NUTRITION IN DIABETIC PATIENTS UNDERGOING CONTINUOUS AMBULATORY PERITONEAL DIALYSIS

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In the pre-dialysis stage, the nutritional management of diabetic patients with chronic renal failure involves mainly caloric and protein intake and control of blood sugar. These aspects are very important because severity of hyperglycemia is correlated with the rate of progression of chronic renal failure, while strict glycemic control can markedly diminish the likelihood of nephropathy and retinopathy in patients with insulin-dependent diabetes (IDDM, type I) (1). Good glycemic control before starting dialysis has been shown to be an independent predictor of survival in patients with non-insulin-dependent diabetes (NIDDM, type II) on continuous ambulatory peritoneal dialysis (CAPD); on the other hand, patients with poor glycemic control before dialysis have increased morbidity and shortened survival (2).

Regarding protein restriction that may delay the progression of renal disease (3), one should avoid overzealous restriction, which would lead to protein malnutrition that may negatively affect outcome during subsequent dialysis. Adequate protein intake is important in end-stage renal disease (ESRD) in diabetic patients treated with either chronic hemodialysis or peritoneal dialysis, because mortality increases in a dose-dependent fashion with the degree of protein malnutrition.

Protein-caloric malnutrition is a major complication of CAPD. An international cross-sectional study of 224 CAPD patients showed that 33% had mild malnutrition and 8% had severe malnutrition (4). In this study, female patients and diabetic patients were malnourished more frequently than male patients and non diabetic patients. Old age, long duration of CAPD, and minimal or absent residual renal function were factors predisposing to severe malnutrition.

Deterioration of nutritional status in CAPD patients commonly begins before the initiation of peritoneal dialysis. The deterioration is mainly due to uremia, anorexia, low-protein diet, underlying disease (such as diabetes mellitus), and the variety of drugs used during the period. Serum albumin, a nutritional indicator, has been observed not to change during dialysis and therefore its predictive meaning for survival seems to be related to the patient's pre-dialysis nutritional status and not to dialysis-induced malnutrition (5).

Because earlier data for patients on CAPD suggested a higher incidence of mild to moderate malnutrition in diabetic patients than in non diabetic patients (6-10), which may account for the former group's worse clinical outcome, this paper will review the various aspects of nutrition/malnutrition in CAPD diabetic patients.

ASSESSMENT OF NUTRITIONAL STATUS

Several studies have established that the subjective global assessment (SGA) (11) accurately reflects nutritional status in dialysis patients. Variables that correlated most frequently with SGA and with one another included plasma albumin, middle arm muscle circumference (MAMC), weight loss, and clinical assessment of muscle wasting and loss of subcutaneous fat. Loss of residual renal function and months on CAPD also correlated with muscle wasting (6).

An index of daily protein intake (DPI) is the protein equivalent of nitrogen appearance (PNA), which can be estimated by urea kinetic modeling from urea and amino acid losses in the dialysate and urine (16,17).
Recently, the Dialysis Outcomes Quality Initiative (DOQI) guidelines for dialysis adequacy (18) recommended that nutritional status of adult PD patients should be assessed on an ongoing basis using PNA and SGA in association with dialysis dose measurements [Kt/Vurea] and weekly creatinine clearance (WCC).

NUTRITIONAL STATUS IN CAPD DIABETIC PATIENTS

**Factors Affecting Nutrition:** Although there is some evidence of increased net anabolism during the first year of CAPD, with weight gain, improvement in anthropometric parameters, and a rise in plasma proteins, prospective studies of total body nitrogen showed a gradual deterioration in nutritional status. Approximately 18%-56% of CAPD patients show anthropometric and biochemical evidence of protein/energy malnutrition (19), while its prevalence is higher in diabetic patients than in non diabetic patients (6-10). This effect may be due to several dialysis-related factors as well as to other chronic complications present in this illness.

