Protein-energy wasting and nutritional requirements in dialysis

Protein-energy wasting is an aspect of chronic kidney disease that is associated with increased risk of morbidity and mortality, and a lower quality of life. Bruno Mafrici and Victoria Armstrong-Brown discuss the nutritional guidelines and recommendations of how to manage these patients, helping them to maintain a healthy nutritional intake.

■ protein-energy wasting ■ chronic kidney disease ■ renal dietetics ■ dialysis

Dialysis is usually required when the kidneys lose 85–90% of their function, and are unable to clear the blood of waste, fluid and electrolytes (National Kidney Foundation (NKF), 2015). Patients may choose hospital/satellite-based haemodialysis (HD) or home dialysis (such as peritoneal dialysis (PD) or home HD), as their treatment option, both of which often require an individually tailored diet to maintain a stable electrolyte balance and ensure a good nutritional status.

Protein-energy wasting

Protein-energy wasting (PEW) refers to the multiple nutritional and catabolic alterations that occur in chronic kidney disease (CKD), and is associated with an increased risk of hospital admissions, morbidity, mortality and impaired quality of life (Carrero et al, 2013; Obi et al, 2015). PEW is not only caused by a decreased energy and protein intake, but also by increased inflammatory cytokines; uraemia-induced alterations; acidosis; the catabolic effect of dialysis, with nutrients losses into the dialysate (such as amino acids and water soluble vitamins); pharmacotherapy, such as prednisolone; and other factors (Kopple, 1999; Carrero et al, 2013; Ikizler et al, 2013).

PEW has been reported in patients on dialysis over the past 20 years, with prevalence rates of 20–70%, depending on the methods used to identify the condition (Fouque et al, 2008). Nutritional requirements (in particular energy and protein) have remained largely unchanged within this timeframe.

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Identification and consequences of protein-energy wasting

Anthropometry parameters in patients on dialysis seem to have improved over the last 30 years (Koefoed et al, 2016). While the reason for this improvement could not be identified, Koefoed et al (2016) suggested that the most likely contributors are the higher prevalence of obesity, less predialytic malnutrition, and an improved focus on nutrition in maintenance of patients on dialysis. Nevertheless, the incidence of PEW is still high and measuring it in patients on dialysis is not simple. The International Society of Renal Nutrition and Metabolism (ISRNM) suggested that no single biochemical marker can diagnose PEW; instead, the use of complementary assessment tools, following trends of individual patients over time, and monitoring of serum biochemistry, fat mass, muscle mass and dietary intake, should all be considered (Fouque et al, 2008).

PEW is characterised by low levels of albumin (<38 g/l), low protein nitrogen appearance (also referred to as protein catabolic rate), progressive falls in post-HD dry body weight, and a body mass index (BMI) of <23 kg/m^2 (Fouque et al, 2008). A BMI below this level has also been associated with greater risk of hospitalisation and mortality (Lopes et al, 2010), and significantly increases the relative risk of death in patients on HD (Dwyer et al, 2005). In addition, pre-HD serum creatinine, urea and phosphate have been used in combination as markers for nutritional status. Levels below the normal range have all correlated with increased risk of hospitalisation and mortality (Kopple, 1997; Combe et al, 2004). Subjective global assessment has been widely used in clinical practice to assess and monitor nutritional status (Steiber et al, 2003; De Mutsert et al, 2009). A study of more than 1500 patients on dialysis assessed using the 7-point subjective global assessment over a period of 7 years showed that low scores (1 and 2) were associated with a high risk of mortality in patients on dialysis (De Mutsert et al, 2009). Other studies have shown strong association between PEW and increased risk of mortality both in PD (Fein et al, 2003; Krishnamoorthy et al, 2015) and HD (Carrero et al, 2013). In addition to the subjective global assessment, a reduction in functional markers, such as hand-grip strength (Vogt et al, 2016) and pinch strength (El-Katab et al, 2016), have also been correlated with an increased risk of death in patients on dialysis. Steiber et al (2015) demonstrated the clinical utility of using a web-based HD-specific nutrition algorithm, including measuring and monitoring outcomes over time, and other models (such as the Renal Nutrition Group and the Parenteral and Enteral Nutrition Group of the British Dietetic Association toolkits) are emerging.

