisma machines, and the need for the circuit to be active at the time of the circuit change. The benefits include the decrease need for repeat transfusions, the minimal change in patient fluid volume changes during the procedure and a decrease of therapy down time. This is due to the fact that Prisma 2 can be primed while the patient remains on Prisma 1 and during the initiation both Prismas are delivering therapy. Down time is estimated at 5 minutes compared to 25 minutes.
Access for Pediatric CRRT

P.D. Brophy\textsuperscript{a}, T.A. Mottes\textsuperscript{a}, U. Patel\textsuperscript{a}, G.M. Barletta\textsuperscript{a}, C.H. Cramer\textsuperscript{a}, T.E. Bunchman\textsuperscript{b}

\textsuperscript{a}University of Michigan, \textsuperscript{b}University of Alabama, Birmingham, USA

The location of vascular access is a local decision with the main sites being either femoral or internal jugular placement. The type and size of vascular access is decided upon by 2 issues, the size of the child (with corresponding size of the blood vessels) and the type of anti coagulation. Due to the extreme range of sizes in children requiring CRRT (2–100kg) the access choice is wide and varied. Triple lumen access provides an extra infusing line for medications or nutrition or alternately provides a site for calcium infusion back to the patient when citrate anticoagulation is utilized. Types of access and flow characteristics used in pediatrics are listed.

**Single Lumen:** In infants the UVC (8.5Fr) and UAC (5.0Fr) have been historically used but newer machines are less forgiving due to these high resistance lines. Single lumen 5 or 6Fr (6–8cm; Cook Critical Care, Bloomington, IN) allow for blood flow rates (BFR) of 30–70mls/min but require multiple access sites.

**Dual Lumen:** 7Fr 10cm (Medcomp, Harlesville, PA, Cook Critical Care, Bloomington, IN) allow for BFRs of 30–70mls/min with arterial resistance of 0–(1/11002)150mmHg and venous resistance of 0–250mmHg. 8Fr 9, 12, 15cm (Kendall, Mansfield, MA), 8Fr 10cm (Arrow International Inc, Reading PA) allow for BFRs of 50–200mls/min with arterial resistance of 0–(1/11002)170mmHg and venous resistance of 0–250mmHg. 9Fr 10cm (Medcomp, Harlesville, PA) allow for BFRs of 50–200mls/min with arterial resistance of 0–(1/11002)170mmHg and venous resistance of 0–250mmHg similar to that of the Kendall 8Fr access. 12.5Fr (Arrow International Inc, Reading PA) allow for BFRs of 100–300mls/min with arterial resistance of 0–(1/11002)230mmHg and venous resistance of 0–250mmHg.

**Triple Lumen:** 7Fr triple lumen CVP 16cm (Medcomp, Harlesville, PA, Arrow International Inc, Reading PA) allow for BFRs of 10–30mls/min with arterial resistance of 0–(1/11002)200mmHg and venous resistance of 0–220mmHg. 12Fr triple lumen 16cm (Arrow International Inc, Reading PA) or 16 or 23cm (Kendall, Mansfield, MA) allow for BFRs of 100–300mls/min with arterial resistance of 0–(1/11002)230mmHg and venous resistance of 0–250mmHg. With the increasing use of citrate anticoagulation the use of triple lumen access will become more common and work in the development of 8Fr triple lumens are in process for Pediatric CRRT.
Regional Citrate Anticoagulation with the Prisma M100 Pre-Pump Infusion Set IMPR

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Continuous renal replacement therapy (CRRT) has been used as an alternative to conventional intermittent hemodialysis in critically ill patients. Many of these patients are at increased risk of bleeding, and the use of heparin as an anticoagulant in CRRT has been associated with a 25–30% incidence of hemorrhage. Heparin is also contraindicated in patients with heparin induced thrombocytopenia. Citrate regional anticoagulation has been shown to be a safe alternative, and various citrate protocols have reported an average CRRT dialyzer lifespan of 29.5 to 45.4h. We have previously described a simplified citrate protocol using 2% trisodium citrate as the prefilter replacement fluid and normal saline as the dialysate. Although we have shown our protocol to be effective with a dialyzer patency of ~60% after 48h, clotting of the extracorporeal circuit antecedent to the replacement fluid port remains a significant complication. We therefore assessed the effect of a modified extracorporeal circuit on dialyzer and circuit patency using our standard 2% citrate protocol. We studied the effect of administering 2% regional trisodium citrate anticoagulation at the level of the vascular access on rates of dialyzer and circuit patency. In the standard Prisma M60 Set (Hospal, France), 2% trisodium citrate is delivered at the replacement fluid port, leaving the antecedent portion of the circuit from the vascular access to the replacement fluid port not anticoagulated. However, in the Prisma M100 Pre-pump Infusion Set (Hospal, France), the replacement solution is delivered close to the vascular access, allowing for anticoagulation of virtually the entire circuit with citrate. Patients were initiated on CRRT using a M60 Set with a blood flow of 150ml/min. Two percent trisodium citrate was delivered at 250ml/h (17.5mM/l) via the prefilter replacement fluid port. The rate was titrated to keep the postfilter ionized calcium in the range of 0.25–0.50mM/L. Normal saline was used as the dialysate at a rate of 1,000–2,000mL/h. Dialyzers were routinely changed after 72h according to the manufacturer’s recommendations. Patients who clotted the extracorporeal circuit excessively (>2 episodes in 24h) despite replacement of the vascular access were switched to the M100 Pre-pump Infusion Set and followed for a further 72h. The platelet count, prothrombin and partial thromboplastin times of the studied patients did not change during use of each setup. A total of five patients were selected using the above criteria for excessive extracorporeal access clotting. The average circuit lifespan using the M100 Pre-pump Infusion Set (trisodium citrate delivered via the prefilter replacement fluid port) was 65±15h compared to 8±5h using the M60 Set (p<0.001). The average number of clotting episodes per patient in a 72-h period using the M100 Pre-pump Infusion Set was 0.4±0.5 compared to 7±0.6 using the M60 Set (p<0.001). We conclude that anticoagulation with 2% trisodium citrate using the Prisma M100 Pre-pump Infusion Set significantly reduces clotting and prolongs lifespan of the extracorporeal circuit based on our observation of five patients who experienced excessive clotting using the standard M60 Set.
Regional Citrate Anticoagulation: Impact on Membrane Survival

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The aim of this study was to evaluate the impact of citrate anticoagulation on membrane survival during CRRT. 58 ARF patients were prospectively studied, from April to October 2002, using synthetic dialysis membranes (PAN 650 SF). CRRT procedures were performed in Prisma (Gambro, Sweden) or FAD100 (BBraun, Brasil) devices. Patients were assigned to 2 different anticoagulation protocols [sodium citrate 4% (SC), enoxaparin (LMWH)] or normal saline 0.9% flush (NSal). Membrane performance was monitored every 24h by urea reduction rate (ultrafiltrate urea/pre-filter urea). Membrane was changed if the result was lower than 0.60. Treatment interruption (including patient death) and cross-over between groups were not considered for analysis. 154 membranes were analysed in 58 patients, as shown in the table. Observed adverse effects were metabolic alcalosis (n=2), citrate intoxication (n=1) in SC group and bleeding (1 event in LMWH group). This study corroborates that regional citrate anticoagulation is effective in extending membrane survival in CRRT.

