Nutritional implications of renal replacement therapy in ICU
Nutritional consequences of RRT

E. Fiaccadori (Italy)
Nutritional consequences of RRT

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"Critical illness"

1. Acute Stress Response
2. Immunological Response
3. Neuroendocrine Response
4. Metabolic Response
5. Iatrogenic Factors

- Trauma/Infection
PEW is a frequent finding in AKI and is associated with increased mortality risk.

In-hospital mortality according to nutritional status in 309 AKI pts.

Nutritional status by SGA (Subjective Global Assessment of nutritional status, Baker JP et al., NEJM 1982; 306:969-72)

Fiaccadori E et al., JASN 1999; 10:581-593
Nutritional support likely to be beneficial in AKI

Effect of acute renal failure requiring renal replacement therapy on outcome in critically ill patients

Philipp G. H. Metnitz, MD, PhD, DEAA; Claus G. Krenn, MD; Heinz Steltzer, MD; Thomas Lang, PhD; Jürgen Ploder, MS; Kurt Lenz, MD; Jean-Roger Le Gall, MD; Wilfred Druml, MD

Table 5. Multivariate predictors: Results of stepwise logistic regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>p Value</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-2.58460</td>
<td>&lt;.001</td>
<td>1.08</td>
</tr>
<tr>
<td>SAPS II score</td>
<td>0.00798</td>
<td>.166</td>
<td>1.08</td>
</tr>
<tr>
<td>Cardiopulmonary resuscitation</td>
<td>0.06160</td>
<td>.004</td>
<td>1.86</td>
</tr>
<tr>
<td>Multiple vasoactive medication</td>
<td>0.02930</td>
<td>&lt;.001</td>
<td>1.34</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>0.02930</td>
<td>&lt;.001</td>
<td>1.34</td>
</tr>
<tr>
<td>Single vasoactive medication</td>
<td>0.01160</td>
<td>.012</td>
<td>1.13</td>
</tr>
<tr>
<td>Treatment of complicated metabolic acidosis/alkalosis</td>
<td>0.00768</td>
<td>.034</td>
<td>1.08</td>
</tr>
<tr>
<td>Care of drains</td>
<td>-0.00883</td>
<td>.002</td>
<td>0.91</td>
</tr>
<tr>
<td>Enteral nutrition</td>
<td>-0.01480</td>
<td>&lt;.001</td>
<td>0.86</td>
</tr>
</tbody>
</table>

SAPS, Simplified Acute Physiology Score.

Variables express the proportion of days on which this activity was performed. The odds ratios reflect the change in the risk of dying during the intensive care unit stay if the proportion of days with intervention increases by 10%.

Metnitz PGH et al., Crit Care Med 2002; 30:2051
Artificial nutrition in AKI can be a difficult task

- Dysmetabolism of critical illness worsened by the acute loss of kidney homeostatic function

- Nutritional approach made difficult by the complexity of the syndrome itself, and by the frequent need of renal replacement therapy (RRT)
• Nutritional support as a key component of the therapeutic strategy of AKI

• Need for a close integration between nutritional support and RRT, taking into account the peculiar effects of RRT on nutritional support delivery
“Metabolic changes in these patients are also determined by the underlying disease and/or comorbidities, by other organ dysfunction, as well as by the modality and intensity of renal replacement therapy (RRT)”

“Renal replacement therapies have profound effects on metabolism and nutrient balances”

The relationship between RRT and nutritional support is complex

Ianus bicefalus, ancient Roman divinity
Vatican Museum, Rome
Nutritional consequences of RRT

- Loss of macronutrients → a cause of underfeeding (negative N balance)?
- Loss of micronutrients → trace element unbalance and hypovitaminosis?
- “Hidden load of nutrients” → a cause of overfeeding?

Effects of nutrients on RRT

- Lipid emulsions and extracorporeal circulation
- Fluid overload and patient’s outcome
Protein catabolic rates in critically ill patients with AKI on RRT

![Bar graph showing protein catabolic rates with references]

Macias WL et al, J Parent Ent Nutr 1996; 20:56
Fiaccadori E et al., Nephrol Dial Transpl 2005; 20:1976
Aminoacid losses during RRT

- Amino acids have small molecular weight (average 140 D, range 75-215)
- RRT can be associated with the loss of up to 10–20 g amino acids per day and up to 5 g/day of proteins, depending on RRT modality and filter type
- With CRRT 10 to 15% of infused aminoacids are lost (up to 15-20% in the case of glutamine, 0.5-6.8 g/day when supplementation is 0.32 g/Kg/day)

