Nutritional Imbalances during Extracorporeal Life Support

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Abstract

Extracorporeal life support has become an integral part of the technologies used in the intensive care. Renal replacement therapy is used daily and extracorporeal membrane oxygenation (ECMO) has become more popular in the recent years with the increasing prevalence of influenza-induced severe respiratory failure. Many years ago, critically ill infants requiring ECMO were found to have the highest rates of whole body protein breakdown ever recorded. However, most of the physicians are not aware of the nutritional consequences of the use of new technologies. The aim of this chapter is to describe the changes induced by artificial membranes and the required therapies to optimize nutritional support.

The quality and technology employed in extracorporeal therapies have improved in terms of biocompatibility of the materials used. Protein oxidation was observed together with cellulose acetate membranes and their switch to polysulfone membrane has decreased inflammation and oxidative stress, too [1, 2]. This progress observed in renal replacement therapy (RRT) can also improve the stress induced by extracorporeal membrane oxygenation (ECMO). This technique is not only increasing whole body protein breakdown [3], but also inducing systemic inflammatory response syndrome, which can be associated with multiorgan failure and mortality [4]. A better knowledge of the metabolic changes observed during these techniques may help prevent some of the complications associated with membrane use.

Nutritional Requirements during Continuous Renal Replacement Therapy

Acute kidney injury (AKI) is one of the most common and severe complications in the ICU, often associated with the failure of other organs. Sepsis is the leading etiologic factor of AKI [5, 6]. The prevalence of AKI in the critically ill is between 10...
and 30%, depending on definition, and 5–10% of the patients suffering from AKI need RRT [6]. Intermittent hemodialysis and continuous renal replacement therapy (CRRT), which is better tolerated by patients with cardiovascular instability, are the most common modalities used for treatment of patients with AKI. There are several ‘hybrid techniques’ of intermittent hemodialysis and CRRT, such as continuous venovenous hemofiltration or hemodiafiltration, extensive daily dialysis, slow low efficient daily dialysis (SLEDD), and high-volume hemofiltration available for treatment of AKI [5, 6]. During hemodialysis, based on diffusion, solutes cross the membrane by concentration gradient between the dialysate fluid and the blood. However, the basic principle of hemofiltration is convection, leading to the removal of small- and middle-sized molecules [7], and ultrafiltration when plasma water is driven by hydrostatic force across a semipermeable membrane [8].

Hypermetabolic state, fluid overload, protein-energy wasting, and inadequate response are the main causes of the poor nutritional status of critically ill patients suffering from AKI (see previous chapter [this vol., pp. 126–135]). For patients undergoing hemodialysis or CRRT, losses of nutrients across a semipermeable membrane due to nonselective solute shifts and supply of same nutrients via replacement fluids could be additional factors inducing profound metabolic derangements [9, 10]. In contrast to normal kidney that reabsorbs nutrients after glomerular filtration, substances such as amino acids, trace elements, and water-soluble vitamins are lost during RRT. Moreover, continuous contact of a patient’s blood with foreign surfaces of the membrane contributes by oxidative stress transforming lipids and proteins [11]. In this context, early nutritional assessment and adequate support may be a crucial part in the management of critically ill patients treated by RRT for AKI.

Energy provision in ICU patients should be individual. Despite the fact that resting energy expenditure (REE) in AKI patients is not elevated, in critically ill patients affected by coexisting conditions like sepsis or heat loss from extracorporeal blood circulation, REE may be increased. The recommended daily caloric intake is 25–35 kcal/kg/day. Overfeeding must be avoided. In these conditions, indirect calorimetry could be used for optimization of metabolic support. It should be noted that precise measurement of REE by indirect calorimetry may be limited in patients receiving RRT due to the removal of carbon dioxide by the membrane [9, 12, 13] and should be limited to stable patients without CO₂ modifications.

Nitrogen balance has an inverse correlation with energy expenditure and is directly associated with hospital outcome [14]. Especially for patients receiving CRRT or using high-flux dialysates, extensive protein losses may be significant (up to 15 g of albumin for each treatment set) [9, 11]. In this context, protein supply can move from 1.5 to 2.0 g/kg/day of protein, connected to metabolic status of patient and type of renal replacement support. A loss of amino acids through the ultrafiltrate/dialysate can be anticipated during CRRT and it has been estimated to be nearly 10% of overall acid supplementation [15]. Intravenous glutamine supplementation is a part of standard care of parenteral nutrition in intensive care. During CRRT, the risk of losses
of glutamine is high, especially during intravenous glutamine supplementations. Recently, recommendations of glutamine supply in critically ill patients receiving RRT has been set to 0.5 g/kg/day (25–35 g/24 h) [16, 17].