Preventing protein-energy wasting

It is important that patients meet their nutritional daily needs in order to prevent PEW; however, those on dialysis often need several dietary modifications in view of any underlying clinical conditions (Carrero et al, 2013). For example, patients with diabetes must consider carbohydrate sources; salt and fluid intake also need to be monitored if patients are to manage hypertension and control intradialytic weight gains. Furthermore, some patients on dialysis may need to follow a low-potassium, low-phosphate diet to reduce symptoms, improve quality of life and increase life expectancy (Durose et al, 2004).

In the authors' experience, meeting nutritional needs in patients on dialysis is challenging: not only because dietary recommendations must have a holistic approach and include a patient's clinical background (not only focusing on the renal dietary guidelines), but also because a patient's nutritional needs are likely to change over time (Sabatino et al, 2016). Therefore, monitoring and reviewing dietetic intervention by measuring meaningful outcomes is essential.

Nutritional requirements in dialysis

Nutritional requirements should include consideration of energy and protein, as well as micronutrients such as phosphate, potassium, vitamins, trace elements (including selenium and zinc) and fluid. Fibre is also an important element of the diet (but not a nutrient per se); this is especially in PD (Sutton et al, 2014), as it may contribute to preventing constipation.

Energy

Indirect calorimetry (IC) is recommended as the gold standard of measuring energy requirements. Where IC is unavailable, an individualised assessment of energy intake goals is recommended (Brown et al, 2010). Recommendations as a result of these assessment are usually based on calories per kg (kcal/kg) body weight.

A small recent study conducted in patients on maintenance HD using IC showed an average daily energy requirement of 31 kcal/kg/day, with an individual variability of 26–36 kcal/kg/day (Shah et al, 2016). *Table 1* shows guidelines for energy requirements in patients on HD and PD, predominantly based on small studies and expert opinion. Adjusting energy requirements according to age, gender, activity levels and presence (or lack) of PEW was suggested by these guidelines. One of the difficulties in this area is that not all recommendations specify how to estimate requirements for patients who are either underweight or obese, and if ideal body weight should be used. Clinical judgement is required when using these guidelines, to help avoid over- or underestimating requirements, and appropriate monitoring of nutritional status should be used to guide any nutritional plan in patients with PEW.

A research group developed predictive energy equations specific to the maintenance HD population in 2014 (Byham-Gray et al, 2014). The researchers found that using albumin, C-reactive protein and creatinine produced a better model for establishing resting energy expenditure than using demographic and anthropometric variables alone. However, as the sample was small, further validation of Byham-Gray et al's (2014) equations is required.

Protein

Protein requirements in the dialysis population are higher than that of the general population (*Table 2*) due to increased losses of protein and catabolism during the dialysis process (Fouque et al, 2007; Ikizler et al, 2013). Higher protein provision has also been associated with better outcomes (Shinaberger et al, 2008). The requirements suggested are based on maintenanceof patients on dialysis and therefore may be higher for hypercatabolic and unwell patients on dialysis. Further research is required in subgroups of the population, such as those with PEW and peritonitis and in obesity, which may lead to an under- or overestimation of actual requirements.