<table>
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<th>LMWH</th>
<th>NSal</th>
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<tbody>
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<td>Patients (n)</td>
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<td>10</td>
<td>31</td>
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<tr>
<td>APACHE II (mean/range)</td>
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<td>15/11–19</td>
<td>15.1/10–22</td>
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<td>Membranes (n)</td>
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<td>82</td>
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<tr>
<td>Time on CRRT (h)</td>
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<td>757</td>
<td>3,763</td>
</tr>
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<td>Membrane survival (h)</td>
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<td>34.4 +23.6*</td>
<td>45.3 +28.3*#</td>
</tr>
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<td>Range</td>
<td>19–168</td>
<td>12–120</td>
<td>6–120</td>
</tr>
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</table>

*, # P<0.001
Citrate Anticoagulation Improves Filter Longevity and Uninterrupted Continuous RRT

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Introduction: Citrate anticoagulation in renal replacement therapy (RRT) is not new, but a protocol that is simple, predictable, and easy to monitor is a valuable adjunct to continuous RRT (CRRT). Continuous venovenous hemodialysis (CVVHD) lends itself well to citrate use, as the blood flow rate (BFR), dialysate flow rate (DFR) and filtration vary only modestly. Methods: The anticoagulation protocol involves ACD solution (3%) infused into the blood line coming from the patient access site toward the CVVHD filter at 1/40 of the BFR (2.5ml or 1.5mmoles/min/100ml BFR), and 20mg/ml CaCl2 infused systemically via a central line at 1/300 of the BFR (0.33ml or 0.6mmole/min/100ml BFR). Anticoagulation of the extracorporeal circuit is achieved by titration of the ACD citrate infusion to maintain an ionized Ca\(^{++}\) (iCa) in the extracorporeal circuit of 0.2–0.4mM, measured in the post-filter blood line returning blood to the patient. Systemic iCa is controlled by titrating the central venous CaCl2 infusion to maintain a systemic iCa of 1.1–1.3mM, measured in the blood entering the extracorporeal circuit upstream from the citrate infusion. Our standard CVVHD includes BFR<200ml/min and DFR=2L/h, using a polysulfone dialyzer (F70NR) and only enough ultrafiltration to maintain optimal systemic fluid balance for the individual patient. This procedure is not a high filtration (CVVH) procedure. Present safety concerns dictate filter changes every 3 days to avoid rupture of the blood line in the blood pump. Results: Results for our first 29 consecutive citrate (C) patients were compared to 29 consecutive heparin (H) patients immediately before use of the citrate protocol. Filter longevity for C patients averaged 2.5 days, only 3/61 filters failing because of clotting in 3 patients. Filter longevity averaged only 1.3 days for H patients (p<0.05), with 44/160 clotted filters in 16 patients. Average total duration of CVVHD was longer for group C (5.7 ds vs. 4.7 ds) due in part to less down time and less filter replacement. Average BUN equilibration between dialysate and blood for group C exceeded 0.9, affording an average solute clearance near 50L/d (clearance=equilibration×DFR+UF). No untoward changes in [Na\(^{+}\)] or [HCO3\(^{-}\)] attributable to citrate infusion were encountered. Both extracorporeal and systemic [Ca\(^{++}\)] were easily controlled, although high total serum calcium (retained citrate- calcium complex) was encountered in most patients with significant liver disease. Conclusion: Citrate anticoagulation using this type of protocol is reliable, effective and easy to monitor, particularly for any slow hemodialysis or hemodiafiltration procedure of the type described here. This protocol utilizes readily available infusion materials with infusion rates adaptable to variable blood flow rate. The protocol not only eliminates heparin and systemic anticoagulation, but also facilitates prolonged and effective CRRT with few side effects for critically ill ARF patients.
Comparison of Outcomes between High Volume Hemofiltration (HVHF) and Continuous Veno-Venous Hemodiafiltration (CVVHDF)

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Over the past five years, continuous veno-venous hemodiafiltration (CVVHDF) has been the CRRT modality of choice in the intensive care units of this tertiary care medical center. Recent studies have suggested a possible survival benefit among critically ill patients with renal failure treated with high volume hemofiltration (HVHF). HVHF, as performed at this center, involved 3L/hr replacement fluid flow rates as compared with standard 1.5L/hr dialysate and hemofiltration flow rates (respectively) in patients treated with CVVHDF. Questions of clinical efficacy, differing practice patterns among consultants, along with increased resource utilization, prompted a comparative evaluation between these two modalities. The goal of this study was to compare single-center case matched outcomes between patients treated exclusively with either HVHF or CVVHDF. Retrospectively, we compared case matched outcomes (30 day mortality and recovery of renal function) using Kaplan-Meier survival curves based on date of initiation of continuous renal replacement therapy. Cases were matched first by age, then by severity of illness (measured as APACHE II scores) and were taken from our CRRT database of 414 patients who received CRRT from October 1, 1997 thru November 30, 2001. Thirteen patients in the HVHF cohort were matched with twelve patients in the CVVHDF cohort. Results of the case matched variables are shown below. Although survival was marginally decreased in the HVHF cohort 38.4 vs. 50%, when studied by Log-Rank this difference was not found to be statistically significant (p=0.907). Likewise, recovery of renal function among those who survived to 1 month after initiation of CRRT was identical (60%). Rational for initiation of CRRT differed substantially between the cohorts. When matched for age and severity of illness, patients treated with HVHF had similar survival and recovery of renal function to patients treated with CVVHDF at this medical center. It is unlikely without tremendous numbers of patients any true advantage of either modality will be found. Further, while the optimal modality of CRRT remains yet to be determined, this preliminary work suggests encouraging survival trends among these critically ill patients.
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<tr>
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<th>HVHF</th>
<th>CVVHDF</th>
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<tr>
<td>Number of patients</td>
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<td>Mean age</td>
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<td></td>
<td>*Overload 23%</td>
<td>*75% Acidosis 66%</td>
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<td></td>
<td>*Acidosis 8%</td>
<td>*Hyperkalemia 42%</td>
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<tr>
<td></td>
<td>*Reperfusion Injury 8%</td>
<td>*Uremia 8%</td>
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<tr>
<td>Mean days of therapy</td>
<td>3.61</td>
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<td>Recovery of renal function at 30 days post initiation of CRRT</td>
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<td>60%</td>
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<td>Alive after 30 days post initiation of CRRT</td>
<td>38.40%</td>
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Continuous venovenous hemofiltration (CVVH) has become increasingly prevalent as a form of renal replacement therapy in acutely ill children in an intensive care setting. Standard heparin anticoagulation for CVVH can often result in increased bleeding and occasional thrombocytopenia. Accordingly, regional citrate anticoagulation has become an important alternative to standard heparin anticoagulation during CVVH. However, there is no universal agreement on how to monitor anticoagulation during citrate infusion. While some centers recommend following post-filter activated clotting time (ACT), others recommend following the post-filter ionized calcium (iCa). **Objective:** The purpose of this study is to evaluate whether the post-filter iCa level correlates with the post-filter ACT in pediatric patients undergoing CVVH with regional citrate anticoagulation. **Design:** Prospective observational study. **Setting:** Pediatric intensive care unit in a tertiary-level children’s hospital. **Subjects:** Pediatric patients undergoing CVVH with regional citrate anticoagulation. Four patients were studied, ranging in ages from 10 months to 13 years. Primary diagnoses included end-stage kidney failure, stem cell transplant in the setting of acute lymphocytic leukemia, and bone marrow transplant in the setting of hemophagocytic syndrome. Indications for CVVH included chronic kidney failure, acute kidney failure, oliguria and hypervolemia. **Interventions:** CVVH with regional citrate anticoagulation using ACD-A solution and replacement solution (generally containing 100meq/L NaCl, 35meq/L NaHCO3, 0–4meq/L KCl and 150mg/L MgSO4 and customized as needed). Citrate infusion generally was started at 1.5×blood flow rate and adjusted to provide a post-filter iCa of 0.25 to 0.4. Calcium chloride (CaCl2) (8g/L) was infused separately into the patient at an initial rate of 0.4×the citrate flow rate to maintain a normal patient iCa of 1.1 to 1.3. No dialysate was used. **Measurements:** The following parameters were measured simultaneously: post-filter iCa, patient serum iCa, post-filter ACT, and partial thromboplastin time (PTT). The hourly citrate and CaCl2 infusion rates also were recorded and normalized per body weight. Measurements were combined from all four patients and analyzed by linear regression. **Results:** No significant correlation was observed between post-filter iCa and post-filter ACT (p = 0.36; n = 43). As expected, no significant correlation was observed between post-filter iCa and patient PTT (p = 0.09; n = 10), since patient anticoagulation is reversed by CaCl2 infusion and normalizing serum iCa. Also as expected, post-filter ACT did not correlate with patient PTT (p = 0.53; n = 12). Citrate infusion rate did significantly correlate with post-filter iCa (p = 0.001; n = 77) but not post-filter ACT (p = 0.16; n = 181). **Conclusions:** Post-filter iCa levels do not correlate with post-filter ACT levels in pediatric patients undergoing CVVH with regional citrate anticoagulation. Since post-filter iCa directly measures the regional effect of citrate during CVVH, caution should be used in following ACT instead of post-filter iCa during regional citrate anticoagulation.
Finite Element Mathematical Model of Solute Transport in Hemofilter Membranes

