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SUMMARY
Among patients with renal failure, those with ARF and critical illness represent by far the largest group undergoing artificial nutrition. ARF, especially in the ICU, seldom occurs as isolated organ failure but rather is a component of a much more complex metabolic environment, in the setting of the multiple organ failure. Nutritional programs for ARF patients must consider not only the metabolic derangements peculiar to renal failure and with the underlying disease process/associated complications, but also the relevant derangements in nutrient balance due to renal replacement therapies, especially when highly efficient renal replacement therapies (RRT) are used, such as continuous veno-venous hemofiltration (CVVH), or prolonged intermittent modalities such as sustained low-efficiency dialysis (SLED). Finally it is to be taken into account that nutrient requirements can change considerably during the course of illness itself (see also guidelines on PN in intensive care).

From a metabolic point of view, patients with CKD or on chronic HD who develop a superimposed acute illness should be considered to be similar to patients with ARF. The same principles in respect of PN should therefore be applied.

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### Summary of statements: Nephrology concern

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<th>Subject</th>
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<tr>
<td>Goals of nutritional support</td>
<td>The primary nutritional goals of PN in ARF should be the same as those in other catabolic conditions in the ICU, such as ensuring the provision of optimal amount of energy, protein and micronutrients, with the aims of prevention of PEW, preservation of lean body mass, maintenance of nutritional status, avoidance of further metabolic derangements, enhancement of wound healing, support of immune function, and reduction in mortality. In the case of ARF patients, nutritional goals could also include the attenuation of their inflammatory status and improvement of the oxygen radical scavenging system and of endothelial function.</td>
<td>C</td>
<td>4</td>
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<tr>
<td>Outcomes</td>
<td>Due to the lack of well-designed randomized controlled trials the evidence regarding the effects of PN on survival and renal recovery remains inconclusive.</td>
<td>C</td>
<td>5</td>
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<tr>
<td>Indications</td>
<td>The indications for and contraindications for PN in ARF are comparable to those in other critically ill patients (see ICU guidelines). PN is appropriate in ARF when G1 tract cannot be used for enteral feeding, when EN is not enough to reach nutrient intake goals.</td>
<td>C</td>
<td>6</td>
</tr>
<tr>
<td>Requirements</td>
<td>Macronutrient requirements are more influenced by the severity of underlying disease, type and intensity of extracorporeal RRT, nutritional status and associated complications, rather than by the ARF itself. Micronutrient requirements have been poorly investigated in ARF patients. In ICU patients with ARF, the enhanced requirements for water-soluble vitamins induced by extracorporeal therapy should be met by supplementing multivitamin products. In line with standard recommendations, because of the possibility of accumulation, patients should be carefully monitored for signs of vitamin A toxicity. Similarly, it has been recommended that vitamin C should not exceed 30–50 mg/day, because inappropriate supplementation may result in secondary oxalosis. Recent data show that prolonged CRRT results in selenium and thiamine depletions despite supplementation at recommended amount.</td>
<td>C</td>
<td>7</td>
</tr>
<tr>
<td>Formula and route</td>
<td>ARF is associated with major fluid, electrolyte and acid–base equilibrium derangements, such as hypo- and hyperkalemia, hyperphosphatemia, and metabolic acidosis. Restrictions of potassium, magnesium and phosphate in PN are however usually unnecessary if the patients are on daily RRT (CRRT, hemodialysis or SLED). Sodium electrolyte levels largely depend on the electrolyte composition of the dialysate/renfluate solutions, and the intensity of RRT. Hyperphosphatemia and hypermagnesaemia can frequently be observed during CRRT or SLED, and should be anticipated.</td>
<td>C</td>
<td>7</td>
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<tr>
<td>Chronic renal failure</td>
<td>An energy intake ≥ 30–35 kcal/kg/day is associated with better nitrogen balance and is recommended in stable CKD patients.</td>
<td>B</td>
<td>12</td>
</tr>
<tr>
<td>Indications</td>
<td>Conservatively treated patients with CKD seldom need PN. Potential indications of PN in CKD patients are similar to the indications for PN in non-renal patients. Malnourished CKD patients requiring nutritional support should only be considered for PN when ONS and EN are impossible or fail to reach nutritional goals. Special attention should be given to CKD requiring PN during periooperative periods.</td>
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<td>13</td>
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<tr>
<td>Formula</td>
<td>When nutritional requirements cannot be met by dietary intake (with or without ONS), in combination with EN or by the enteral route alone, the goals of PN in CKD patients are: (a) prevention and treatment of PEW leading to cachexia; (b) ensuring the provision of optimal levels of energy, essential nutrients and trace elements; and (c) attenuation of disease (CKD) progression through protein or phosphate restriction.</td>
<td>C</td>
<td>14</td>
</tr>
<tr>
<td>Monitoring</td>
<td>Standard formulae are adequate for the majority of patients. However, requirements can differ and have to be assessed individually.</td>
<td>C</td>
<td>15</td>
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<tr>
<td>PEW is very common in patients undergoing maintenance hemodialysis; its prevalence varies from 20% to 70% according to the nutritional parameters considered. Although initiation of dialysis results in an initial improvement in nutritional indices, some dialysis-specific factors, like impairment of subjective well-being, loss of nutrients, protein catabolism and inflammation are relevant for the high incidence of PEW.</td>
<td>C</td>
<td>18</td>
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<tr>
<td>Outcomes</td>
<td>In acute ily HD patients the requirements are the same as in ARF patients. Macronutrient requirements of metabolically stable patients include nitrogen delivery of 1.1–1.5 g/kg per day and energy of 30–40 kcal/kg per day.</td>
<td>C</td>
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<td>C</td>
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<tr>
<td>Due to dialysis-induced losses, water-soluble vitamins should be supplemented: folic acid (1 mg/day), pyridoxine (10–20 mg/day) and vitamin C (30–60 mg/day). Vitamin D should be given according to serum calcium, phosphorus and parathyroid hormone levels. Routine hemodialysis does not induce significant trace-element losses. However, in depleted patients, zinc (15 mg/day) and selenium (50–70 µg/day) supplementation may be useful.</td>
<td>C</td>
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<td>PEW is recognized as an independent determinant of morbidity and mortality in HD patients.</td>
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<td>Large randomized, controlled trials are needed to evaluate the effects of IDPN on quality of life, hospitalization rate and survival. Retrospective studies suggest that IDPN may reduce hospitalization rate and survival. Randomized controlled trials evaluating the effect of IDPN are needed.</td>
<td>B</td>
<td>24</td>
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<tr>
<td>Acutely ill patients with CKD on dialysis should be treated in a similar manner to those with ARF. Standard amino acid solutions can be used for IDPN in non-acute ill malnourished HD patients. The energy supply should combine carbohydrate and fat. The use of specific parenteral solutions is not yet supported by controlled data.</td>
<td>C</td>
<td>25</td>
<td></td>
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<td>C</td>
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<tr>
<td>In acutely ill patients with CKD on dialysis the route for PN should be the same as in ARF patients. In non-acutely ill malnourished HD patients, IDPN is infused through the venous line during dialysis.</td>
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<td>C</td>
<td>28</td>
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<tr>
<td>In acutely ill patients with CKD on dialysis the decision to use PN should be based on the same criteria as in ARF patients.</td>
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<td>29</td>
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<tr>
<td>In acutely ill patients with CKD on dialysis the decision to use PN should be based on the same criteria as in ARF patients.</td>
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<td>In non-acutely ill malnourished HD patients with mild PEW as defined by insufficient spontaneous intake; dietary counseling, and, if necessary, ONS should be prescribed.</td>
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<tr>
<td>In patients exhibiting severe PEW, with spontaneous intakes more than 20 kcal/day: dietary counseling and ONS should be prescribed; IDPN is indicated in patients unable to comply with ONS; EN can be necessary when ONS or IDPN fail to improve nutritional status.</td>
<td>C</td>
<td>32</td>
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<tr>
<td>In patients exhibiting severe PEW, with spontaneous intakes less than 20 kcal/day, or in stress conditions; both ONS and IDPN are generally able to provide satisfactory nutritional supply and are not recommended; daily nutritional support is necessary and EN is preferred to PN; central venous PN is indicated when EN is impossible or insufficient.</td>
<td>C</td>
<td>33</td>
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<tr>
<td>Since CAPD patients usually have better residual renal function, several uricemic symptoms and metabolic abnormalities are less pronounced than in patients on HD therapy. However peritoneal losses of various nutrients are significant while absorption of glucose from the dialysate is enhanced.</td>
<td>C</td>
<td>34</td>
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<tr>
<td>Indications</td>
<td>Acutely ill CAPD patients have the same nutritional requirements as ARF patients. Macronutrient requirements of metabolically stable patients include nitrogen delivery of 1.1–1.5 g/kg per day and energy of 30–40 kcal/kg per day. Intravenous PN has been poorly investigated in CAPD patients. Present data suggest that PN should be limited to malnourished and stressed CAPD patients, or patients with severe encapsulating peritonitis, when nutritional requirements cannot be ensured by oral or enteral routes. In acutely ill patients with CKD on dialysis the decision to use PN should be the same as in ARF patients. In CAPD patients presenting with mild PEW as defined by insufficient spontaneous intakes, dietary counseling, and, if necessary, ONS should be prescribed. In patients exhibiting severe PEW, with spontaneous intakes more than 20 kcal/day; dietary counseling and ONS should be prescribed; IPPN may be considered in patients unable to comply with ONS; EN can be necessary when ONS are unable to improve nutritional status. In patients exhibiting severe PEW, with spontaneous intakes less than 20 kcal/day, or in stress conditions: daily nutritional support is necessary and EN should be preferred to PN; central venous PN is indicated when EN is impossible or insufficient. In acutely ill patients with CKD on dialysis, the goal of PN is to reduce protein catabolism and nutritional depletion-associated morbidity and mortality. In chronically undernourished CAPD patients IPPN aims to improve quality of life and to reduce PEW-related complications, hospitalization rate and mortality.</td>
<td>C</td>
<td>30</td>
</tr>
<tr>
<td>Goals of PN</td>
<td>During central venous PN the energy supply should combine carbohydrate and fat. Amino acid based PD solutions can be used for IPPN in non-acutely ill malnourished CAPD patients. The use of specific formulae for parenteral mixtures is not yet supported by controlled data.</td>
<td>C</td>
<td>31</td>
</tr>
<tr>
<td>Route</td>
<td>The special form of PN unique to CAPD patients is Intraperitoneal Parenteral Nutrition (IPPN). IPPN is shown to improve nitrogen balance and nutritional parameters. When nutritional requirements cannot be ensured by oral or enteral routes, IPPN can be proposed in stable CAPD patients. In acutely ill patients with CKD on CAPD the route for PN should be the same as in ARF patients. In these patients a combined use of PN and IPPD, using an amino acid based PD solution can be suggested.</td>
<td>B</td>
<td>32, 36</td>
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1. Preliminary remarks