Salt and fluid

For patients on dialysis, a low-salt diet of <6 g/day (NKF, 2015; Joint British Diabetes Societies, 2016; Luis et al, 2016) can reduce thirst, helping with the management of hypertension and intradialytic weight gain (Lindley, 2009). In practice, recommendations are individualised and some patients require <5 g/salt a day (Lindley, 2009), while others may need a temporary relaxation of restriction to improve nutritional intake. Standard equations to estimate fluid requirements (such as 30–35 ml/kg body weight) are not useful in dialysis. These requirements depend on the patient's dry weight, blood pressure,

Table 1. Energy requirements in patients on dialysis

Guidelines	Haemodialysis	Peritonial dialysis
National Kidney Foundation (2000) Kidney Disease Outcomes Quality Initiative	30–35 kcal/kg/day	35 kcal/kg/day (including kcal from dialysate)
European Society for Clinical Nutrition and Metabolism (Cano et al, 2006)	35 kcal/kg/day	35 kcal/kg/day
European Best Practice Guidelines (Fouque et al, 2007)	30–40 kcal/kg/ideal body weight (IBW)/day	Not applicable
American Society for Parenteral and Enteral Nutrition (Brown et al, 2010)	35 kcal/body weight (BW)/day (20–40 kcal/kg/BW)	35 kcal/body weight (BW)/day (20–40 kcal/kg/BW)
International Society of Renal Nutrition and Metabolism (Ikizler et al, 2013)	30–35 kcal/kg IBW per day, based on physical activity level	30–35 kcal/kg IBW per day, based on physical activity level
British Dietetic Association Renal Nutrition Group (Naylor et al, 2013)	Not applicable	30–35 kcal/kg of IBW per day, based on physical activity level
Australian systematic review (Ash et al, 2014)	35 kcal/kg/IBW/day for those <60 years; 30–35 kcal/kg/IBW/day for those >60 years	35 kcal/kg/IBW/day for those <60 years; 30–35 kcal/kg/IBW/day for those >60 years

dialysis prescription, residual renal function and clinical condition. From clinical experience, recommendations on fluid restriction can vary widely across different renal units; for example between 500–1000 ml a day in patients on HD, and up to 1500 ml in PD. Advice on fluid restriction should always be given in combination with lowering salt intake (Tomson, 2001).

Fluid and salt restrictions needs to be taken into account when developing a nutritional plan for patients who require nutritional support. For example, supplementing dietary intake with large volumes of full-fat milk may not be appropriate in view of fluid restrictions. The amount of salt in standard oral nutritional supplements (ONS) and enteral feed is negligible; however, fluid content needs to be considered. A high-protein, high-energy, low-volume, low-phosphate and low-potassium supplement is advised by clinical guidelines (National Institute for Health and Care Excellence (NICE), 2013) and in the literature (Ikizler et al, 2013). If patients struggle to meet their energy and protein requirements with a fluid restriction, the dialysis prescription may need to be increased to accommodate nutritional support. This decision must involve patients, as the increased frequency of dialysis is likely to affect a patient's quality of life.

Phosphate

Dietary phosphate should be restricted to 800–1000 mg (26–32 mmol) in patients on dialysis (NKF, 2003). In practice, patients should achieve a phosphate serum level between 1.1–1.7 mmol/l and aim towards a normal range where possible, as studies have shown an association between hyperphosphatemia and mortality in dialysis (Kidney Disease: Improving Global Outcomes, 2009; Renal Association, 2015). NICE (2013) guidelines for hyperphosphatemia in CKD suggested offering information about controlling intake of phosphate-rich foods while avoiding malnutrition by maintaining a higher protein intake.

Protein and phosphate have a direct relationship: the higher the protein content in food, the higher the phosphate content. This is true for animal protein, which has a high biological value, and therefore should not be restricted. However, processed foods containing additives and preservatives are high in phosphate and may provide little nutritional value (Kalantar-Zadeh et al, 2010; Benini et al, 2011). A combination of decreased serum phosphorus and increased protein intake is linked to the best clinical outcomes, whereas a low serum phosphorus and protein intake has the worst outcomes in patients on HD (Ikizler et al, 2013).

In the context of PEW, patients present with a very small appetite and limited intake, including dietary phosphate. The evidence also suggests that a low level of phosphate (<1.1 mmol/l) is correlated with an increase in relative risk of mortality (Noordzij et al, 2006). Therefore, when assessing patients with PEW, both high- and low-phosphate levels are equally important.