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Previous mathematical models of hemofilter solute transport have usually employed lumped compartmental representations and uniform membrane processes, and have required a number of assumptions for analytical efficiency. These models often do not address regional variations in membrane transport, convection-diffusion interaction, and region-dependent processes such as backfiltration. These influences are of particular importance in therapies such as high-volume hemofiltration. In order to overcome these limitations, we developed a finite element model of hollow fiber membrane transport that incorporates both momentum and mass transport. The geometry is based on the specifications of the AN69S hollow fiber hemofilter (Gambro), and modeled as a 2-D axisymmetric region with distributed blood, membrane and dialysis phases. Navier-Stokes equations were used for momentum transport in blood and dialysis phases, Brinkman equations for porous flow for membrane momentum transport, and the convection-diffusion equation for mass transport in all phases. Blood was treated as a non-Newtonian fluid, and local hematocrit and protein concentration were incorporated for viscosity and osmotic pressure determinations. Anisotropic solute diffusivity and Brinkman permeability coefficients were used to simulate membrane channel transport. Boundary conditions were established for pressure, velocity and concentration at membrane boundaries. The model was solved with FEMLAB (Comsol, Inc.). The model simulates transport of small solutes in aqueous medium. Model parameters can be adjusted to simulate various hemofilter operating conditions. Model performance parallels that of experimental data for comparable hemofilters. Simulations of fluid flux and protein concentration were conducted, and support the osmotic pressure theory as a singular basis for limitation of fluid flux in hemofilter membranes.
Results of Peritoneal Equilibration Test during the First Months of CAPD

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It was suggested that peritoneal permeability changes during the initial course of peritoneal dialysis (PD) treatment and the first peritoneal equilibration test (PET) results may not be adequate for further analyses of differences in peritoneal membrane permeability, closely related to biocompatibility of PD solutions and PD complications. In this study we undertook a task to compare the results of PET obtained no later than one month from the continuous ambulatory peritoneal dialysis (CAPD) beginning and those shown after 5–7 months of CAPD treatment. In the retrospective analysis, from 150 PD patients two groups were selected. Group I included patients in whom PET was performed during the first month of CAPD treatment (n=41); group II consisted of patients who underwent PET after finishing 5 months of CAPD treatment but dialyzed no longer than 7 months (n=60). In group I there were 14 women and 27 men, being on CAPD through 0.47±0.26 months. Group II included 23 women and 37 men, dialyzed for 6.02±0.57 months. In the prospective study, in 27 CAPD patients (10 women, 17 men) the first PET was performed during the first month of CAPD (0.40±0.25 months) and the second PET was done after 5–7 months (6.28±0.42 months) of CAPD treatment. Values of D4/P2 creatinine, D4/D0 glucose and dialysate drain volumes were analysed in prospective studies and retrospective ones as well. The results of PET were considered as the stable ones when the difference between the first and the second values were no greater than±10%. In the retrospective analysis there were no significant differences in peritoneal transport between both groups, but slightly higher V-M transport (D4/P2 creatinine 0.61±0.14 vs. 0.65±0.19) and M-V transport (D4/D0 glucose 0.38±0.12 vs. 0.33±0.12) was observed in group II. In group I a correlation between drain volume and D4/D0 glucose (r=+0.433, p=0.005) was shown; in group II drain volume was related to D4/D0 glucose (r=+0.289, p=0.025) and D4/P2 creatinine (r=−0.261, p=0.043) as well. Percentual distribution of low, low-average, high-average and high transporters was not statistically different between both groups. In the prospective studies, a significant increase in V-M peritoneal permeability was shown when D4/P2 creatinine was compared in the first (0.61±0.15) and the second (0.68±0.18) PET (p=0.027) in all patients (n=27). Increased V-M permeability occurred in 12 of 27 patients (44%); in other 12 persons (44%) permeability remained unchanged and in 3 patients (12%) it was decreased. In patients who revealed a decrease in peritoneal permeability the initial D4/P2 was significantly higher (0.83±0.67) than in those with stable (0.62±0.12, p=0.021) or increasing permeability (0.55±0.14, p=0.021). The M-V peritoneal permeability did not show significant changes during the first 5–7 months of CAPD treatment. Significantly higher drain volumes at 5–7 months of CAPD treatment (2,500±141ml vs. 2,304±122ml, p=0.039) were observed in patients with decreased peritoneal permeability compared to patients in whom peritoneal permeability increased. There were no significant changes in peritoneal transport and drain volume related to patients’ gender. Our results indicate that changes in the peritoneal permeability during the first months of CAPD treatment occur independently on initial peritoneal transport rates. Changes in peritoneal transport are associated with significantly different ultrafiltration volumes.
Simplified Regional Anticoagulation for Continuous Veno-Venous Hemodiafiltration

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**Background:** Regional anticoagulation with trisodium citrate for continuous veno-venous hemodiafiltration (CVVHDF) is an effective and safer alternative to heparin, in patients at high risk for bleeding. Current protocols using trisodium citrate with calcium free dialysate and a separate systemic intravenous calcium infusion are cumbersome and labor-intensive. **Purpose:** In search for a simpler and effective technique, we evaluated Anticoagulant Citrate Dextrose – Formula A (ACD-A) solution (3% – trisodium citrate 2.2% and citric acid 0.8% – Baxter Healthcare, Deerfield, IL, USA) as a regional anticoagulant for CVVHDF in combination with calcium containing dialysis solution. **Methods:** ACD-A solution was initiated at 150ml/hr via a ‘Y’ connection at the junction of double lumen hemodialysis catheter and prefilt er tubing of Gambro PRISMA M100 set with AN69 hemofilter. The rate was adjusted to maintain postfilter ionized calcium (iCa) between 1.0–2.0mg/dl. Calcium chloride (10%) solution was administered intravenously every 6 hours to maintain systemic serum iCa between 3.5–4.0mg/dl. The vascular access consisted of a double lumen catheter placed in femoral, internal jugular or subclavian vein. Blood flow rate was set at 150ml/min. Dianeal low calcium peritoneal dialysis solution (Ca 2.5mEq/L, Na 132mEq/L, Cl 95mEq/L, Mg 0.5mEq/L, lactate 40mEq/L, 1.5% dextrose, Baxter Healthcare, Deerfield, IL, USA) was delivered at 500ml to 1,000ml/hr. Normal saline (Na 154mEq/L, Cl 154mEq/L) was used as replacement fluid at 500 to 1,000ml/hr. The PRISMA M-100 set was changed every 96 hours even if the circuit was patent. During the period of January 2001 to September 2002, 38 patients (8 females, 30 males) in intensive care unit received citrate based CVVHDF in combination with calcium containing dialysate. Thirty patients had acute renal failure, 5 had acute on chronic renal failure and 3 had end stage renal disease. Heparin was contraindicated because of recent major surgery in 16 patients and severe thrombocytopenia and/or coagulopathy in 8 patients. Fourteen patients were considered high risk for systemic anticoagulation due to the severity of the underlying disease. **Results:** CVVHDF was performed for a total of 394 days using 149 M100 sets. The average length of treatment was 10.5±0.15 days (range 2–46 days) using ACD-A at the mean rate of 159±0.16ml/hr (17.97±0.02mmol per hour) and calcium containing dialysate at the mean rate of 679.6±4.14ml/hr. The mean hemofilter life span was 63.5±3.12hours. Twenty percent of the hemofilter were patent at 96 hours, 23% clotted before 96 hours, 26% were discontinued before 96 hours for reasons other than clotting and 25% of were lost due to catheter malfunctioning. Seventy five percent, 61%, 49% and 26% of hemofilters were patent at 24, 48, 72 and 96 hours respectively. Mean serum concentration of sodium, bicarbonate, total calcium and ionized calcium at 48 hours post initiation of CVVHDF was 137.95±0.3mmol/L, 26.83±0.10mmol/L, 9.07±0.02mg/dl and 3.47±0.01mg/dl respectively. The change in serum concentration was statistically significant for bicarbonate and ionized calcium from the base level. Serum sodium was more than 145mmol/L in 5 patients and more than 150mmol/L in one. None of the patients had symptomatic hypocalcaemia (arrhythmia, seizures) and the lowest serum ionized calcium was 2.8mg/dl. Mean daily calcium administered per patient was 10.8±8.7mEQ. Metabolic alkalosis requiring 0.1N HCL infusion was observed in 5 patients. **Conclusion:** Our simplified technique of regional anticoagulation with 3% trisodium citrate with calcium containing dialysate is not associated with increased hemofilter clotting and obviates the need for systemic calcium infusion and provides an alternative to calcium free dialysate.
**Normocarb™ as a Replacement Fluid for Convective Clearance In CVVH**