The present guidelines address the indications for parenteral nutrition (PN) in renal patients with malnutrition in a similar way to the previously published guidelines on enteral nutrition (EN). As mentioned in these EN guidelines, patients with renal failure represent a heterogeneous group and their nutritional requirements vary according to the clinical setting. A large body of evidence supports the use of the enteral rather than the parenteral route for nutrient administration. However, PN can be useful in renal patients and one of the goals of these guidelines is to characterize its indications. Most of the available studies on PN in patients with renal failure are uncontrolled and only address metabolic parameters and nutritional status. Only a few studies address “hard” end points such as outcome, hospital stay, incidence of complications and recovery of renal function.

As the development of guidelines on the basis of evidence-based medicine criteria is rarely possible for this patient group, the following recommendations should therefore be regarded mainly as expert opinion.

The recent research findings concerning syndromes of muscle wasting, malnutrition, and inflammation in individuals with chronic kidney disease (CKD) or acute kidney injury (AKI) have led to a need for new terminology. Recently, an expert panel from the International Society of Renal Nutrition and Metabolism recommended the term ‘protein-energy wasting’ (PEW) for loss of body protein mass and fuel reserves in AKI as well as in CKD. This term is used in this paper. PEW should be diagnosed if three characteristics are present: low serum levels of albumin, serum retinol-binding protein, low serum levels of albumin, low levels of albumin, reduced muscle mass (muscle wasting or sarcopenia, reduced mid‐arm muscle circumference).

Patients: subjects with renal failure present a heterogeneous group of patients, in whom nutritional needs can differ fundamentally; they are thus discussed separately:

- patients with acute renal failure (ARF),
- patients with chronic kidney disease (CKD),
- patients on hemodialysis therapy (HD) including continuous renal replacement therapies (CRRT),
- patients on continuous ambulatory peritoneal dialysis.

(1) Does acute renal failure exert a major impact on metabolism relevant for nutritional therapy?

ARF not only affects water, electrolyte and acid-base metabolism but also induces global changes in the “milieu intérieur”, with specific alterations in protein, amino acid, carbohydrate and lipid metabolisms. Additionally, it exerts a pro-inflammatory reaction and has a profound effect on the anti-oxidative system (Grade B). ARF, especially in the ICU setting, rarely represents an isolated disease process. Metabolic changes in these patients are also determined by the underlying disease and/or co-morbidities, by other organ dysfunction, as well as by the modality and intensity of renal replacement therapy (RRT).

Comment: important specific metabolic abnormalities associated with ARF are:

- protein catabolism,
- alteration of metabolism of specific amino acids, peripheral insulin resistance,
- reduction of lipolysis and impaired fat clearance,
- depletion of the antioxidant system,
- induction of a pro-inflammatory state,
- immunodeficiency.

Protein catabolism is the metabolic hallmark of ARF. The metabolism of various amino acids is abnormal, several non-essential amino acids (e.g. tyrosine) become conditionally essential, and there are alterations in the intra- and extra-cellular amino acid pools as well as in the utilization of exogenously infused amino acids.