Diabetes mellitus itself does not seem to be a risk factor for increased malnutrition in patients undergoing maintenance hemodialysis (20). However, diabetic patients often begin dialysis already malnourished (21), probably because their energy intake is commonly below the recommended daily allowance. In addition, this situation can be aggravated on CAPD by the greater protein peritoneal losses that are present in diabetic patients than in non diabetic patients (22).

Young et al (6) reported a higher incidence of mild to moderate malnutrition in diabetic patients than in non diabetic patients, but found no differences between the diabetic and non diabetic patients in the severely malnourished group. It has been suggested that the smaller number of diabetic patients who progress to severe malnutrition may reflect the lower survival rates for these patients (23) or a tendency for diabetic patients undergoing CAPD to retain greater residual function (24).

The most important cause of inadequate nutrition in many CAPD patients is underdialysis, which can lead to anorexia and poor protein intake. However, even in the well-dialyzed patient, other factors (reviewed below) may lead to a concurrent decrease in protein and calorie intake and therefore to the development of malnutrition (Table 1 and Table 2).

**Peritoneal Dialysis Adequacy, Nutritional Status, and Clinical Outcome:** The statistical relationship between normalized dietary protein intake (nPNA) and small-solute clearance (Kt/V) provides indirect evidence of the link between peritoneal dialysis adequacy and nutritional status (25-26) and suggests that an increase in the dialysis dose (Kt/V) may increase dietary protein intake (nPNA) by increasing appetite (27-29).

The relationship between malnutrition and increased morbidity and mortality is not necessarily a causal one. A number of comorbid conditions, frequently present in diabetic CAPD patients, such as vascular complications, severe cardiovascular disease, gastrointestinal and liver diseases, and other systemic diseases, are accompanied by malnutrition and have

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**TABLE 1**

Etiology of Malnutrition in Diabetic Continuous Ambulatory Peritoneal Dialysis Patients

<table>
<thead>
<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>Underdialysis</td>
</tr>
<tr>
<td>Anorexia</td>
</tr>
<tr>
<td>Gastroparesis</td>
</tr>
<tr>
<td>Hyperglycemia — Poor glycemic control</td>
</tr>
<tr>
<td>Dialysate protein losses</td>
</tr>
<tr>
<td>Inadequate diet (protein) and energy supply</td>
</tr>
<tr>
<td>Recurrent peritonitis</td>
</tr>
<tr>
<td>Residual renal function decline</td>
</tr>
</tbody>
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**TABLE 2**

Factors Affecting Nutrition in Diabetic Continuous Ambulatory Peritoneal Dialysis Patients

