

Management of Protein and Energy Intake in Dialysis Patients

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Abstract. Malnutrition is not uncommon in patients with end-stage renal disease treated with maintenance dialysis. The presence of several abnormal parameters of nutritional status are reported to be predictive of poorer outcomes in these patients, compared to dialysis patients without evidence of

malnutrition. This article describes methods that may be used to recognize the presence of malnutrition in end-stage renal disease patients and the management of protein and energy intake. Whether the correction of malnutrition will improve outcomes, such as morbidity and mortality, is unknown.

Malnutrition is a serious concern in patients with end-stage renal disease (ESRD) who are treated with maintenance dialysis. The reason for concern is the association between evidence for malnutrition and poor patient outcome. Reduced serum concentrations of albumin, creatinine, and cholesterol have been associated with an increased relative risk of death in maintenance hemodialysis patients (1). Reduced serum albumin, prealbumin, creatinine, and cholesterol at the commencement of dialysis treatment may be predictive of reduced survival in either hemodialysis patients or, with the exception of serum cholesterol, peritoneal dialysis patients (2,3). These findings have increased awareness of the importance of nutrition in people treated with maintenance dialysis.

Causes of Malnutrition

Malnutrition is not uncommon in dialysis patients and the causes are numerous. The dialysis procedure itself results in losses of nutrients into dialysate and, independent of these losses of nutrients, appears to result in an increase in catabolism during hemodialysis (4–6). Lim and coworkers concluded that, overall, the hemodialysis treatment was a catabolic event because of amino acid losses into dialysate and decreased protein synthesis during treatment (5). The presence of metabolic acidosis, which is common in patients with ESRD, may also be associated with increased catabolism in these patients (7).

Amino acids are lost into dialysate (8), and, with high flux dialyzers, protein losses are also increased (9). Losses of vitamins into dialysate also occurs (10). Symptoms of uremia include anorexia, nausea, and vomiting, and these symptoms are not always well controlled in maintenance dialysis patients, leading to reduced dietary protein and energy intake. Falken-

hagen and coworkers demonstrated that maintenance hemodialysis patients who self-selected their diets were in danger of developing protein-calorie malnutrition (11). Patients with ESRD treated with either hemodialysis or peritoneal dialysis demonstrate altered patterns of food intake (12). The cause of reduced appetite is not entirely understood, but elevated serum leptin or other factors, which suppress appetite, may be involved. All of these abnormalities can result in the development of malnutrition.

Diagnosis of Malnutrition

Unfortunately, the diagnosis of malnutrition is not straightforward. The presence of malnutrition is not recognized with a single test or an evaluation at a single time point and, therefore, it is necessary to screen patients for the presence of malnutrition with a variety of measures and to carry out this investigation on a regular basis. Also, the presence of renal disease can confound several routine measures of nutritional status. Thus, it is necessary to carry out measures of protein status and body composition, as well as measures of nutritional intake, to identify the presence of malnutrition.

Serum albumin, which is widely used to measure protein stores, may be altered by the coexistence of acute, catabolic illnesses, including underlying infection, which is common in dialysis patients. The coexistence of a chronic access infection (either peritoneal catheter or hemodialysis vascular access) or other infection may lower the serum albumin concentration due to reduced liver synthesis of albumin in response to an increase in production of acute phase reactants. Yeun and Kaysen have shown that the serum albumin concentration is predictive of both albumin losses into dialysate, as well as production of C-reactive protein, which is associated with inflammation. This demonstrates that serum albumin may not always reliably measure nutritional status (13). Despite the excellent correlation of serum albumin with mortality, at least one investigation has questioned the value of serum albumin as a marker of nutritional status in patients treated with continuous ambulatory peritoneal dialysis (CAPD) (14).

Serum prealbumin also is predictive of outcome in patients at the commencement of dialysis treatment (15), and, due to its relatively short half-life, is frequently used to determine the

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response to nutrition interventions. However, in patients with ESRD, the serum prealbumin is spuriously elevated. This is due to abnormal metabolism of the prealbumin-retinol binding protein complex (16). It is recommended that when prealbumin is used to monitor the nutritional status or the response to a nutritional intervention in the dialysis population, the goal of therapy should be a prealbumin level equal to or greater than 29 mg/dl (17). As with serum albumin, prealbumin also declines in response to an acute catabolic illness, since liver synthesis of proteins is directed to the synthesis of acute phase reactants.

In the pre-ESRD population, serum transferrin appears to be a useful measure of nutritional status; however, serum transferrin is altered in states of iron deficiency, and the common occurrence of iron deficiency associated with the use of recombinant human erythropoietin in the management of anemia in maintenance dialysis patients makes this measure less reliable (18).