There is hyperglycemia, caused both by peripheral insulin resistance and the activation of hepatic gluconeogenesis. In
contrast to the situation in patients with CKD and healthy subjects, this increased glucose formation cannot be suppressed by exogenous nutrient supply. Insulin resistance, as defined by hyperglycemia despite high insulin concentrations, may be associated with increased risk of mortality in critically ill patients with ARF.4

Alterations in lipid metabolism are characterized by hypertriglyceridemia due to an inhibition of lipolysis; exogenous fat clearance after parenteral or enteral administration of lipids can therefore be reduced.5

Additional features include induction of a pro-inflammatory state and impaired immune competence. The plasma concentrations of water-soluble vitamins are reduced and the activation of vitamin D3 is impaired, contributing to secondary hyperparathyroidism. Vitamins E and A and selenium levels are low and there is a profound depression of the antioxidant system.

(2) Do renal replacement therapies alter nutrient metabolism in ARF patients?

Renal replacement therapies have profound effects on metabolism and nutrient balances (Grade B).

Comment: continuous renal replacement therapies (CRRT), and especially CVVH and veno-venous hemodiafiltration (CVVHDF) or sustained low-efficiency dialysis (SLED) have become the treatment modality of choice in the critically ill patients with ARF. Because of their continuous or prolonged nature and the high efficiency, these therapies may exert a negative influence on electrolyte and nutrient balance.6

CRRT cause a significant loss of water-soluble, low molecular weight substances including several nutrients. In CVVH/CVVHDF there is a loss of about 0.2 g amino acids/l of ultra filtrate (up to 10–15 g amino acids per day), and of 5 g and 10 g/day of proteins, depending on RRT modality and filter type.7,8 Water-soluble substances such as vitamins are also lost in significant amounts.6 There are however no lipid losses across the filter.

The administration of large amounts of lactate as substitution fluid, or citrate as anticoagulant, can cause complications such as hyperlactacidemia or metabolic alkalosis. CRRT also frequently induces electrolyte derangements, e.g. hypophosphatemia, hypomagnesaemia etc.12

(3) Does nutritional status influence outcome in ARF patients?

Poor nutritional status is a major risk factor for morbidity and mortality, thus determining outcomes (Grade B).

Comment: a prospective cohort study in 309 patients with ARF showed that severe under nutrition, as evaluated at admission by subjective global assessment (SGA), was present in 42% of patients.13 In this study, in-hospital length of stay and mortality were increased in patients presenting with severe malnutrition, as defined by SGA. Moreover, under nutrition was a predictor of in-hospital mortality independently of complications and co-morbidities.

(4) What are the goals of PN in ARF?

The primary nutritional goals of PN in ARF should be the same as those in other catabolic conditions in the ICU, such as ensuring the provision of optimal amount of energy, protein and micronutrients, with the aims of prevention of PEM, preservation of lean body mass, maintenance of nutritional status, avoidance of further metabolic derangements, enhancement of wound healing, support of immune function, and reduction in mortality (Grade C). In the case of ARF patients, nutritional goals could also include the attenuation of their inflammatory status and improvement of the oxygen radical scavenging system and of endothelial function5 (Grade C).

(5) Are outcome studies available? Does PN influence renal function, recovery of renal function or patient outcome?

Due to the lack of well-designed randomized controlled trials the evidence regarding the effects of PN on survival and renal recovery remain inconclusive (Grade C).

Comment: most of the randomized controlled trials (RCTs) concerning nutritional support in ARF used PN as the route of nutrient delivery. However, the possible effects of nutritional support on reducing the morbidity and mortality of ARF patients and improving recovery of ARF are still to be demonstrated, due to both the heterogeneity/complexity of the syndrome, and major methodological flaws of the available studies. The effect of PN on mortality has been analyzed in four studies. In a retrospective study,14 PN was associated with a better outcome, while in three prospective studies15–17 no survival advantages were demonstrated. However, these studies were flawed by methodological problems including suboptimal selection of patients, population heterogeneity, and lack of stratification for severity of illness, nutritional status, RRT dose received, use of historical controls, quantitative and qualitative inadequacy of caloric and nitrogen intake. In a prospective randomized trial assessing calorie and protein needs of critically ill anuric patients requiring CRRT, nitrogen balance was positively related to protein intake and more likely to be attained with protein intakes of more than 2 g/kg/day. Moreover, nitrogen balance was directly associated with both ICU and hospital outcome, as for every 1 g/day increase in nitrogen balance survival increased by 21%.11 However, most patients were receiving both PN and EN, and the latter had a statistically significant outcome advantage by multiple regression analysis.

Several nutrients have an important impact on renal function. Experimental studies have reported that intravenously or enterally administered amino acids increase renal plasma flow and creatinine clearance.18 No specific information is available on the possible beneficial effects in ARF patients; however in one clinical study EN was superior to PN in this respect.19

(6) When is parenteral nutrition indicated in ARF?

The indications for and contraindications to PN in ARF are comparable to those in other critically ill patients (see ICU guidelines). PN is appropriate in ARF when the GI tract cannot be used for enteral feeding, or when EN is not enough to reach nutrient intake goals (Grade C).

Comment: in the past PN was thought to be the preferred route of nutritional support in patients with ARF. However, in recent years EN has become the preferred modality of nutrition support; moreover, even small amounts of enterally provided diets can help to support intestinal function. In the case of EN in ARF patient’s under delivery of enteral formulae due to complications is not frequent with the use of commercially available formulae, but it may be difficult to achieve the higher protein intake usually recommended in ARF. Thus parenteral amino acid supplementation may therefore be required, especially in ARF patients on CRRT.20

(7) Are substrate requirements altered in patients with ARF?

Macronutrients

Macronutrient requirements are more influenced by the severity of underlying disease, type and intensity of extracorporeal RRT, nutritional status and associated complications, rather than by the ARF itself (Table 1).11,2
A positive nitrogen balance was more likely to be obtained with nitrogen balance was positively related to protein intake, and patients receiving an isocaloric regimen – in most cases by EN – is unknown. ARF is a highly catabolic state, and normalized protein amounts to only 130% of predicted energy expenditure multiple organ failure the energy expenditure (EE) of critically ill anticipated.12

Table 1
Nutritional requirements in patients with ARF (from Refs. 1,12).