There are several explanations for depletion of trace elements and water-soluble vitamins in patients with AKI receiving RRT. The activity of plasma glutathione peroxidase can be low due to a decreased synthesis in renal parenchyma, selenium deficiency, and removal from plasma by an extracorporeal circuit. According to Berger et al. [10], all trace elements were found in effluent fluids, but selenium had the highest concentration. Zinc is also lost during convection or ultrafiltration, but due to high concentrations of zinc in replacement fluid (especially in bicarbonate solution), the total balance remains positive [9, 10]. Concentration of other trace elements like chromium and copper are also low. Concentration of thiamine, folic acid, and vitamin C in these patients are decreased mainly due to losses of these micronutrients through the semipermeable membrane. Daily supplementation of thiamine should be greater than 1.5 times the standard doses administered in parenteral nutrition. Vitamin C and folic acid losses can reach 100 mg/d and 600 nmol/day, respectively, for patients receiving CRRT. Up to 150–200 mg of vitamin C is recommended for these patients [18, 19]. On the other hand, supplementation of fat-soluble vitamins is not recommended [9]. During continuous venovenous hemofiltration, glucose losses may reach up to 60 g/day. Increasing the rate of replacement fluids and highest concentration of glucose can decrease glucose losses [6]. Tables 1 and 2 summarize the nutrient losses and requirements of the ICU patient undergoing CRRT.

**Extracorporeal Membrane Oxygenation**

ECMO is a prolonged type of cardiopulmonary bypass and is an available technique for short-term support of patients suffering from severe pulmonary and cardiovascular dysfunction.
Patients receiving ECMO are severely ill patients. These patients are usually treated by high doses of vasoactive agents (especially in venoarterial ECMO), need prolonged ICU hospitalization, and receive heavy sedation and sometimes high doses steroids. These drugs impair gastric emptying and the ability to start enteral feeding and to reach the calorie target. Few studies have addressed nutritional support for critically ill newborns treated by ECMO, and the same is true for adult patients, too. In one single hospital retrospective study, Lukas et al. [20] demonstrated that most of the 48 patients receiving ECMO had inadequate nutritional support. Scott et al. [21] showed that early enteral feeding (first 24–36 h of initiating ECMO) was well tolerated and safe for patients treated by venovenous ECMO for severe respiratory failure. A Swiss team [22] demonstrated that patients after cardiopulmonary bypass requiring high doses of vasopressors tolerated enteral feeding successfully.

Accurate assessment of nutritional support may be problematic. Indirect calorimetry is not possible. The techniques of indirect calorimetry are based on measurement of oxygen consumption (\(V_\text{O}_2\)) and carbon dioxide production (\(V_\text{CO}_2\)), as well as minute volume [15]. \(\text{CO}_2\) removal across the extracorporeal membrane cannot be identified by indirect calorimetry and the level of REE during ECMO can cause inaccuracies.

The guidelines for initiation and maintenance of nutritional support for patients receiving ECMO are not available. The enteral route is always preferred in critical patients, and if it can be tolerated while administrating high doses of vasopressors, it can also be prescribed during ECMO therapy. The use of prokinetics such as metoclopramide and/or erythromycin is indicated, like in the general ICU population,

**Table 2. Nutrient intake in AKI on RRT [9]**

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Description</th>
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<tbody>
<tr>
<td>Amino acids</td>
<td>Loss of up to 10–20 g amino acid/day, depending on RTT modality and filter type 10–15% of infused amino acids are lost with CRRT</td>
</tr>
<tr>
<td>Glutamine</td>
<td>Loss up to 10–15% (0.5–6.8 g) with CVVH when supplementation level is 0.32 g/kg/day</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Up to 600 μmol/day (100 mg/day) during CVVH</td>
</tr>
<tr>
<td>Folic acid</td>
<td>Up to 600 nmol/day during CVVH</td>
</tr>
<tr>
<td>Thiamine</td>
<td>More than 1.5 times the daily provision of the vitamin from standard TPN solution during CVVHD</td>
</tr>
<tr>
<td>Trace elements</td>
<td>Selenium, chromium, copper and zinc can be loss from plasma by convection</td>
</tr>
<tr>
<td>Selenium</td>
<td>Negative selenium balance associated with CVVH equivalent to twice the daily intake from standard formula TPN</td>
</tr>
</tbody>
</table>

TPN = Total parenteral nutrition; CVVH = continuous venovenous hemofiltration; CVVHD = continuous venovenous hemodialysis.
to prefer the enteral route. If the gastric residue is larger than 500 ml and duodenal tube is not applicable, parenteral nutrition will be prescribed. In this context, nutritional support must be based on the latest evidence-based guidelines for critically ill patients.

Conclusions

In the critically ill patient requiring extracorporeal therapy, special attention should be given to the nutrients lost during therapy and to the inflammation induced by the membranes. Nutritional support can replace the nutrients missing and modulate the inflammation.

References