Potassium

Potassium levels need to be taken into consideration when advising on nutritional support. Hyperkalaemia can be caused by underdialysis and non-compliance with diet. The renal association suggest that predialysis potassium levels should be between 4–6 mmol/l in HD patients, and that this is associated with the lowest risk of death (Mactier et al,

Table 2. Protein requirements in patients on dialysis

Guidelines	Haemodialysis	Peritonial dialysis
National Kidney Foundation (2000) Kidney Disease Outcomes Quality Initiative	>1.2 g/kg/day	1.2–1.3 g/kg/day
European Society for Clinical Nutrition and Metabolism (Cano et al, 2006)	1.2–1.4 g/kg/day; 1.5 g during periods of illness (high biological value of at least 50%)	1.2–1.5 g/kg/day (high biological value of at least 50%)
European Best Practice Guidelines (Fouque et al, 2007)	1.1–1.2 g/kg/day	Not applicable
American Society for Parenteral and Enteral Nutrition (Brown et al, 2010)	1.2 g/kg/day	1.3 g/kg/day
International Society of Renal Nutrition and Metabolism (Ikizler et al, 2013)	1.2 g/kg ideal body weight (IBW), with at least 50% of protein intake being of high biological value	1.2 g/kg IBW, with at least 50% of the protein intake being of high biological value
British Dietetic Association Renal Nutrition Group (Naylor et al, 2013)	1.1 g/kg/day (and no more than 1.4 g/kg of body weight (BW) per day in maintenance dialysis)	1.0–1.2 g/kg/day (and no more than 1.4 g/kg of BW per day in maintenance dialysis)
Australian systematic review (Ash et al, 2014)	1.1 g/kg IBW/day, with at least 50% of the protein intake being of high biological value	1.0–1.2 g/kg IBW/day

2011). In patients with potassium lever >6 mmol/l, a potassium intake of 50–70 mmol or 1 mmol/kg of ideal body weight is recommended (Fouque et al, 2007).

Patients with hyperkalaemia and PEW should be advised to follow a high-energy diet that continues to limit high-potassium items. Patients who are malnourished may develop low levels of potassium due to inadequate oral intake, especially if they are on automated PD. In these patients, dietary restrictions should, therefore, be relaxed to avoid hypokalaemia.

High or low potassium dialysate in patients on HD (to optimise serum potassium levels) should be discussed with the multidisciplinary team if levels are still suboptimal following dietary advice.

Other nutrients

In addition to phosphate and potassium, other nutrients (such as vitamins and trace elements) may be considered; however, the evidence on this is far from clear. Although some guidelines suggest that water-soluble vitamins should be supplemented in patients on HD, in view of the risk of deficiency with the dialysis process and a restricted diet (Fouque et al, 2007), others suggest that supplementation should be made on an individual basis. More research is needed in patients on HD (Tucker et al, 2015) and PD (Jankowska et al, 2016). In clinical practice, many centres in the UK provide all patients on HD with a water-soluble vitamin supplement.

Some guidelines suggest to limit vitamin A provision for patients on HD to 700–900 µg/day, in view of the elevated levels of retinol and retinol-binding protein in patients on HD (Fouque et al, 2007). However, a large observational study by Espe et al (2011) showed a strong association between low retinol and retinol-binding protein concentrations and sudden cardiac death and all-cause mortality in patients with diabetes on HD. This suggests that lower levels of retinol many be more harmful than higher levels in patients on HD with diabetes, but it is important to note that the low-retinol plasma concentrations in HD patients were still above the recommended retinol plasma concentrations in healthy individuals (Espe et al, 2011). In clinical practice, vitamin A levels are rarely measured (with the exception of long-term enteral and parental nutrition), and more research is needed before clear guidelines can be made.