<table>
<thead>
<tr>
<th>Route of nutrition</th>
<th>Protein (essential and non-essential amino acids)</th>
<th>Energy (non-protein calories)</th>
<th>Carbohydrates</th>
<th>Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conservative therapy, mild catabolism</td>
<td>0.6–0.8 (max. 1.0) g/kg/d</td>
<td>20–30 kcal/kg/d</td>
<td>3–5 (max. 7) g/kg/d</td>
<td>0.6–1.2 (max. 1.5) g/kg/d</td>
</tr>
<tr>
<td>Extracorporeal therapy, moderate catabolism</td>
<td>1.0–1.5 g/kg/d</td>
<td></td>
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<tr>
<td>CRRT, severe hypercatabolism</td>
<td>Up to maximum 1.7 g/kg/d</td>
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</tbody>
</table>

*Adapted to catabolism levels and to individual needs in case of underweight or obesity.*

Micronutrient requirements have been poorly investigated in ARF patients. In ICU patients with ARF, the enhanced requirements for water-soluble vitamins induced by extracorporeal therapy should be met by supplementing multivitamin products (C). In line with standard recommendations, because of the possibility of accumulation, patients should be carefully monitored for signs of vitamin A toxicity. Similarly, it has been recommended that vitamin C should not exceed 30–50 mg/day, because inappropriate supplementation may result in secondary oxalosis. These recommendations deserve some comment (see below). Recent data show that prolonged CRRT result in selenium and thiamine depletions despite supplementation at recommended amounts22,23 (A).

**Electrolytes**

ARF is associated with major fluid, electrolyte and acid–base equilibrium derangements, such as hypo- and hypernatremia, hyperkalemia, hyperphosphatemia, metabolic acidosis.12,24 Restrictions of potassium, magnesium and phosphate in PN are however usually unnecessary if the patients are on daily RRT (CRRT, hemodialysis or SLED). Serum electrolyte levels largely depend on the electrolyte composition of the dialysate/reinfusate solutions, and the intensity of RRT. Hypophosphatemia and hypomagnesaemia can frequently be observed during CRRT or SLED, and should be anticipated.12

Comment: since renal regulatory functions are impaired, tolerance of excessive substrate delivery is severely hampered (amino acids, trace elements, vitamins, etc) (C).25,26

**Macronutrients**

No major modifications of energy metabolism are associated with ARF per se, as the more relevant effects on energy expenditure are usually due to acute co-morbidities and complications.27 In mechanically ventilated patients, no differences were found in resting energy expenditure due to the presence of ARF.28 Even in multiple organ failure the energy expenditure (EE) of critically ill patients amounts to only 130% of predicted energy expenditure (PEE).

The optimal amount of protein supplementation in ARF patients is unknown. ARF is a highly catabolic state, and normalized protein catabolic rates (nPCR) of 1.4–1.8 g/kg/day have been reported in ARF patients on artificial nutrition (PN or EN or a combination of both regimens).29–32 Few data are currently available on the effects of high protein intake on nitrogen balance in ARF patients. In an uncontrolled interventional study, only 35% of patients achieved a positive nitrogen balance with nutrient intakes of 2.5 g/kg/day of protein and 35 kcal/kg/day of energy.10 In a cross-over study on ARF patients receiving an isocaloric regimen – in most cases by EN – nitrogen balance was positively related to protein intake, and a positive nitrogen balance was more likely to be obtained with intakes of more than 2 g/kg/day.11 However, no data are currently available from RCTs on this topic, and evidence concerning the safety of high protein intakes in critically ill patients with ARF is lacking. Finally, it should be emphasized that hypercatabolism in ARF patients is unlikely to be overcome by increasing protein or amino acid intake alone.

The optimal energy to nitrogen ratio has not been clearly defined in ARF patients, although, in a retrospective study of patients undergoing CVVH, linear regression analysis predicted less negative or weakly positive nitrogen balance values at protein intakes of 1.5 g/kg/day if non–protein energy intake was set at about 25 kcal/kg/day.44 Increased calorie to nitrogen ratio is not associated with better nitrogen balance. At protein intakes of 1.5 g/kg/day, increasing energy provision up to 40 kcal/g/day does not improve nitrogen balance estimates compared with 30 kcal/kg/day; instead, more severe metabolic complications of artificial nutrition (hypertriglyceridermia, hyperglycemia) can be observed.33

ARF patients on RRT and PN should receive at least 1.5 g/kg/day of protein. 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.

**Micronutrients**

All patients who require PN containing macronutrients will also require micronutrients as part of the regimen. However, some specific aspects should be considered. Experimental ARF is associated with an increase in plasma retinol.34 Although retinol intoxication was not reported in ARF patients, signs of potential vitamin A toxicity should be carefully sought during supplementation. Inappropriate vitamin C supplementation may result in secondary oxalosis.35 However, supplies higher than 50 mg/day may be necessary in ICU patients given a report of losses during CRRT of 600 μmol/day (i.e. 100 mg/day) of vitamin C and of 600 nmol/day of folate in the ultrafiltrate.36 Trace elements, which mainly circulate in a protein-bound form, appear to be less affected by ultrafiltration.36 However, Klein et al. reported significant losses of magnesium and calcium, necessitating greater supplies than were provided in standard PN formulae.23 Additional zinc was not required,21 but recent data from Berger et al. strongly argue for an increase in selenium and thiamine intake to at least double the recommended dietary allowances.22

(8) Are disease-specific formulae required for PN in ARF patients?

Standard formulae are adequate for the majority of patients (C). However, requirements can differ and have to be assessed individually. When there are electrolyte derangements, three-in-one formulae without electrolytes or customized formulae can be advantageous (C).

Comment: special nutrient formulations are more expensive and appear to offer no clinical benefit in most patients with ARF undergoing RRT. Thus, standard parenteral formulae (both amino acids and commercial three-in-one nutrient admixtures) can be employed (C). In some patients, three-in-one nutrient admixtures without electrolytes, now commercially available, can be used with caution, or customized according to patient needs. Whether immune enhancing diets (immunonutrition) should be given in ARF patients remains unclear.

(9) Which route for PN in ARF patients?

For short time periods, peripheral PN can be used in ARF patients, according to fluid restriction needs and calorie/protein
goals, but due to the need for fluid restriction and the high osmolarity of more concentrated commercial three-in-one admixtures, PN in ARF patients, especially those in the ICU, often needs to be infused centrally (C).

(10) Which decision tree for nutritional support in ARF?

The use of PN in ARF patients could represent (a) a complementary short-term nutrition strategy in patients on EN, especially in the case of inadequate protein intake; (b) a first choice when the enteral route is compromised from severe gastrointestinal complications.

A suggested decision tree for nutritional support in ARF patients with PEW might be (C):

Is the gastrointestinal tract functioning normally?

If the answer is yes:

(1) increase dietary intake by augmenting energy and protein through tube feeding,

(2) if patient’s nutritional goals (in most cases protein needs) are not achieved, start PN.

If the answer is no:

(1) Start with PN. The PN can be:

(a) peripheral PN: in cases of short-term therapy, with or without fluid restriction depending on concomitant complications and with the purpose of supplementing immediate needs,

(b) central PN: in cases of long-term therapy, with fluid restriction.

(2) When gastrointestinal function returns PN should be tapered gradually towards the use of enteral feeding or dietary intake if suitable.

2. PN in stage III–V non-dialyzed CKD

2.1. Introduction

PN is rarely used in adults with CKD treated conservatively in situations outside the intensive care unit, unless the patient suffers from severe protein-energy wasting or has severe gastrointestinal or other complications. Systematic trials are therefore not available and recommendations are based on expert opinion only.

(11) Does CKD have an influence on nutritional status and are there any metabolic alterations that influence nutritional therapy?