It is appropriate to choose one measure of protein status and to avoid measuring a host of serum proteins. Serum albumin is clearly the most commonly used measure of protein status, correlates well with mortality, and is readily available in clinical laboratories. However, when initiating a nutritional intervention, it may be useful to use a serum protein measure with a more rapid turnover, such as serum prealbumin, and to use this measure over time to assess the patient's response to the nutritional intervention.

Measures of body composition, such as anthropometry, bioelectrical impedance analysis, dual-energy x-ray absorptiometry, and subjective global assessment, have all been reported to be useful to assess nutritional status in people with ESRD treated with maintenance dialysis. Anthropometry has been used for years in healthy subjects, as well as in people treated for ESRD with maintenance dialysis, and anthropometric reference values have been established for patients with ESRD (19).

Subjective global assessment was originally developed for use in the acute hospital setting, but is also useful as a measure of nutritional status in the CAPD population (20,21).

All of these measures of body composition have limitations. Anthropometry is subject to significant inter-operator error and may be affected by skin turgor. It is important that good quality skinfold calipers be used for skinfold measurements. Bioelectrical impedance analysis is not as useful as early reports would have indicated (22), since it is a better measure of body water than it is a measure of body composition. Dual-energy x-ray absorptiometry can differentiate fat from fat-free mass, but requires special equipment that is not always available (23). Since anthropometry is both widely available and requires only a simple instrument, it is readily applicable in most dialysis clinics, and therefore currently may be the most useful measure of body composition.

Nutritional intake should also be frequently assessed in dialysis patients. Renal dietitians are well trained to determine nutrient intake from food records, and computer programs exist that can quickly and accurately translate dietary food intake into accurate amounts of protein and energy. Dietary recall

over 1 to 3 d is commonly used, but the longer the period of recall, the more likely the patient will become bored with keeping a diary, and this may compromise the information obtained. Dietary history does not require much work on the part of the patient, but its accuracy depends on the patient's memory. The normalized protein equivalent of nitrogen appearance (nPNA) has also been used to assess dietary protein intake in stable patients who are in neutral nitrogen balance.

Nutritional status should be assessed on a regular basis in all dialysis patients, so that any decline in nutritional status can be quickly addressed. Serum proteins should be monitored monthly to every 3 mo, anthropometry should be carried out every 6 mo, and food intake from dietary history, food records, and nPNA should be assessed simultaneously.

Management of Malnutrition

Once malnutrition occurs, patient outcomes may decline. Therefore, prevention of malnutrition becomes very important. Patients must be prescribed adequate protein and energy to prevent the development of malnutrition. Although no studies exist to demonstrate that prevention of malnutrition will change patient outcomes such as morbidity or mortality, the clear association between poor nutritional status and increased risk of death strongly suggests that malnutrition should be avoided.

Dietary Protein Intake

Dietary protein intake has been the subject of a number of studies, as a strategy to slow the progression of ESRD, to reduce uremic symptoms, and to evaluate the appropriate dietary protein requirements of people with ESRD treated with maintenance dialysis therapy. The issues surrounding use of diet to reduce symptoms of uremia and to delay the progression of ESRD are beyond the scope of this discussion.

For an understanding of the protein requirements for people treated with maintenance dialysis, one can look at those studies carried out in metabolic units to determine the level of dietary protein intake that will result in neutral or positive nitrogen balance. Studies by Blumenkrantz *et al.* and Bergstrom *et al.* in CAPD patients demonstrate that nitrogen balance is negative with diets providing less than 1.2 g protein/kg body wt per d (24,25). This requirement is higher than that recommended for healthy subjects, which is about 0.8 g/kg per d. In hemodialysis patients, there are no randomized, prospective trials that examine dietary protein intake and outcomes. However, several studies carried out by measurement of nitrogen balance demonstrate that approximately 1.2 g/kg per d of high biologic value protein is associated with positive nitrogen balance (4,26,27).

These higher protein requirements may be due to losses of protein and amino acids into dialysate, or the catabolic effect of the hemodialysis procedure. Several studies report losses of approximately 1 to 2 g of protein into dialysate with conventional hemodialyzers, but may be higher with high-flux dialyzers (9). Losses of amino acids into hemodialysate average 6 to 12 g per treatment (8). Losses of proteins into dialysate are higher with peritoneal dialysis compared to hemodialysis, and

are reported to be approximately 5 to 15 g/d, and protein losses increase with episodes of peritonitis (28). These data lead to the recommendation that dietary protein intake for patients treated with peritoneal dialysis should be approximately 1.3 g protein/kg body wt per d, to be certain that all patients receive adequate protein intake (24–26).