Kuhlmann MK et al., Anaesthetist 2000; 49:353-8
Berg A et al., Int Care Med 2007; 33:660-6
Btaiche EF et al., Pharmacotherapy 2008; 28:600-613
In CVVHD, aminoacid losses are about 20% of nitrogen intake
“Protein intake should be increased to compensate for the protein and amino acid losses during RRT of about 0.2 g/kg/day, taking into account also that about 10–15% of infused amino acids in PN during RRT are lost in the dialysate/ultrafiltrate”

RRT and loss of micronutrients

- Trace elements
- Vitamins
- Electrolytes
Original Communications

Trace Element Loss in Urine and Effluent Following Traumatic Injury

Catherine J. Klein, PhD, RD, CNSD1; Forrest H. Nielsen, PhD2; and Phylis B. Moser-Veillon, PhD, RD3

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Original Article

Trace element removal during in vitro and in vivo continuous haemodialysis

Mariann D. Churchwell1, Deborah A. Pasko2, Imad F. Btaiche2, Jinesh C. Jain3 and Bruce A. Mueller2

1Department of Pharmacy Practice, College of Pharmacy, University of Toledo, Toledo, OH, 2Department of Clinical Sciences, College of Pharmacy, University of Michigan, Ann Arbor, MI, USA, 3Senior Scientist Hartford Waste Treatment and Immobilization Plant, Richland, WA, USA from the Renal Replacement Therapy Kinetics Study Group
Trace elements during CRRT in AKI

- In general, daily supplementation with standard doses of parenteral multitrace element preparations results in enough trace elements to overcome the amount lost by CRRT.

- No data on whether multitrace element preparations give the patients on CRRT the optimal dose of trace elements.
Copper, selenium, zinc, and thiamine balances during continuous venovenous hemodiafiltration in critically ill patients\textsuperscript{1–3}

Mette M Berger, Alan Shenkin, Jean-Pierre Revelly, Eddie Roberts, M Christine Cayeux, Malcolm Baines, and Rene L Chioléro

Conclusions: CRRT results in significant losses and negative balances of selenium, copper, and thiamine, which contribute to low plasma concentrations. Prolonged CRRT is likely to result in selenium and thiamine depletion despite supplementation at recommended amounts. \textit{Am J Clin Nutr} 2004;80:410–6.
Vitamin losses during CRRT in AKI

In ICU patients with AKI, plasma levels of water-soluble vitamins, such as vitamin C, thiamine and folic acid, may be lower than normal [51,56], due mainly to the losses occurring through the extracorporeal circuit: in CVVH vitamin C losses can reach up to 600 µmol/day, i.e. 100 mg/day, and folate losses up to 600 nmol/day [51–56]; in CVVHDF thiamine losses may amount more than 1.5 times the daily provision of the vitamin from standard total parenteral nutrition solutions.

Recommended vitamin C administration in patients with AKI is 50–100 mg/day; higher intakes (up to 150–200 mg) may be needed when continuous modalities of RRT are used. No supplementation of fat-soluble vitamins is usually necessary in AKI.

Fiaccadori E et al., NDT Plus 2009, in press
Problems with electrolytes in highly efficient RRT modalities

• Risk for hypophosphatemia with SLED or CRRT

• Low risk for hypokalemia if potassium in SLED dialysis fluid or CRRT fluids is 4 mmoles/L
Hypophosphatemia and phosphate supplementation during continuous renal replacement therapy in children

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¹Pediatric Intensive Care Unit, Hospital General Universitario Gregorio Marañón, Madrid, Spain and ²Statistics, Preventive Medicine and Quality Assurance Service, Hospital General Universitario Gregorio Marañón, Madrid, Spain

- 68% of pts had hypoP during CRRT vs 12% at the start
- 36% had hypoP when P was supplemented, vs 85% with no P supplementation during CRRT
- Supplementation by sodium phosphate 0.8 mmol/L in both replacement fluid and dialysis solution

*Kidney International* (2009) 75, 312–316
Serum phosphorus levels during SLED^ (normal values 0.85-1.6 mmol/l)

^SLED is sustained low efficiency dialysis

SLED* 8 hours/day
SLED** 10 hours/day
Serum phosphorus levels during SLED

(normal values 0.85-1.6 mmol/l, or 2.5-5 mg/dL)

mmol/L

1. SLED* 8 hours/day
2. SLED** 10 hours/day

i.v. P supplementation

SLED* 8 hours/day
SLED** 10 hours/day
Estimating glucose caloric impact of CRRT utilizing regional citrate anticoagulation with ACD-A