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Historically programs have used pharmacy made solutions with a bicarbonate base to use as replacement fluids for convective clearance in CVVH. Many programs have reported pharmacy solution errors with near fatal or fatal consequences. The FDA Modernization Act of 1997 (www.fda.gov/opicom/backgrounders/modact.htm) in the section under Pharmacy Compounding states, *The Act creates a special exemption to ensure continued availability of compounded drug products prepared by pharmacists to provide patients with individualized therapies not available commercially.* This allows for Normocarb™ (Dialysis Solutions Incorporated, Richmond Hills, Ont) to be used as a replacement fluid for it needs to be compounded. From March 2002 to October 2002, 5 children (age range new born to 17yrs, wt range 3.2–107kg) underwent either CVVH with Normocarb™ (2 newborns on ECMO) or CVVHDF (14, 15, 17 y/o) with Normocarb™ as both dialysis and replacement fluid. The indications for the newborns were sepsis while in the older aged group 2 pts (14 and 17 y/o) had rhabdomyolysis with hypercatabolism while the 14 y/o had sepsis with hypercatabolism. The newborns on ECMO had a HF-400 in line with IV pump for prefilter Normocarb™ infusion and with IV pump for ultrafiltrate control; in this system heparin was used for anticoagulation. The 3 older children were on the PRISMA (Gambro Healthcare, Lakewood, CO) with a M-60 (14 y/o) or M-100 (15, 17 y/o) with the PRISMA in the CVVHDF mode with Normocarb™ with KPhos (2meq/L) and KCL (2meq/L) in both the dialysis bag (at 2.5liters/hr) and in the replacement bag (at 2liters/hr); all received citrate anticoagulation. No complications were found related to the Normocarb™ as replacement, but cost was diminished and safety was ensured. The use of identical additives to the Normocarb™ helps to minimize confusion at bedside. We conclude that Normocarb™ is a safe and reasonable solution for CVVH when convective clearance is needed.
Anticoagulation for Pediatric CRRT: A Report from the ppCRRT Registry Group

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Refinement of CRRT circuit anticoagulation (ACG) methods has been an active area of clinical research in critically ill adult patients over the last decade. While most pediatric (ped) centers have experience with heparin-based (hepACG) ACG protocols, heparin may not be ideal for the critically ill patient (pt), since pts may experience systemic anticoagulation as a result. The ppCRRT Registry now reports the first ped data comparing circuit life and side effects using hepACG vs. a citrate-based regional ACG method (citACG). The 5 ppCRRT centers practice according to local protocol; 3 centers used hepACG, one center used citACG, and one center changed from hepACG to citACG in 7/02. Heparin doses were adjusted to keep activated clotting times between 180 and 240 seconds. Regional citACG was accomplished in CVVH-D mode with ACD-A infusion into circuit arterial line to maintain circuit ionized calcium between 0.25–0.5mmol/L and a central calcium chloride infusion to keep patient ionized calcium between 1.1 and 1.3mmol/L. 78 ped pts (mean age 9.6±7.6yrs) required 261 CRRT circuits comprising 10,274 hours of CRRT from 1/1/01 to 10/31/02. 161 circuits used hepACG (6,976 hours), 70 circuits used citACG (2,521 hours) and 30 circuits used no ACG (777 hours). Mean circuit life and % circuits functioning at 72 hours using each method are shown in the Table. Log-rank analysis (circuits stopped for patient test, change to hemodialysis, or scheduled circuit change were censored) showed no circuit survival difference between hepACG and citACG, but circuits with no ACG functioned for shorter duration (p<0.001) than circuits with ACG. 20/70 citrate ACG vs. 35/161 heparin ACG circuits clotted (p=NS). No side effects were reported using citrate ACG. 6 pts receiving hepACG had systemic bleeding, 4 of which lead to discontinuation of hepACG. Our ppCRRT Registry data show that (1) both hepACG and citACG protocols lead to similar circuit survival times and (2) side effects were rare for hepACG and did not occur with citACG. We suggest that citACG may be preferable to hepACG for CVVH-D in ped pts with systemic bleeding.

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<th>hepACG</th>
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<tr>
<td>Mean circuit duration (hrs)</td>
<td>43.2±26.9</td>
<td>36.0±28.8</td>
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<tr>
<td>% circuits functional at 72 hours</td>
<td>60</td>
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Conditioning of Blood Prime Using Prisma® – Based CVVHD for Pediatric Patients

T.A. Mottes, D.A. Pasko, B.A. Mueller

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A blood prime is required to fill the extracorporeal circuit when CVVHD is used in children <10kg. This blood is frequently hyperkalemic and should be “conditioned” via dialysis prior to CVVHD initiation to correct potassium concentrations and prevent administration of a potassium bolus. The purpose of this study was to determine the efficacy of a CVVHD blood-conditioning regimen for use prior to CVVHD initiation in children. Methods: Two in vitro CVVHD Prisma circuits (M60; Hospal) were primed with expired human blood and a bicarbonate-based dialysate containing potassium 3mEq/L. Blood conditioning was performed in a recirculating mode with Qb=180mL/min and Qd=41.67mL/min for 30 minutes. Arterial and venous blood and dialysate were sampled at 0, 2.5, 5, 7.5, 10, 15, 20, and 30 minutes to assess potassium, sodium, and chloride content. Electrolyte clearance was calculated and time to normalized electrolyte concentrations was determined. Results: Initial blood concentrations were K=25.8mEq/L (experiment 1) and 24.1mEq/L (experiment 2), Na=144mEq/L (exp. 1) and 175mEq/L (exp. 2), Cl=86mEq/L (exp. 1) and 130mEq/L (exp. 2). Mean ± SD clearances for the three electrolytes were 36.41 ± 4.04mL/min, 39.05 ± 4.25mL/min, and 42.8 ± 5.16mL/min for potassium, sodium, and chloride respectively. All blood electrolyte concentrations were at ‘normal’ concentrations by 5 minutes. Conclusion: Blood primes for Prisma®-based CVVHD can be conditioned at Qb 180mL/min and Qd 41.67mL/min for 5 minutes before CVVHD initiation to ensure normalized K, Na, and Cl concentrations before CVVHD initiation.
Conditioning of Blood Prime using Diapact®-Based CVVHD for Pediatric Patients