The uremic syndrome leads to PEW. The causes are summarized in Table 2.

Strategy of nutritional intervention in CKD patients is determined by specific metabolic alterations (A):

- insulin resistance
- abnormal plasma lipid clearance
- metabolic acidosis
- hypocalcaemia and hyperphosphatemia
- secondary hyperparathyroidism, uremic bone disease
- impairments of vitamin D3 activation
- hyperkalemia
- renal anemia
- chronic inflammatory reaction
- Activation of protein catabolism due to enhanced catabolism in intercurrent acute illness, acidosis and inflammation.

<table>
<thead>
<tr>
<th>Causes of protein-energy wasting in patients with CKD.</th>
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<tbody>
<tr>
<td>Reduced oral intake</td>
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<tr>
<td>Restrictive dietary regimen</td>
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<tr>
<td>Uremic toxicity</td>
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<tr>
<td>Micronflammation (MIA-syndrome)</td>
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<tr>
<td>Metabolic acidosis</td>
</tr>
<tr>
<td>Endocrine factors (Insulin resistance, hyperparathyroidism, elevated plasma leptin etc.)</td>
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<tr>
<td>Gastrointestinal factors (gastroplegia, impaired absorption etc.)</td>
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</table>

Comment: one important factor is anorexia. The uremic syndrome is associated with loss of appetite and a variety of gastrointestinal adverse effects, which result in reduced nutritional intake. There is a direct correlation between renal insufficiency and the reduction of spontaneous oral nutrient intake. Moreover, protein restricted diets can result in PEW, if not closely monitored.

Metabolic acidosis in uremia is an important factor for the activation of protein catabolism. Alkalinization therapy is thus standard in the treatment of CKD patients.

Intercurrent acute illnesses and/or the chronic inflammatory state augment protein catabolism can compromise the efficacy of nutritional support (type 2 malnutrition: “MIA-syndrome” = malnutrition – inflammation – atherosclerosis).

Nutritional therapy cannot logically be separated from other metabolic interventions, such as the therapy of secondary hyperparathyroidism or correction of metabolic acidosis. In diabetic patients accurate management of glucose metabolism and of hypertension is mandatory. Intercurrent disease (e.g. infections) must be treated.

(12) What are the nutritional requirements of CKD patients?

An energy intake > 30–35 kcal/kg/day is associated with better nitrogen balance and is recommended in stable CKD patients (A). Recommendations for protein intakes are given in Table 3-1 and mineral requirements of metabolically stable patients are summarized in Table 3-2 (Table 4) (B).

Loss of protein due to proteinuria exceeding 1 g/d should lead to compensatory additions to daily protein intake such as by the calculation of protein/AA intake needed based on ideal body weight (kg × 0.6 – 0.8 × proteinuria).

The nutritional requirements of acutely ill CKD patients are dealt with as in ARF (see above).

(13) Which CKD patients might need PN?

Conservatively treated patients with CKD seldom need PN. Potential indications of PN in CKD patients are similar to the indications for PN in non-renal patients. Malnourished CKD patients requiring nutritional support should only be considered for PN.

<table>
<thead>
<tr>
<th>Table 3</th>
</tr>
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<tbody>
<tr>
<td>Recommendations for protein supply in adult patients with non-dialysis CKD (g/kg/day):</td>
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<tr>
<td>GFR &gt; 25–70 ml/min</td>
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<tr>
<td>GFR &lt; 25 ml/min</td>
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</table>

ESBPEN, European Society for Clinical Nutrition and Metabolism; NKF, National Kidney Foundation; EAA, essential amino acids; GFR, glomerular filtration rate; HBV, high biological value; KA, ketoanalogues.

By now, because EAA are already not used, very low protein diets are most often 0.3–0.4 g protein/kg/day + KA.
hypo-
patients from these reports should be considered as severely malnourished.

(19) Does HD in addition to CKD have effects on nutritional status?

Although initiation of dialysis results in an initial improvement in nutritional indices, some dialysis-specific factors, like impairment of subjective well-being, loss of nutrients, protein catabolism and inflammation are relevant for the high incidence of PEW.

Comment: the high prevalence of PEW which is observed at the onset of HD treatment is the consequence of a reduction in nutrient intake which occurs early in the course of renal failure and worsens with its progression, and to renal failure-associated metabolic disturbances.\(^\text{54,58}\) A survey of the outcome of nutritional status in patients on maintenance HD showed improvements in food intake, nutritional markers and body composition during the first years of HD therapy.\(^\text{60}\) However, after this initial improvement, the time on dialysis becomes directly associated with a significant decline in all measured nutritional parameters.\(^\text{50}\) Moreover, despite adequate dialysis dose and protein intake, long-term HD survivors develop lower BMI and poorer anthropometric status than their short-term HD counterparts.\(^\text{51}\)

In addition to the above mentioned factors seen in CKD, anorexia is a major cause for the development of PEW in HD.\(^\text{52}\) Chronic inflammation, which is present in 35–50% of HD patients, may also contribute to PEM.\(^\text{53,54}\) Inflammation is linked to uremic factors (infection, cardiovascular disease) and also with certain dialytic factors (e.g. water purity, biocompatibility, access site infection). Regardless of the mechanisms, inflammation has many adverse metabolic and nutritional effects which include anorexia, increased whole-body and muscle protein catabolism, decreased anabolism due to disruption of the GH and IGF-1 axis and cytokine-mediated increased energy expenditure.\(^\text{55}\) However, it is noticeable that in two recent studies concerning HD patients, no correlation was found between either energy or protein intake and inflammatory markers.\(^\text{56,57}\)

Intercurrent disease processes such as infections enhance catabolism and must be treated consistently. Other “treatable” causes of PEM include acidosis, hyperparathyroidism and gastroparesis.\(^\text{58}\) Lastly, because of the addition of socio-economic, psychological and specific problems of aging, elderly patients are at increased risk for the development of PEW.\(^\text{59}\)

(20) Does HD have an additional impact on metabolism or substrate requirements?

In patients with terminal renal failure on HD, the metabolic alterations due to CKD are not completely compensated by HD therapy; fluid and electrolyte problems are aggravated and several dialysis-associated factors become relevant. The dialysis procedure is itself a catabolic event as confirmed by stable isotopic techniques. Energy expenditure is increased during hemodialysis sessions.

Comment: the dialysis procedure is a catabolic event as confirmed by stable isotopic techniques.\(^\text{60,61}\) Nitrogen balance is approximately neutral on non-dialysis days and negative on dialysis days in relation to free amino acid and peptide losses into the dialysate (8–12 g and 1–3 g per session respectively); increased protein breakdown and reduction of protein synthesis also occurs.\(^\text{21}\) This cumulative negative nitrogen balance is at least partly responsible for the high prevalence of loss of lean body mass observed in long-term HD patients.\(^\text{62}\)

In addition, energy expenditure is increased during HD treatment in relation to alteration of substrate oxidation with diminished carbohydrate and increased lipid and amino acid oxidation. Glucose losses into the dialysate (approximately 25 g per session) may also contribute to PEW in patients with a reduced dietary intake. Lastly, dialysis losses of water-soluble vitamins, carnitine and trace elements can account for frequent deficiencies observed in HD patients.\(^\text{63}\)

(21) What are the nutritional requirements in HD patients?