• ACD-A, a commonly used citrate formulation for regional anticoagulation in CRRT, contains 2.45% dextrose

• All standard CRRT prescriptions with ACD-A resulted in net positive glucose caloric delivery

• CRRT-delivered caloric load ranged from 30 to 328 Kcal per day (mean 183 Kcal), 2-21% of estimated caloric needs

Macnowski J et al., Blood Purif 2009, 27:290A
Problems with increased glucose calorie load in AKI patients

• Increased insulin needs
• Higher glucose levels

Higher glucose levels associated with higher risk of death in AKI

Fig. 3. Risk profile for glucose level in quartiles ($n = 509$). The analysis was adjusted for demographics, renal function, and severity of illness ($P = 0.025$). Values in histogram bars represent median baseline glucose values of the respective quartiles (in mmol/l).

Basi S et al., Am J Physiol 2005; F259-F264
Nutritional consequences of RRT

- Loss of macronutrients → a cause of underfeeding?
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Effects of nutrients on RRT

- Lipid emulsions and extracorporeal circulation
- Fluid overload and patient’s outcome
Any problem with filters and circuits when lipid emulsions are infused during renal replacement therapy?

The answer is “no”
Shortened Hemofilter Survival Time due to Lipid Infusion in Continuous Renal Replacement Therapy

Amir Kazory\textsuperscript{a}  William L. Clapp\textsuperscript{b}  A. Ahsan Ejaz\textsuperscript{a}  Edward A. Ross\textsuperscript{a}

\textsuperscript{a}Division of Nephrology, Hypertension, and Transplantation and \textsuperscript{b}Department of Pathology, University of Florida, Gainesville, Fla., USA

500 ml/24 hours of a 20\% lipid emulsion (LCT only)

Serum triglyceride levels 1713 mg/dL
Fig. 1. Electron micrograph illustrating ‘layering effect’. A layer of electron-neutral material (top) consistent with lipid is situated adjacent to clumps of electron-dense material composed of fibrin. ×3,400.

Fig. 2. Electron micrograph illustrating clumps of fibrin and lipid droplets with neutral electron density and spherical character. ×17,500.

Serum triglycerides during TPN in AKI patients

n = 103

TPN > 7 days, MCT/LCT 20% 250-500 ml/day, 24 hour continuous infusion

Internal Medicine & Nephrology Dept.
Parma University Medical School
No effects of parenteral nutrition with lipid emulsions on filter duration in AKI on sustained low-efficiency dialysis (SLED)

- 273 SLED in 37 ICU patients with AKI
- Prescribed duration 8 hours/treatment
- PN with all-in-one system
- 20% MCT/LCT 250-500 ml/day
Nutritional support means fluids

• Whatever is the route of delivery, fluid intake is increased by nutritional support

• Whatever is the route of nutrient delivery the mean fluid intake requested to target nutritional needs can be 1500-2000 ml/day in the adult
Fluid overload associated with increased mortality risk in AKI

Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury

Josée Bouchard¹, Sharon B. Soroko¹, Glenn M. Chertow², Jonathan Himmelfarb³, T. Alp Ikizler⁴, Emil P. Paganini⁵ and Ravindra L. Mehta¹, Program to Improve Care in Acute Renal Disease (PICARD) Study Group

¹Division of Nephrology and Hypertension, Department of Medicine, University of California San Diego, San Diego, California, USA; ²Division of Nephrology, Department of Medicine, Stanford University School of Medicine, Palo Alto, California, USA; ³Division of Nephrology, Department of Medicine, University of Washington, Seattle, Washington, USA; ⁴Division of Nephrology, Department of Medicine, Vanderbilt University, Nashville, Tennessee, USA and ⁵Division of Nephrology, Department of Medicine, Cleveland Clinic Foundation, Cleveland, Ohio, USA
Figure 1 | Cumulative probability of survival by fluid overload status. (a) Kaplan-Meier survival estimates by fluid overload status at dialysis initiation. There was a significant difference in survival among patients with or without fluid overload at dialysis initiation ($P = 0.005$). (b) Kaplan-Meier survival estimates by fluid overload status at AKI diagnosis in non-dialyzed patients. There was a significant difference in survival among patients with or without fluid overload ($P = 0.04$).
Conclusions

- The relationship between nutritional support and RRT is complex and should be analyzed by looking at both faces of the coin
- Nutritional support may contribute to a positive fluid balance → need for careful integration between nutrition and RRT (earlier RRT start and “dry” patients?)