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A blood prime is required to fill the extracorporeal circuit when CVVHD is used in children <10kg. This blood is frequently hyperkalemic and should be ‘conditioned’ via dialysis prior to CVVHD initiation to correct potassium concentrations and prevent administration of a potassium bolus. The purpose of this study was to determine the efficacy of a CVVHD blood-conditioning regimen for use prior to CVVHD initiation in children. **Methods:** Four in vitro CVVHD Diapact circuits (M60; Hospal) were primed with expired human blood and a bicarbonate-based dialysate containing potassium 3mEq/L. Blood conditioning was performed in a recirculating mode without ultrafiltration for 30 minutes (Qb=200mL/min and Qd=33mL/min). Arterial and venous blood and dialysate were sampled at 0, 2.5, 5, 7.5, 10, 15, 20, and 30 minutes to assess potassium, sodium, and chloride content. Electrolyte clearance was calculated and time to normalized electrolyte concentrations was determined. **Results:** Initial blood concentrations were K=21.3mEq/L (experiments 1 & 2) and 9.6mEq/L (experiments 3 & 4), Na=164mEq/L (exp. 1 & 2) and 162mEq/L (exp. 3 & 4), Cl=142mEq/L (exp. 1 & 2) and 148mEq/L (exp. 3 & 4). Mean±SD clearances for the three electrolytes were 30.88±2.78, 33.39±0.14, and 33.29±0.21ml/min for potassium, sodium, and chloride respectively. All blood electrolyte concentrations were at ‘normal’ concentrations by 7.5 minutes. **Conclusion:** Blood primes for Diapact®-based CVVHD in small children can be conditioned adequately at Qb200ml/min and Qd 33ml/min for 7.5 minutes to ensure normalized K, Na, and Cl concentrations before CVVHD initiation.
Cost-Analysis of an Interdisciplinary Protocol for Continuous Veno-Venous Hemodiafiltration (CVVHDF) in Intensive Care Units

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The cooperative work of Dialysis and Intensive Care (ICU) staffs can improve the treatment of critically ill patients with acute renal failure, as ICU nurses are particularly trained to the complex management of these patients, whereas Dialysis staff has the best expertise with blood purification. On this basis, we implemented an interdisciplinary program for CVVHDF in ICU patients, whose main details are reported below. About 200 patients were treated in July 1st 1998 through November 1st 2002. Clinical management of both renal disease and CVVHDF was made by nephrologists, in a close relationship with Intensivists. Technical assistance to CVVHDF was performed by both dialysis nurses (start / end of treatment, technical assistance, emergencies) and ICU personnel (ancillary manoeuvers, fluids and anticoagulant supplies, scheduled blood sampling). Main features: 

- **Machine**: Hospal Prisma\textsuperscript{®}, Filter AN69 0.9m\textsuperscript{2}; 
- **QB**: 150ml/min; 
- **QD**: 2L/h; 
- **QHDF**: 0.5L/h; bicarbonate buffered fluids; 
- **treatment length**: 3.9±4.4 days/pts; 
- **life of the circuit**: 36±15h.

To calculate the expenditure of this CVVHDF management, both technical costs (extracorporeal circuit, dialysate and HDF-fluids, priming solutions, heparin, double-lumen catheter, disposable devices) and staff costs (average time for nurse and medical surveillance, multiplied by their respective salaries) were considered. The daily cost of CRRT was 266.96 (1=about 1$); of which, 78% for devices and 22% for human resources. Nurse interventions required 141 minutes per day, 55% of which (77min) supplied by ICU nurses and 45% (64min) by Dialysis nurses. On average, CVVHDF management required less than 1min/nurse/hour for both Dialysis and ICU nurses. The co-operation between Dialysis and Intensive Care Units improved the use of human resources and allowed us to supply CRRT to all critically ill patients with acute renal failure. Being the time for the technical assistance shared among Dialysis- and ICU-nurses in such a way, additional personnel was not required for CVVHDF. As the higher expenditure was due to the cost of technical devices, it can be reasonably assumed that, in the near future, even the availability of economic resources will no longer represent a limitation against the widespread use of continuous therapies in ICU.
Technical Characteristics of Pediatric CRRT: A Report of the Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) Registry Group

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ppCRRT Registry Group, USA

We report mechanical and technical characteristics for 77 pediatric CRRT subjects from the ppCRRT Registry. Catheter data are shown in table 1. CRRT modality and solute clearance are shown in table 2. Mean blood flow (Q_B) was 100ml/min (range 15–200ml/min); mean Q_B per body weight was 4ml/kg/min (range 1.1–22ml/kg/min). Nutritional data from 23 subjects/84 circuits showed mean protein intake of 1.7g/kg/d (range 0–4g/kg/d) and mean caloric intake of 40.3kcal/kg/d (range 3–90kcal/kg/d). In 261 CRRT circuits/10,274 hours of therapy time, there were 35 reported complications (other than filter clotting). 20/35 complications were mechanical (e.g., blood leak, pump failure, calibration error). 15/35 complications were patient events possibly related to CRRT (11 bleeding, 2 hypotension, 2 other). Of 11 circuits complicated by bleeding, 10 circuits had heparin anticoagulation, 1 no anticoagulation. Review of Registry data indicates a broad range for catheter size, Q_B and solute clearance, demonstrating the clinical variability seen in those critically ill children who require CRRT. Femoral catheter site was most commonly used. The majority of treatments employed diffusion-based methods. CRRT complications were few; bleeding, when reported, was most often associated with heparin and never with citrate. Ongoing data analysis as the Registry matures will permit more detailed description of pediatric CRRT methods and a more complete evaluation of various techniques in relation to outcome.

Table 1
Catheter size and location related to body weight

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<th>Patient body weight</th>
<th>Catheter size (Fr)</th>
<th>Catheter location</th>
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<tbody>
<tr>
<td></td>
<td>7 8 9 10 11.5 12 12.5 Femoral Internal Subclavian jugular</td>
<td></td>
</tr>
<tr>
<td>&lt;5kg (n=7)</td>
<td>3 2 1 1 *3 *3 *3 3 1</td>
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<td>5–10kg (n=5)</td>
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<tr>
<td>&gt;60kg (n=14)</td>
<td>*6 3 5 11 1 1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>8 9 6 18 23 4 9 64 7 6</td>
<td></td>
</tr>
</tbody>
</table>

Table 2
CRRT modality and calculated solute clearance

<table>
<thead>
<tr>
<th>Modality</th>
<th>n</th>
<th>Calculated solute clearance* (mean (range))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ml/min</td>
</tr>
<tr>
<td>SCUF</td>
<td>9</td>
<td>*2.3 (0.5–5.1)</td>
</tr>
<tr>
<td>CVVH</td>
<td>42</td>
<td>15.5 (1.1–35.1)</td>
</tr>
<tr>
<td>CVVHD</td>
<td>184</td>
<td>19.5 (1.9–48.3)</td>
</tr>
<tr>
<td>CVVHDF</td>
<td>26</td>
<td>32.6 (13.0–65.4)</td>
</tr>
<tr>
<td>All modalities</td>
<td>261</td>
<td>19.6 (0.5–65.4)</td>
</tr>
</tbody>
</table>

*Solute clearance (K) calculated as the sum of CRRT effluent, as follows: K = ΣQeff(1−QD/Qufnet+QR(prefilter)+QR(postfilter))/(QB/QB(prefilter))
Continuous Venovenous Hemofiltration with Citrate-Based Replacement Fluid Is Safe