In acutely ill HD patients the requirements are the same as in ARF patients. Macronutrient requirements of metabolically stable patients as estimated by NKF, ESPEN and EDTA are summarized in Table 5 (B).

Mineral requirements are given in Table 6 (B). Due to dialysis-induced losses, water-soluble vitamins should be supplied: folic acid (1 mg/day), pyridoxine (10–20 mg/day) and vitamin C (30–60 mg/day) (C, 13,66). Vitamin D should be given according to serum calcium, phosphorus and parathyroid hormone levels. Routine hemodialysis does not induce significant trace-element losses. However, in depleted patients, zinc (15 mg/day) and selenium (50–70 μg/day) supplementations may be useful.

Comment: a meta-analysis of published nitrogen balance studies that estimated basal or maintenance requirements and/or the adequacy of specific nitrogen intakes in healthy adults has been published.\(^\text{64}\) The average requirement of protein for healthy adults has been estimated at 0.65 good-quality protein/kg/day and the recommended dietary allowance (97.5th centile) at 0.83 g.\(^\text{64}\) Although a neutral or positive nitrogen balance can occur in HD patients at an intake of 0.9–1.0 g protein/kg/day, it has been proposed by the NKF,\(^\text{45}\) ESPEN,\(^\text{21}\) and EDTA\(^\text{67}\) that a higher protein intake, from 1.1 to 1.4 g/kg/day, is needed in HD patients. Phosphorus intake should be limited to 10–15 mg/kg/day. As phosphorus and protein are combined in nutrients with a ratio of 10–13 mg phosphorus/g protein, most HD patients who have an adequate protein intake will need phosphate binders to prevent an increase in serum phosphorus. A renal dietician is best placed to help the patient choose nutrients low in phosphorus.\(^\text{63}\)

A number of descriptive studies have reported energy intakes to be frequently as low as 22–24 kcal/kg/day contributing to PEW by depleting body adipose stores and by favoring negative nitrogen balance, despite the recommended daily energy intake of 30–40 kcal/kg/day according to age, gender and physical activity.

Due to abnormal metabolism and dialysis-induced losses, supplements of water-soluble vitamins have been recommended. Infection, surgery, and a glucose-rich infusion may especially increase the need for thiamine. The typical dietary intake of 0.5–1.5 mg/day can be supplemented with a daily oral dose of 1–5 mg of thiamine hydrochloride.\(^\text{63}\) Vitamin E may also be prescribed to patients at high cardiovascular risk at a daily dose of 800 IU of alpha-tocopherol.\(^\text{68}\)

(22) Does protein-energy wasting in patients on HD have an impact on morbidity and mortality?

PEW is recognized as an independent determinant of morbidity and mortality in HD patients.

Comment: it is estimated that the annual mortality rate in malnourished hemodialysis patients is close to 30%.\(^\text{69,70}\) Epidemiological studies have shown a strong association between nutritional status and subsequent morbidity and mortality among HD patients, albumin and transthyretin showing the strongest predictive value.\(^\text{71–74}\) It is notable that these different markers are also influenced by the inflammatory state of the patient. Changes in nutritional variables over a few weeks provide additional prognostic information.\(^\text{75,76}\) PEW is not a direct cause of morbidity and mortality but rather contributes to a fatal outcome by worsening the adverse effects of cardiovascular disease and infection which
are the commonest causes of death in HD patients.\textsuperscript{77,78} The protective effect of high BMI on morbidity and mortality risk, which is part of the so-called reverse epidemiology, indirectly confirms the importance of nutritional factors in the outcome of HD patients.\textsuperscript{79,80}

(23) Is PN indicated in HD patients?

In acutely ill patients with CKD on dialysis, PN is indicated as in those with ARF (C). Nutritional support is indicated in undernourished HD patients as defined by low nutritional indices, mainly BMI less than 20 kg/m\textsuperscript{2}, body weight loss more than 10% over 6 months, serum albumin less than 35 g/l and serum transthyretin less than 300 mg/l (C). IDPN improves nutritional status in undernourished HD patients (A). In outpatients, if nutritional counseling and oral nutritional supplements (ONS) are unsuccessful, IDPN should be proposed (C).

Comment: IDPN typically provides 800–1200 kcal three times weekly, in the form of glucose and fat emulsion and 30–60 g of protein.\textsuperscript{81} IDPN improves energy and protein balance, and albumin synthesis rate.\textsuperscript{82,83} In more than thirty studies, including five prospective, randomized, controlled trials, IDPN has been shown to improve nutritional parameters.\textsuperscript{84–87} However in a recent randomized controlled trial in 182 undernourished HD outpatients, the addition of IDPN to standard ONS did not further improve nutritional status.\textsuperscript{88} These data suggest that IDPN should be proposed only in undernourished HD out patients with poor compliance to ONS or not tolerating it. Moreover, oral ONS and IDPN can generally only provide the equivalent of 7–8 kcal/kg/day and 0.3–0.4 g protein/kg/day. As shown in Fig. 1, when PEW is associated with spontaneous intakes lower than 0.8 g protein and 20 kcal/kg/day, daily nutritional support is needed to ensure recommended nutritional intakes.\textsuperscript{89} In these conditions, EN should be preferred to PN.\textsuperscript{1} One group in whom central venous PN should however be considered is the HD patient with acute catabolism in whom oral and enteral nutrition is not possible. These patients should be treated metabolically and nutritionally like ARF patients.

(24) What are the goals of PN in HD patients?

In acutely ill patients with CKD on dialysis, the goal of PN is to reduce protein catabolism and nutritional depletion-associated morbidity and mortality. In chronically undernourished HD patients, IDPN aims to improve quality of life and to reduce PEW-related complications, hospitalization rate and mortality.

Large randomized, controlled trials are needed to evaluate the effects of IDPN on quality of life, hospitalization rate and survival. Retrospective studies suggest that IDPN may reduce hospitalization rate (B) and survival (B). Randomized controlled trials evaluating the effect of IDPN are needed.

Comment: the effect of IDPN on quality of life was assessed in a cohort of 23 patients before and after four months of IDPN. Although the IDPN improved serum albumin levels, aside from improved sleep patterns, no significant improvement in quality of life could be demonstrated.\textsuperscript{89} A reduction of hospitalization rate was reported in a retrospective study of 45 patients with low serum albumin given IDPN for 6 months.\textsuperscript{90} Three retrospective studies reported that in malnourished, hypoalbuminemic HD patients, IDPN improved survival.\textsuperscript{69,70,91} Based on these three studies, it was estimated that the relative risk reduction in mortality with intradialytic parenteral nutrition (IDPN) ranged from 0.48 to 0.74.\textsuperscript{92} However, the need for randomized controlled trials evaluating the effect of IDPN on outcome has been underlined by many authors.\textsuperscript{92,93} The FineS study aimed to evaluate in a randomized, intention-to-treat fashion, the effect on survival of a one-year IDPN in 182 malnourished HD patients receiving oral supplements. The two-year survival was not influenced by the addition of IDPN to ONS. Independent from the nutritional support, the improvement of nutritional status as assessed by serum transthyretin, was associated with an increased survival.\textsuperscript{98}

(25) Are outcome studies available?