Renal dietetic management of protein-energy wasting on dialysis

Identifying PEW in patients on dialysis is a multidisciplinary responsibility, and both the medical and nursing teams should refer at-risk patients to the renal dietitian for assessment, based on their clinical judgement with or without the support of nutritional screening tools. Renal dietitians are ideally placed to assess the causes of malnutrition and suggest strategies to improve nutritional intake. However, the treatment of PEW is complex, and is important that is not considered in isolation but incorporated in a multidisciplinary team approach. *Figure 1* summarises the treatments available for PEW.

Input from renal dietitians has been associated with an improvement in nutritional status and dietary intake in patients on HD (Campbell et al, 2009). A food first approach, with or without food fortification, should always be a key nutritional intervention to improve energy and protein intake. A 'little and often' style of eating should be recommended, along with energy-dense snacks. Fortification with butter, double cream and sugar (where appropriate) can also add extra calories. Caution should be used when recommending hard cheese, processed meat products and milk powder, however, as they can be high in potassium, phosphate and salt.

Oral nutritional supplements

Renal-specific ONS can be used as food fortification to meet a patient's energy and protein requirements without compromising electrolytes. In practice, however, patients may be able to relax dietary restrictions based on their potassium and phosphate levels. Stratton et al's (2005) systematic review found that ONS significantly improve total dietary energy and protein intake. A more recent study showed that their use was also associated with a significant reduction in hospital admission (Cheu et al, 2013). Sezer et al (2014) found that renal-specific ONS significantly improved nutritional parameters in malnourished patients with CKD, and were found to have an improved inflammatory status and reduced erythropoietin requirements when compared to a control group.

ONS should be considered in conjunction with food fortification to improve nutritional intake; however, choice of ONS must be influenced by patient preference and nutritional deficit, in addition to fluid, potassium and phosphate restrictions. It is also worth noting that many over-the-counter commercially available nutritional supplements are not always suitable for patients on dialysis due to their elevated potassium, phosphate and fluid content.

Table 3 summarises some of the products currently available in the UK. For many patients on HD, a low-volume, low-electrolyte, high-protein, high-calorie supplement may be appropriate to meet energy and protein requirements. Those on PD with good residual function may be able to use a higher volume and higher electrolyte supplement due to better clearance. High-protein supplements may also be useful when added to food for patients with PEW and a poor tolerance of supplements in larger volumes.

Ikizler et al (2013) described the substantial anabolic role of ONS, reporting studies that included regular meals during dialysis, oral supplementation taken at home or during dialysis, and oral amino acid tablets. They also showed that ONS may improve weight, lean body mass, quality of life and physical functioning. However, they added that larger studies are needed to assess the effect of oral supplements with hospitalisation rates and mortality.

Evidence has also shown that eating during dialysis can be beneficial in improving nutritional markers