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Background: Regional anticoagulation with trisodium citrate is an effective form of anticoagulation for continuous renal replacement therapy (CRRT). The fear of insufficient clearance of sodium citrate from the blood has limited the use of sodium citrate with hemofiltration (CVVH). Recently, a simple system for regional citrate anticoagulation for CVVH was described in which citrate was delivered in predilution replacement fluid. In a population of patients at high risk of bleeding using heparin anticoagulation, we evaluated our 1 year experience using up to 3L/h of citrate-based replacement fluid. Methods: Standard solution (trisodium citrate 13.3mmol/liter, sodium chloride 100mmol/liter, magnesium chloride 0.75mmol/liter and 0.2% dextrose) was delivered at a fixed rate of 2 to 3L/h in pre-filter mode of a Diapact (B Braun) device. Ultrafiltration was increased beyond this rate by adding the volume of all other parenteral solution plus desired net UF. A central calcium chloride infusion was used to maintain a normal systemic iCa++. We retrospectively reviewed the outcomes and complications associated with this protocol in 71 patients treated over the past year, evaluating the efficacy and safety of this technique and patient mortality. Results: Clinical data of 71 patients (age =59±15 years, 65% male and 62% Caucasian) who underwent a total of 507 CVVH patient-days was analyzed. There were no episodes of significant bleeding or citrate toxicity. Seventy percent of patients died for reasons unrelated to CRRT. A mean life span of filters was 33±19hours (n=24). Control of fluid, electrolyte balance and azotemia, analyzed in a subset of 36 patients, was excellent (table 1). Conclusions: CVVH with sodium citrate replacement fluid of up to 3L/h is a safe and efficient technique in patients at high risk of bleeding.
## Table 1

<table>
<thead>
<tr>
<th></th>
<th>CVVH day 1</th>
<th>CVVH day 2</th>
<th>CVVH day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine, mg/dl</td>
<td>3.3±1.4</td>
<td>2.7±1.5</td>
<td>1.9±0.7</td>
</tr>
<tr>
<td>BUN, mg/dl</td>
<td>73±34</td>
<td>56±29</td>
<td>41±20</td>
</tr>
<tr>
<td>Serum total Ca, mg/dl</td>
<td>7.9±1.0</td>
<td>8.7±1.2</td>
<td>9.9±1.2</td>
</tr>
<tr>
<td>Serum ionized Ca, mmol/L</td>
<td>1.05±0.14</td>
<td>1.14±0.15</td>
<td>1.24±0.09</td>
</tr>
<tr>
<td>Serum Na, mmol/L</td>
<td>140±6</td>
<td>138±5</td>
<td>137±6</td>
</tr>
<tr>
<td>Serum CO2, mmol/L</td>
<td>23±5</td>
<td>24±4</td>
<td>23±5</td>
</tr>
<tr>
<td>Serum K, mmol/L</td>
<td>4.3±0.5</td>
<td>4.2±0.4</td>
<td>4.3±0.6</td>
</tr>
<tr>
<td>Serum phosphorus, mg/dl</td>
<td>5.2±1.8</td>
<td>4.3±1.2</td>
<td>3.6±1.0</td>
</tr>
</tbody>
</table>
Randomised Controlled Trial Enoxaparin versus Heparin in Continuous Renal Replacement Therapy

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ICU Epworth Hospital Richmond, Australia

**Background:** Anticoagulation is an important aspect CRRT. Unfractionated heparin (UFH) is commonly employed, but low molecular weight heparins (LMWH) may offer potential advantages, such as decreased coagulation studies and decreased bleeding. There is little published information on LMWH in CRRT. The aim of this randomised study was to compare UFH with enoxaparin as anticoagulation for CRRT. **Methods:** Patients requiring CRRT for ARF, who had no contraindication to anticoagulation, were eligible. Patients were randomised to titrated heparin infusion, adjusted to a goal APTT of 45, or fixed dose enoxaparin (0.5mg/kg bolus followed by 1.0mg/kg/day). Haemofiltration was standardised to CVVHDF, with 1,000ml/hr dialysate, 750ml/h predilution and 125ml per min blood flow. The primary outcome measure was haemofilter survival time. Secondary measures included APTT level, anti-Xa levels, change in haemoglobin and platelets, incidence of bleeding and number of transfusions. **Results:** Twenty-nine patients (87 filters) were randomised, fourteen (36 haemofilters) to heparin (mean ± SD, age 74.7 ± 5.1, Apache II Score 26.2 ± 4.0) and 15 patients (51 haemofilters) to enoxaparin (age 77.5 ± 10, Apache II Score 27.3 ± 6.0). Median (range) APTT level was 49s (24–216s) for heparin, and anti-Xa level was 0.29IU/ml (0–0.87IU/ml) for enoxaparin. We found no significant difference in filter life between the two groups. Median (range) haemofilter life was 23.5h (1.50–74h) for heparin and 25.3h (0.75–72.8h) for enoxaparin. Kaplan-Meier derived mean haemofilter survival time was 36.0 hours for heparin and 36.1 hours for enoxaparin (p = 0.27 Log rank). There was no significant change in haemoglobin concentration or platelet count with either drug. There was one episode of major bleeding during 989 hours of heparin (0.024/24h) and four episodes during 1,476h of enoxaparin (0.065/24h). **Conclusions:** Although enoxaparin is an effective anticoagulant for CRRT, we were unable to demonstrate that it offers any real advantage over unfractionated heparin.
Hospital Reimbursement and Cost Benefits of CRRT

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\textsuperscript{b}University of Alabama at Birmingham,  
\textsuperscript{c}University of Michigan Health Systems, USA,  
\textsuperscript{d}Gambro, Lund, Sweden

Hospitals can be reimbursed for CRRT, the amounts of which depend on facility billing methods and sources of reimbursement. Hospitals are reimbursed either by government programs, such as Medicare and Medicaid, or by private insurance. Medicare reimbursement for hospitalization is based on a Diagnostic Related Group (DRG) code assigned by the hospital upon discharge. The code is substantiated by the ICD-9 codes assigned by physicians. Medicare reimburses a lump-sum amount (per-case payment), based on the DRG, regardless of length of stay, medication, therapy, or labor. Private insurance companies pay either contract or usual, customary, and reasonable (UCR) rates for items billed, depending on if it is an HMO/PPO or traditional plan. Hospitals can obtain reimbursement from private insurance by billing via line item for disposables, medication, solutions, and labor. In addition, hospitals may bill a setup fee to capture labor and maintenance costs. The costs of CRRT are related to the initial expenditure of the machinery (~$22,000 as compared to ~$18,000 for a hemodialysis machine), vascular access (~$50–100.00), tubing and membranes (~$100.00–150.00/72hrs or treatment as opposed to ~$30.00/4hrs treatment on hemodialysis), anticoagulation (cost of heparin or citrate is minimal but may affect life of circuit effective disposable costs), dialysis solutions (7.00/liter×2liters/hr×24hrs (~336.00/day) when compared to HD which runs 500–800ml/min ×4hrs at an average cost of $100.00/day) and labor (average of 1hr/day of dialysis staff time×3 days of CRRT vs. 18hrs of dialysis staffing time if a patient is on HD for those same 3 days). Again, disposables (vascular access, filter, tubing, solutions, and anticoagulation) can be billed via line item to private insurance. The cost benefits of CRRT include decreasing labor and use of ancillary services, reducing length of stay, and decreasing technology requirements (medication and other therapies). An effective CRRT treatment will last 72hrs requiring minimal staff involvement. In addition, use of dedicated CRRT equipment does not require the use of hemodialysis staff (ancillary services). Studies published by Gettings et al. [Intensive Care Med 1999;25:805–813] and Schetz et al. [Adv Ren Replace Ther 2002;9:282–289] have shown that early initiation of CRRT decreases time on ventilators (technology) and length of stay, both of which translate into significant cost savings on the total hospitalization. Center data has shown that comparison of daily hospital cost of CRRT is ~$450.00 while daily cost of Hemodialysis is ~$660.00. Two separate studies have evaluated the total cost of CRRT on hospital bills. In a study published by Goldstein et al. [Pediatrics 2001;107: 1309–1312], the cost of CRRT was, on average, 0.9% of the total bill. In a study published by Mehta et al. [Kidney Int 2001;60:1154–1163], the cost of CRRT was comparable to cost of IHD, yet the net fluid and solute control on CRRT was improved. Gettings et al showed a reduction in length of stay by approximately 6 days and a reduction of days required of CRRT by initiating CRRT early vs. late. If the total cost of CRRT for a patient's hospitalization equals approximately one day of ICU, then decreasing it by even one day can balance the cost. Conclusion: The costs of IHD and CRRT are comparable, but the benefits of CRRT lead to significant cost savings when evaluating the total cost of hospitalization. An aggressive CRRT program can decrease hospitalization costs by reducing length of stay, use of ancillary services and labor, and technology (medications and other therapies). Hospitals can be reimbursed for CRRT, the amount of which depends on the source of payment and hospital billing methods. Administrators are encouraged to examine the various billing methods when initiating a CRRT program to ensure charges are adequately captured.
Continuous Venovenous Hemodiafiltration vs. Hemodialysis as a Renal Replacement Therapy in Patients with Acute Renal Failure in the Intensive Care Unit