Acutely ill patients with CKD on dialysis should be treated in a similar manner to those with ARF (C).

Standard amino acid solutions can be used for IDPN in non-acutely ill malnourished HD patients (C). The energy supply should combine carbohydrate and fat (C). The use of specific parenteral solutions is not yet supported by controlled data.

Comment: HD patients are characterized by numerous abnormalities of nutrient metabolism concerning both amino acid and energy metabolism. These metabolic abnormalities should be taken into account for amino acid, carbohydrate and fat supply during IDPN. HD patients have abnormalities of essential amino acids, branched-chain amino acids, tyrosine and sulphur amino acids.\textsuperscript{94–96} Moreover, HD sessions are responsible for a decrease in the total plasma amino acid concentration which is known to alter protein synthesis.\textsuperscript{97,98} It has been shown that the intradialytic infusion of amino acids prevents the decrease in plasma amino acid concentration and the subsequent decrease in protein synthesis.\textsuperscript{82} No controlled study has yet addressed the use of specific amino acid formulae.
Both glucose and lipid metabolism are altered in HD patients. The use of hypertonic glucose is limited by insulin resistance, glucose intolerance and the risk of post-dialysis hypoglycemic accidents. Therefore, despite the fact that exogenous lipid clearance is reduced, fat is the preferred fuel in HD patients during the post-absorptive phase. Other arguments to provide fat emulsions in association with glucose during PN in HD patients are (a) the essential fatty acid deficiency reported in HD patients; (b) the high energy/volume ratio of fat emulsions and their isosmolarity which make their intravenous peripheral infusion well-tolerated; (c) the lack of effect of fat emulsions on dialysis efficacy.

(27) Which route for PN in HD patients?

In acutely ill patients with CKD on dialysis the route for PN should be the same as in ARF patients (C).

In non-acutely ill malnourished HD patients, IDPN is infused through the venous line during dialysis.

Comment: IDPN is a cyclic PN given (usually) three times weekly through the venous line of the dialysis circuit. The following technical rules have been proposed in order to ensure optimal tolerance (C): (a) IDPN should be infused at constant rate during a typical 4 h dialysis session; (b) IDPN delivery should be progressively increased from 8 ml/kg/IDPN (representing 500 ml in a 60 kg patient) during the first week, to a maximum of 16 ml/kg/IDPN without exceeding 1000 ml/HD; (c) IDPN should be associated with controlled ultrafiltration, volume for volume; (d) 75 mmol Na should be added per liter of IDPN solution in order to compensate Na losses due to ultrafiltration.

(28) Which decision tree for nutritional support in HD patients?

In acutely ill patients with CKD on dialysis the decision to use PN should be based on the same criteria as in ARF patients (C). In non-acutely ill malnourished HD patients, Fig. 1 proposes a decision tree for the management of PEW according to HD patient nutritional assessment (C).

- In patients presenting with mild PEW as defined by insufficient spontaneous intake, dietary counseling, and, if necessary, ONS should be prescribed.
- In patients exhibiting severe PEW, with spontaneous intakes more than 20 kcal/day: dietary counseling and ONS should be prescribed; IDPN is indicated in patients unable to comply with ONS; EN can be necessary when ONS or IDPN fail to improve nutritional status.
- In patients exhibiting severe PEW, with spontaneous intakes less than 20 kcal/day, or in stress conditions: both ONS and IDPN are generally unable to provide satisfactory nutritional supply and are not recommended; daily nutritional support is necessary and EN should be preferred to PN; central venous PN is indicated when EN is impossible or insufficient.

Comment: the following measures for longitudinal monitoring of nutritional status in maintenance dialysis patients can be proposed based on the ESPEN, US National Kidney Foundation and EBPG recommendations: dietary interviews every 6 months; body mass index and nPNA monthly; serum albumin and transthyretin, anthropometrics every 1–3 months as needed according to nutritional status. Unstable and high-risk patients may require monitoring at shorter intervals. Severe PEW, compromising the middle-term prognosis can be detected by a decrease in BMI below 20, a body weight loss more than 10% within 6 months and the alteration of protein markers of malnutrition such as serum albumin < 35 g/l, transthyretin < 300 mg/l.

Alternative treatments for protein-energy wasting in dialysis have also been developed and may be proposed when nutritional support is insufficient. Daily dialysis which was shown to induce an
improvement in spontaneous alimentation and nutritional status, should be assessed as a therapy for PEW in selected patients. The administration of nandrolone decanoate was demonstrated to increase muscle mass, as assessed by pre-dialysis creatinine and DEXA, and muscle performance. Exercise combined with IDPN, as compared with IDPN alone, was shown to promote net muscle protein accretion. These data argue in favor of a multimodal treatment of PEW in dialysis, combining nutritional support, exercise and anabolic agents. Such a therapeutic approach of PEW in dialysis should be tested to obtain an optimal treatment of PEW.

4. Specific aspects of parenteral nutrition in patients on continuous ambulatory peritoneal dialysis (CAPD)

4.1. Introduction

The prevalence and prognostic influence of PEW is similar in CAPD and HD patients. Therefore, the CAPD patients should have the same nutritional monitoring (see above). PN in CAPD patients is mainly characterized by the development since the beginning of the nineties of a specific route for nutrient delivery: intraperitoneal parenteral nutrition (IPPN). IPPN, which mainly consists of the intraperitoneal administration of 1.1% amino acid-based solution, is now demonstrated to improve protein metabolism and nutritional markers in stable CAPD patients. IPPN should be integrated into the nutritional management of CAPD patients, taking into account spontaneous alimentation, nutritional supplementation and compliance with ONS and EN.

(29) Do CAPD patients have specific metabolic characteristics?

Since CAPD patients usually have better residual renal function, several uremic symptoms and metabolic abnormalities are less pronounced than in patients on HD therapy. However peritoneal losses of various nutrients are significant while absorption of glucose from the dialysate is enhanced.

Comment: therapy-associated losses of proteins during CAPD are higher than in HD, as are losses of protein-bound substances, such as trace elements. Protein losses have been reported to be approximately 10 g/day and amino acid losses from 3 to 4 g/day, including 30% of essential amino acids. Protein losses are about 15 g/day in moderate peritonitis, and can reach 100 g/d in severe peritonitis. In patients treated by APD, a somewhat higher 24 h dialysate protein losses compared to previous reports among continuous ambulatory PD patients has been reported. In these patients more frequent monitoring of nutritional parameters has been suggested and the use of 1.1% amino acid-based solution proposed. Elimination of water-soluble substances is lower than in HD.