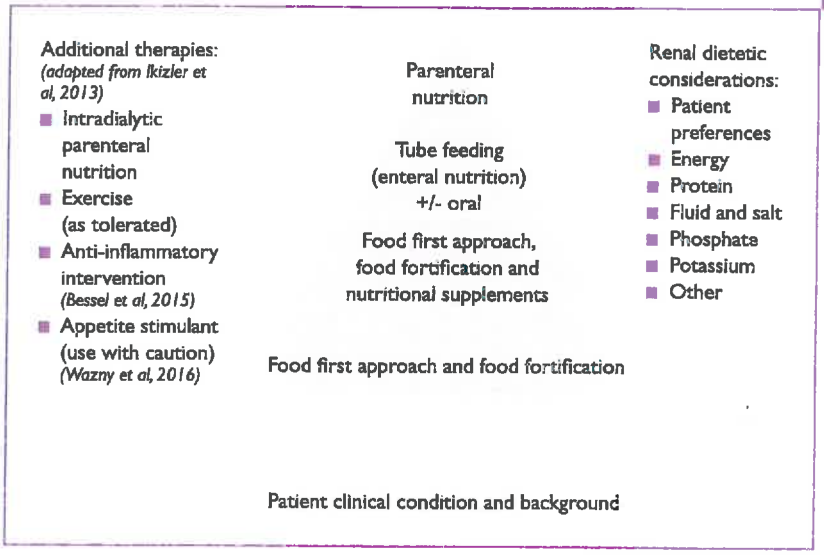

Figure 1. Dietary management scheme for protein-energy wasting

in patients with malnutrition (Caglar et al, 2002). It is also known that protein loss-induced catabolism can still be seen 6 hours after dialysis (Ikizler et al, 2002). Moreover, it has been found that the use of ONS during HD reduces mortality (Lacson et al, 2012; Weiner et al, 2014). Interestingly, these studies did not take into account renal dietetic input, patient level of motivation and oral intake while not on dialysis; the question remains if ordinary food provision could have the same effect as an ONS (Wright et al, 2012).

In addition to food fortification and ONS, other strategies (such as enteral feeding and intradialytic parenteral nutrition) may be used with patients with PEW (Ikizler et al, 2013).

The Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines for nutrition in CKD are due to be published later this year and will offer a deeper review of renal dietary recommendations for this patient group (ISRNM, 2017).

Conclusion

Each member of the multidisciplinary team has a responsibility for the prevention, identification, assessment, management and monitoring of PEW in patients on dialysis. ONS that are high in calories and protein, and lower in electrolytes and fluid, play a role in the management of these patients. Further research focusing on renal dietetic advice and ONS intervention linked with clinical outcomes (including nutritional, clinical, cost and patient-related outcomes) is needed to establish the efficacy of these treatment options, and their impact on mortality. **JKC**

Conflict of interest: this article was supported by Stanningley Pharma; the opinions expressed within this

Table 3. Comparison of some oral nutritional supplements

Product (company)	Presentation volume (ml or g)	Energy (kcal)	Protein (g)	Potassium (mmol)	Phosphorus (mmol)
Calogen Extra (Nutricia)	120 ml	480	6.0	16.5	7.80
Complan (Nutricia)	57 g (made with 200 ml full-fat milk)	380	15.5	18.0	15.00
Ensure Compact (Abbott)	125 ml	300	13.0	6.9	6.90
Foodlink Complete (Nualtra)	57 g (made with 200 ml full-fat milk)	386	18.3	22.0	17.10
Forticreme Complete (Nutricia)	125 g	200	11.9	5.7	4.50
Fortijuce (Nutricia)	200 ml	300	7.8	0.5	0.80
Fortisip Compact Protein (Nutricia)	125 ml	300	18.0	3.4	12.10
Fresubin Protein Energy Drink (Fresenius)	200 ml	300	20.0	6.6	7.80
Nephro HP (Abbott)	220 ml	396	17.8	5.9	5.10
ProSource Plus Liquid (Nutrinovo)	30 ml	100	15.0	0.3	3.96
Protifar (Nutricia)	2.5 g (1 scoop)	9	2.2	0.1	0.60
Renapro Powder (Stanningley Pharma)	20 g	74	18.0	0.4	0.30
Renapro Shot (Stanningley Pharma)	60 ml	82	20.0	0.3	0.03
Renilon 7.5 (Nutricia)	125 ml	250	9.4	0.7	0.10

Note: nutritional values will slightly vary depending on flavour

article are those of the authors, who do not recommend any specific nutritional products.

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Key points

- Nutritional requirements in dialysis have remained unchanged over the past 20 years
- Protein-energy wasting is linked to an increased in mortality and morbidity in patients on dialysis
- Patients on dialysis who require nutritional support require a renal dietitian assessment and close monitoring of their nutritional status
- There is a need to report and share nutrition-related objective outcome measures to establish the effectiveness of existing strategies in this area

CPD reflective questions

- What are the key nutritional parameters to identifying and monitoring protein-energy wasting?
- What are the main differences between the nutritional requirements of patients on haemodialysis compared to patients on peritoneal dialysis?
- When considering oral nutritional supplements, what dietetic consideration should the member of the multidisciplinary team take into account?

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