J.W. Chang, W.S. Yang, J.W. Seo, S.-K. Park
University of Ulsan, Asan Medical Center, Seoul, Korea

Hemodialysis (HD) and continuous venovenous hemodiafiltration (CVVHDF) have been adopted for renal replacement therapy (RRT) in patients with acute renal failure (ARF). Although CVVHDF has the hemodynamic stability, an effective volume removal, and a superior metabolic control, previous studies reported no definite improvement of survival rate by CVVHDF compared to HD. We assumed because that they did not analyze the survival rate under the stratification of disease severity. In this retrospective study, we evaluated the clinical outcome of patients with ARF in the ICU who were treated with CVVHDF vs. HD, under the stratification of disease severity by APACHE III score system and the number of organ failure. A total of 148 ICU patients with ARF underwent HD (M:F = 70:25, 45 ± 17 years) or CVVHDF (M:F = 42:11, 52 ± 18 years). Patients' severity of illness was investigated at the initiation of RRT and on the 3rd day and presented by APACHE III score system. The number of organ failure was checked at the initiation of RRT. The overall survival rate was 46% in HD group and 21% in CVVHDF group (p = 0.002). It was that CVVHDF was applied to the more severe patients who had longer periods using ventilator (p = 0.002) and/or vasopressor (p < 0.001), higher numbers of organ failure (p < 0.001), and higher initial APACHE III scores (p < 0.001). At the APACHE III scores over 103, survivors existed in the only CVVHDF group (13%), none in the HD group (0%). However, according to the number of organ failure, the survival rate was 9% in the HD group and 36% in the CVVHDF group (p = 0.035) in the patients with kidney and two other organs failure. In conclusion, overall mortality of the CVVHDF group was higher than that of the HD group. But, this could be explained that CVVHDF was applied to the more severe cases. In contrast, CVVHDF might give a survival chance to the severe ARF patients with the APACHE III score over 103, especially and it could be more useful than HD as a RRT if the number of organ failure was three, tolerable degree of severity for CVVHDF.
Continuous Hemodiafiltration (CHDF) and Oncotic Agents Therapy Can Be a New Therapeutic Strategy for ARDS

Department of Emergency and Critical Care Medicine, Graduate School of Medicine, Chiba University, Japan

Aim: It is generally accepted that increased capillary and alveolar permeability caused by a variety of humoral mediators and resultant pulmonary interstitial edema (PIE) play a major role in the pathogenesis of ARDS. When oncotic agents were administered for reducing PIE through increasing colloid osmotic pressure (COP), the oncotic agents may leak to the extravascular space and PIE may be exacerbated in the state of hyperpermeability, such as ARDS. If the causative humoral mediators can be removed and the capillary and alveolar permeability can be normalized, the administration of oncotic agent can increase COP and reduce PIE. We have claimed that CHDF can remove various humoral mediators from the blood stream and that CHDF and oncotic agents administration can reduce PIE through the removal of water in blood and concomitant water refilling from the extravascular space. The present study was undertaken to investigate the efficacy of the CHDF and oncotic agents therapy as a new therapeutic strategy for ARDS. Methods: Thirty-eight ARDS patients who received the CHDF and oncotic agents regardless of their renal function in addition to the conventional treatment were entered in this study. Changes in respiratory index (RI), central venous pressure (CVP), COP and the blood levels of tumor necrosis factor-alpha (TNF-alpha), interleukin-6 (IL-6) and interleukin-8 (IL-8) with 3 days of this combination therapy were measured. Twenty-six ARDS patients treated with intermittent hemodialysis in addition to the conventional treatment served as controls and the 28-day survival was compared between the two groups. Results: COP increased significantly and 1,600±2,500mL water could be removed from the patients without changing CVP with 3 days of the CHDF and oncotic agents therapy. The average administered FFP volume and albumin weight as oncotic agents for 3 days were 2,900±1,800mL and 44.7±59.9g, respectively. The blood levels of TNF-alpha, IL-6 and IL-8 decreased significantly for 3 days. RI was also improved significantly. There were significant and positive correlations between the degree of the decrease in the blood level of TNF-alpha, IL-6 and the degree of the improvement in RI. The 28-day survival was 64.5% in the combination therapy group and 34.6% in the intermittent hemodialysis group, respectively (p<0.05). Conclusions: These results indicate that the CHDF and oncotic agents therapy effectively reduces PIE and consequently improves the survival of ARDS patients. Thus, we conclude that the CHDF and oncotic agents therapy can be a new therapeutic strategy for ARDS.
Determination of the Optimum Ultrafiltration Rate

N. Hemasilpin\textsuperscript{a}, M. Polycarpou\textsuperscript{b}, J.J. Bissler\textsuperscript{a}

\textsuperscript{a}Cincinnati Children’s Hospital Research Foundation, Cincinnati, OH, USA
\textsuperscript{b}Department of Electrical Engineering and Computer Sciences, University of Cincinnati, OH, USA

Intradialytic hypotension is a critical morbidity associated with hemodialysis. The hypotensive condition is due, in large part, to intravascular volume contraction caused by an excessive fluid removal rate. Ultrafilter tolerance is attributed to the kinetic balance of the patient’s lymphatic return and the ultrafiltration rate. The lymphatic return system not only supplies the excess fluid that needs to be removed, but also helps regulate the blood pressure before the nervous and the humoral pressure regulating mechanisms are triggered. The blood pressure that is regulated by the lymphatic return from the interstitial fluid has its transient time response affected by a property called vascular stress-relaxation. Therefore, a precise quantitative knowledge of lymphatic return rate and vascular stress-relaxation property is essential for optimizing a physiologically appropriate ultrafiltration rate. To this end, we have designed a method of modeling both the lymphatic return rate and the vascular stress-relaxation property. We have derived a set of dynamical equations to represent the cardiovascular system including capillary dynamics, lymphatic flow, interstitial fluid dynamics, and vascular stress-relaxation property based on physiological data. This set of equations allows the prediction of the blood pressure response during ultrafiltration.
Multiple Use of a CVVH Machine in a Small Pediatric Center
Children's Hospital of Eastern Ontario, USA