Because peritoneal solutions with a high glucose content are used as standard in CAPD, this method is associated with a glucose uptake of 100–200 g/d, which is further increased during peritonitis. Consequently, total energy intake is usually normal or even enhanced.

(30) How are body composition/nutritional state affected in CAPD patients?

The enhanced loss of proteins or amino acids can induce protein PEW and deficiencies of micronutrients. Due to the increased glucose load, body weight may even increase in CAPD patients but this reflects an increase in body fat mass only and masks a loss in lean body mass. The high glucose load is also responsible for induction or aggravation of diabetes, hypertriglyceridemia in 60% of patients, and increased LDL and VLDL cholesterols.

(31) What are the nutritional requirements of CAPD patients?

Acutely ill CAPD patients have the same nutritional requirements as ARF patients. The requirements of metabolically stable patients are summarized in Tables 5 and 6 (C).

Comment: recommended energy intakes in CAPD patients, 35 kcal/kg/d, including glucose uptake from peritoneal fluid, which represents approximately 8 kcal/kg/day. Estimated protein requirements are 1.2 g/kg/day, including 50% of high biological value proteins.

(32) Is PN indicated in CAPD patients?

Intravenous PN has been poorly investigated in CAPD patients. Present data suggest that PN should be limited to malnourished and stressed CAPD patients, or patients with severe encapsulating peritonitis, when nutritional requirements cannot be ensured by oral or enteral routes. The special form of PN unique to CAPD patients is Intraperitoneal Parenteral Nutrition (IPPN). IPPN is shown to improve nitrogen balance and nutritional parameters (A). When nutritional requirements cannot be ensured by oral or enteral routes, IPPN can be proposed in stable CAPD patients (C).

Comment: in the particular setting of encapsulating peritonitis central venous PN may be necessary. IPPN was made easier by the use of a dialysate with 1.1% amino acid concentration. Metabolic studies during intravenous infusion of (2H3) and intraperitoneal leucine (13C) showed that intraperitoneal amino acids were incorporated in protein synthesis. More recently, combined amino acid and glucose dialysate was shown to improve protein anabolism in renal failure patients on CAPD. An analysis of 11 studies of intraperitoneal AA infusions, including 4 randomized trials, showed an improvement of nitrogen balance and nutritional parameters in 4 cohort series. Intraperitoneal amino acid therapy in non-acute malnourished CAPD patients was reported to improve nitrogen balance, serum transferrin and fasting morning plasma amino acid pattern. In one randomized study nutritional improvement was only observed in hypoalbuminemic patients. In a 3-year, randomized, prospective, controlled study of amino acid dialysate 60 patients were assigned randomly to either replace one exchange daily with amino acid dialysate or to continue with dextrose dialysate. Dietary protein intake increased in the amino acid group. Biochemical nutritional parameters including nPNA, albumin and cholesterol decreased in the dextrose group but remained stable or increased in the amino acid group. The nutritional benefit of the amino acid dialysate appeared more prominent in women, whose lean body mass and body mass index were maintained with amino acids but not with dextrose alone. This study, however, did not show a significant effect of amino acid dialysate on patient survival.

(33) What are the goals of PN in CAPD patients?

In acutely ill patients with CKD on dialysis, the goal of PN is to reduce protein catabolism and nutritional depletion-associated morbidity and mortality. In chronically undernourished CAPD patients IPPN aims to improve quality of life and to reduce PEW-related complications, hospitalization rate and mortality.

(34) Are outcome studies available?

Studies to document the improvement in the morbidity and mortality of CAPD patients with these interventions are still needed and require large multi-centre trials. Amino acid-enriched dialysate in peritoneal dialysis improves nutritional parameters of
malnourished patients but an ability to improve patient survival is questioned. Retrospective studies suggest that IPPN may reduce hospitalization rate (B) and improve survival (B).

Comment: very few papers address the effect of PN on morbidity and mortality in CAPD patients. Adequate nutrition is an important challenge for dialysis patient outcome. Nutritional status must be regularly assessed and treated if necessary. Recent data showed the effectiveness of PN in reducing morbidity and mortality in malnourished HD patients (see above). Although the same results could be expected in CAPD patients, no prospective data demonstrate an effect of PN on CAPD patient outcome.

(35) Which PN formulae should be used in CAPD patients?

During central venous PN the energy supply should combine carbohydrate and fat (C). Amino acid-based PD solutions can be used for IPPN in non-acutely ill malnourished CAPD patients (A). The use of specific formulae for parenteral mixtures is not yet supported by controlled data. Very few randomized trial have been published on PN in CAPD patients and these studies have only really addressed the energy supply. A random-order cross-over study was performed in eight APO patients to compare in two periods of 7 day each, amino acid plus glucose dialysate versus glucose as control dialysate. Whole-body protein turnover was determined using a primed continuous infusion of 1-[1–13C]leucine, and 24 h nitrogen balance studies were performed. During amino acid plus glucose dialysate rates of protein synthesis and net protein balance were improved compared to controls. Another study demonstrated that the use of a new 0.6% amino acid/1.4% glycerol-containing dialysate solution was safe and well-tolerated. Glucose load was reduced significantly and dialysate CA125 levels improved significantly. Ultrafiltration was comparable with that of a 2.27% glucose solution.

(36) Which route for PN in CAPD patients?

In acutely ill patients with CKD on CAPD the route for PN should be the same as in ARF patients (C). In these patients a combined use of PN and IPPD, using AA based PD solution can be suggested (B). In non-acutely ill malnourished CAPD patients, the preferred route is via the peritoneum (B). Comment: IPPN can be associated with hypokalemia and hypophosphatemia. Some patients may also develop mild acidosis. These possible side effects underline the need for close monitoring during this treatment.

(37) Which decision tree for nutritional support in CAPD patients?

In acutely ill patients with CKD on dialysis the decision to use PN should be the same as in ARF patients (C). In non-acutely ill malnourished CAPD patients, a decision tree similar to that of malnourished HD can be proposed (C).

- In patients presenting with mild PEW as defined by insufficient spontaneous intakes, dietary counseling, and, if necessary, ONS should be prescribed.
- In patients exhibiting severe PEW, with spontaneous intakes more than 20 kcal/day; dietary counseling and ONS should be prescribed; IPPN may be considered in patients unable to comply with ONS; EN can be necessary when ONS are unable to improve nutritional status.
- In patients exhibiting severe PEW, with spontaneous intakes less than 20 kcal/day, or in stress conditions; daily nutritional support is necessary and EN should be preferred to PN; central venous PN is indicated when EN is impossible or insufficient.

Comments: nutritional support in CAPD patients include dietary counseling, ONS, EN, PN and IPPN, which consists of the intraperitoneal administration of amino acids. ONS were shown to improve protein and calorie intakes. Conflicting data have been reported regarding patient compliance with ONS and their nutritional efficacy. Moreover the effects of EN and PN are poorly documented in adult CAPD patients.

Conflict of interest

Conflict of interest on file at ESPEN (espenjournals@espen.org).

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