Energy Intake

Energy intake is also critical in dialysis patients. Several studies have demonstrated that the energy requirement in these patients is not different from that of healthy subjects. Therefore, it is important that energy intake be maintained at normal levels in dialysis patients. The recommended daily energy intake for dialysis patients is 35 kcal/kg body wt per d (28). It should be noted that patients treated with peritoneal dialysis absorb calories from the glucose in the dialysis fluid and this should be included in the calculation of dietary energy intake. Approximately 90% of the glucose is absorbed during dwells over 8 h, and about 70% is absorbed during shorter dwells; therefore, one can easily calculate the amount of carbohydrate absorbed in each exchange. For example, if the dialysis fluid has a dextrose concentration of 2.5%, then a 2-L bag contains 25 g/L or 50 g of dextrose for each exchange. If 70% is absorbed, then $0.7 \times 50 = 35$ g of dextrose is absorbed. Because dextrose has a caloric value of 3.4 kcal/g, $35 \text{ g} \times 3.4 \text{ kcal/g} = 119$ kcal is absorbed from each 2-L bag of 2.5% dextrose dialysis fluid. More precise information regarding the absorption of dextrose from dialysate for an individual patient can be derived from the peritoneal equilibration test data.

If patients are unable to consume the required protein and energy intake from the diet, more aggressive measures should be undertaken to ensure adequate intake. These measures may include the addition of dietary protein and energy supplements. Dietary supplements have the advantage of being fairly inexpensive and simple to administer. Several of the available supplements have been formulated specifically for dialysis patients. It is recommended that supplements that are calorie dense and low in phosphorous be selected for use. A large retrospective analysis of dietary supplements in dialysis patients demonstrated that their use was associated with an increased serum albumin level in those patients with a low serum albumin, as well as increases in body weight and anthropometric measures (29). However, despite these results, many patients are not compliant with the use of supplements. This may be because in the United States, the cost of such supplements is borne by the patient, or because they may be unpalatable or monotonous. It is important that patients be carefully monitored for compliance when supplements are prescribed. In addition, patients must be instructed not to use supplements to replace meals.

If oral supplements cannot be tolerated, tube feedings should be considered. Use of tube feeding is widely accepted in pediatric patients, but is rarely used in adults. Perhaps nephrologists believe that adults with poor dietary intake will refuse tube feedings, but in practice, tube feedings can be very effective in improving nutritional status in malnourished patients (30). In patients undergoing maintenance hemodialysis, the

calories and amino acids can be administered into the venous drip chamber of the dialysis tubing during the dialysis procedure. This has the advantage of ensuring compliance, and the infused fluid can be removed during the dialysis procedure. Two retrospective studies have demonstrated improved survival from this procedure (31,32). One randomized, prospective study has demonstrated an improvement in nutritional status when a mixture of amino acids and lipids was infused during each hemodialysis procedure for a period of 3 mo (33). However, other studies have failed to demonstrate improvement in nutritional status when these solutions are administered (34). This may be due to the fact that many patients studied did not demonstrate malnutrition, or that the period of study was too short.

Amino acids can also be infused into the peritoneum during the peritoneal dialysis procedure. In two studies that used a mixture of essential and nonessential amino acids in place of dextrose as the osmotic agent, nitrogen balance became more positive and those patients with evidence of malnutrition demonstrated improvement in nutritional status (35,36).

In summary, malnutrition has serious consequences for patients with ESRD treated with maintenance dialysis and should be managed vigorously. As a first step, it is important to recognize the presence of malnutrition. This requires a nutritional assessment on an ongoing basis, as described above.

Although a large body of data exists to demonstrate that increasing intake will improve measures of nutrition status, no studies exist to determine whether provision of additional protein and calories to reach target recommendations will change the outcomes of mortality and morbidity. No randomized, prospective, controlled trials have been carried out to examine this question. Such trials would be very costly and take years to complete. However, the benefits of an adequate diet would seem to outweigh the potential risks of overfeeding. The main risk of increasing protein and calorie intake may be the need for an increase in the dialysis dose or an increase in the dose of phosphate binder therapy. This does not seem to offer any substantially increased risks or costs. It is therefore recommended that every effort be made to ensure that patients consume an adequate diet. This may require a relaxation of some of the usual dietary restrictions. It also requires an effort by the dietitian to help patients understand the requirements and remain sensitive to patients' ethnic food habits. These efforts should result in well-nourished and well-dialyzed patients, as well as improved patient outcomes.

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