The cost of a CVVH machine is not negligible and small centers may have only one machine available. The number of CVVH treatments in children is limited and in our center with a catchment area of 2.5 million inhabitants the frequency amounts to 10–15 treatments per year. Yet, there is trained staff available to operate the machine and who needs to maintain the skills. Therefore, we were interested whether the CVVH machine (Baxter BM25) can be safely used for other extra-corporeal circulation procedures like plasma exchange. Case Report: A 3-year old boy (17kg body weight) was admitted to the hospital with steroid resistant nephritic syndrome (NS). After 6 weeks of daily steroid therapy renal biopsy was performed showing minimal change NS with IgM but no demonstration of focal segmental glomerulosclerosis. He developed renal insufficiency with anuria and required hemodialysis. After two weeks, his renal function improved but no remission was obtained even after starting Cyclosporine. Therefore, plasma exchange was indicated in order to remove the hypothetical plasma permeability factor and induce remission. In our center, plasma exchange therapy has been traditionally performed using centrifugation method, involving a very large extracorporial volume, necessitating blood priming and being frequently associated with severe complications including severe hypocalcemia. Therefore, the Edwards Life Sciences/Baxter BM25 machine with Asahi plasma filters (Plasmalfo Plasma Separator, made of cellulose di-acetate, inside diameter 330microns, priming volume 65mL) and pediatric tubing was used to replace 1.5 times plasma volume with albumin 5%. A total of 6 procedures were performed, duration of each was approximately 2 hours. During each plasma exchange, 10mL of 10% calcium gluconate per L of albumin was administered in continuous IV infusion into the venous port to counteract citrate added to the albumin solution. No serious adverse effects were observed and all procedures were extremely well tolerated. Unfortunately, no remission was obtained with plasma exchange therapy but the machine – filter set-up for plasma exchange proved to be safe for use in small children where centrifugation method may be associated with serious adverse effects. This approach could also be used for immunoabsorption and lipidapheresis. In conclusion, the existing CVVH equipment (Baxter BM25) can be used with safety to perform plasma exchange therapy. In addition, there is no need for additional training of nursing personnel trained initially for CVVH only.
Early CVVHDF Increases Survival from Bone Marrow Transplant ARDS

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Stanford University, Palo Alto, CA, USA

Purpose: Respiratory failure in immunosuppressed children carries a 50% mortality rate; after bone marrow transplantation (BMT) mortality remains as high as 96%. Conversely, mortality in pediatric respiratory failure generally has improved (<8%). We hypothesized that early institution of hemodiafiltration would improve survival from ARDS after BMT or severe induced immunosuppression. Methods: ARDS was defined as respiratory failure (PaO2/FiO2 < 200, lung injury score > 2.5) in a relevant setting (chemotherapy, total body irradiation). Respiratory support consisted of mechanical ventilation, oxygen, small tidal volumes, and permissive hypercapnia. Continuous venovenous hemodiafiltration (CVVHDF) with citrate anticoagulation was prescribed to achieve a clearance of 50 mL/min/1.73 m² (ultrafiltrate production + volume of dialysate solution). Early CVVHDF was instituted coincident with intubation, regardless of renal status (mean serum creatinine 1.36 ± 0.67 mg/dL) or fluid balance, in five consecutive children with severe immunodeficiency (4 BMT, 1 chemotherapy). Results: Five children had ARDS (PaO2/FiO2 98 ± 45, lung injury score 3.28 ± 0.38). All five were treated with early hemodiafiltration and achieved resolution of their lung disease and were extubated. Of these, four survived, while one died of persistent severe autonomic instability from a midbrain lesion. Mean intravenous fluid infusion rate was 870 ± 624 mL/kg/day. Ultrafiltrate volume was 30 ± 19 mL/kg/hr. Clearance achieved by CVVHD was 53 ± 20 mL/min/1.73 m². After extubation, three survivors (BMT) were supported with hemodialysis until renal function recovered (28, 22, and 16 days post extubation). The fourth survivor (leukemia) retained normal renal function. Conclusions: CVVHDF may have dramatically improved respiratory recovery and survival in a small group of severely immunosuppressed patients with ARDS. Strict fluid balance alone is unlikely to explain the effect. Hemodiafiltration may play an immunomodulatory role. The immuno-activity that fuels respiratory failure in this setting is of a moderate degree; hemodiafiltration may remove active chemicals to attenuate the inflammatory process. An expanded pilot study and eventually a controlled trial are needed to test this approach, which may have wider applicability in adult and pediatric hematology–oncology and bone marrow transplantation.
Combination of Hemoperfusion and Continuous Venovenous Hemofiltration in Treatment of Severe Tetramine Poisoning

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Objective: To evaluate the removal of tetramine from the plasma of severely poisoned patients treated by combination of hemoperfusion (HP) and continuous venovenous hemofiltration (CVVH). Methods: Eighteen patients were diagnosed as severe tetramine poisoning and were treated by additional blood purification except routine medical therapy. Blood purification procedures included HP using activated charcoal for 3–5 hours and consecutive CVVH for 24–36 hours. Tetramine concentration was detected in plasma pre-, post-HP, and during CVVH, plasma pre-, post-filter, ultrafiltration at 2nd hour and 12th hour were also detected. Results: HP procedures were performed using 2 adsorbents in 14 patients, and using 1 adsorbent in 4 patients. Plasma tetramine concentration reduced from 0.124 ± 0.082 mg/L to 0.080 ± 0.055 mg/L after HP, reduction rate was 42.9 ± 14.0% in patients using 2 adsorbents, and was 34.7 ± 13.8% in patients using 1 adsorbent (p > 0.05). Consecutive CVVH were performed in 16 patients. During CVVH, mean plasma tetramine concentration in 2nd hour was 0.078 ± 0.064 mg/L, in 12th hour was 0.074 ± 0.059 mg/L, and ultrafiltration sieving coefficient in 2nd and 12th hour was 0.839 ± 0.409, 0.686 ± 0.253, respectively. Plasma tetramine concentration at 2nd hour of CVVH declined in 15 patients (mean reduction rate 13.2 ± 12.1%), but increased slightly in 1 patient (increasing rate 9.52%); at 12th hour of CVVH, plasma concentration declined in 13 patients (mean reduction rate 29.8 ± 14.5%), but increased slightly in 3 patients (mean increasing rate 11.05 ± 8.00%). Conclusion: HP therapy can significantly decrease plasma tetramine concentration, and reduction rate difference between patients using 2 adsorbents and using 1 adsorbent is not obvious. CVVH is also effective in removal of tetramine, and can attribute to attenuating rebound of plasma tetramine concentration after HP.
Remote Monitoring of CVVH Performed in Intensive Care Units (ICU)
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SCDU Nefrologia, Dialisi e Trapianto Renale, Ospedale S Giovanni Batti, Turin, Italy

CVVH performed in ICU without the direct assistance of trained personnel is increasingly used for Acute Renal Failure treatment. Although devices used are safe enough to automatically control continuous sessions, some doubts could raise about the safety and feasibility of these treatments. In our Centre a computerised control has been developed, based on the following main points: (a) CCVH devices using a microprocessor for real time computations (KT/V, pre-dilution, etc) and handling the communication protocol through a serial port connected to (b) a microprocessor-based signal concentrator used for translating all the different communication devices protocols in a standardised format (Universal Medical Information Bus) and able to remotely transfer all the data through (c) a 33.6KBit/s modem connected via hospital’s PSTN telephone line to (d) a PC (class Pentium I/H11001) located inside the dialytic facility and running a specialised supervising software. The software is able to simultaneously monitor 25 dialysis machines plus those located remotely in the ICUs, thus allowing the management of a single ‘virtual’ dialysis facility including different rooms and units. This system is operating with different features: (a) direct monitoring of dialytic parameters (blood and effluent flow rates, venous, pre-filter and trans-membrane pressure, total ultrafiltration volume, pre- and post-dilution flow) and internal computations (urea clearance, filtration fraction, KT/V); (b) transmission of alarms from the device and setting of logical alarms on received data; (c) control on CVVH devices, session duration, efficiency and comparison between scheduled and actual results; (d) review of previous sessions and data storage. Furthermore, recording is effected without any personnel burden, even when the telephone connection is off. In conclusion, the remote monitoring of CVVH is representing a useful, low cost and logical improvement in the management of these long duration, out-sighted but life-saving treatments.