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
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<tbody>
<tr>
<td>Effects of uremia — Inadequate dose of dialysis</td>
</tr>
<tr>
<td>Anorexia</td>
</tr>
<tr>
<td>Glucose intolerance</td>
</tr>
<tr>
<td>Hyperinsulinemia</td>
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<tr>
<td>Reduced peripheral sensitivity to insulin</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
</tr>
<tr>
<td>Effects of the peritoneal dialysis procedure</td>
</tr>
<tr>
<td>Abdominal discomfort — Fullness feeling</td>
</tr>
<tr>
<td>Slow gastric emptying</td>
</tr>
<tr>
<td>Absorption of glucose from the dialysate</td>
</tr>
<tr>
<td>Continuous energy supply</td>
</tr>
<tr>
<td>Anorexia</td>
</tr>
<tr>
<td>Protein and amino acid losses</td>
</tr>
<tr>
<td>Hyperinsulinemia</td>
</tr>
<tr>
<td>Hyperdyslipoproteinemia</td>
</tr>
<tr>
<td>Peritonitis</td>
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<tr>
<td>Residual renal function decline</td>
</tr>
<tr>
<td>Effects of diabetes mellitus</td>
</tr>
<tr>
<td>Autonomic nervous disturbances</td>
</tr>
<tr>
<td>Gastroparesis</td>
</tr>
<tr>
<td>Hyperglycemia — Poor glycemic control</td>
</tr>
<tr>
<td>Amino acid alterations?</td>
</tr>
<tr>
<td>Formation of abnormal glycosylated proteins?</td>
</tr>
<tr>
<td>Toxic effects on peritoneum?</td>
</tr>
<tr>
<td>General factors</td>
</tr>
<tr>
<td>Unpalatable or inadequate diet</td>
</tr>
<tr>
<td>Inadequate energy supply</td>
</tr>
<tr>
<td>Inflammation, infection, sepsis</td>
</tr>
<tr>
<td>Medications</td>
</tr>
<tr>
<td>Psychosocial and socioeconomic factors — Anorexia</td>
</tr>
<tr>
<td>inability of adequate diet intake</td>
</tr>
</tbody>
</table>
an unfavorable prognosis. In such patients, malnutrition is a maker of illness, but not the direct cause of death. Thus, according to the United States Renal Data System (USRDS) 1997 report (30), among dialysis patients, diabetic patients have substantially higher adjusted death rates owing to acute myocardial infarction, cardiac arrest, other cardiac causes, septicemia, cerebrovascular disease, and hyperkalemia than non diabetic patients. Cachexia is a rare cause of death (3.1% in patients aged over 64 years, 2% in diabetic patients, and 1.7% in non diabetic patients). Malnutrition is not listed among the causes of death even though it may have contributed to the high death rate (23.8% of diabetic ESRD patients versus 14.1% of non diabetic ESRD patients). Also, malnutrition and failure to thrive may have contributed to withdrawal of dialysis or to death from unknown causes (19).

Anorexia: Underdialysis, metabolic acidosis, hyperglycemia, the feeling of fullness owing to the presence of dialysate in the abdomen, and loss of residual renal function may contribute to anorexia in CAPD patients. The presence of dialysate in the abdomen may cause a full feeling that may decrease appetite and slow gastric emptying. This effect is more prominent in diabetic patients who also suffer from gastroparesis. Such patients should empty the abdomen just before meals. In addition, these patients may better tolerate small, frequent meals.

Gastroparesis: Gastroparesis, which is common in diabetic patients, may affect as many as 20% to 30% of those with end-stage renal disease (31) and may contribute to decreased food intake by delaying gastric emptying.

Eisenberg et al (32), who investigated clinical and laboratory features and risk factors for diabetic gastroparesis (DGP) in 226 diabetic patients on chronic dialysis, found that 106 patients (43%) had DGP, diagnosed by persistent vomiting that improved with the use of prokinetic agents. Type I diabetic patients had DGP more frequently than type II diabetic patients (70% versus 37%), while logistic regression analysis identified long duration of diabetes and poor glycemic control as risk factors for this complication. Moreover, DGP was associated with high frequency of other diabetic complications, low serum albumin and creatinine, and high morbidity and mortality.

When gastroparesis is suspected from the history, the rate of gastric emptying can be accurately assessed by radionuclide solid-phase gastric emptying scans (33). Diabetic gastroparesis has been successfully treated with erythromycin (34) or newer prokinetic medications, such as cisapride (35). One may choose the optimal therapeutic agent based upon its effectiveness in improving the scanning results after intravenous administration. The gastric emptying response to intravenous doses of metoclopramide (5 mg) and to erythromycin elixir by mouth (200 mg) was assessed in 5 CAPD non diabetic patients with hyperalbuminemia and occult gastroparesis (36). In peritoneal administration of metoclopramide (5 10 mg per 2 L bag of dialysate) or erythromycin (100 mg per 2 L bag of dialysate) was also successful in relieving symptoms (37).

Severe hiccups have also been reported as an unusual cause of malnutrition with a particularly bad prognosis (38), although they may improve after an increase in the dialysis dose.

Hyperglycemia -Glucose Absorption: Although CAPD patients generally have fewer dietary restrictions than those treated with hemodialysis, the frequent use of hypertonic peritoneal dialysis fluids may lead to an increase in glucose absorption, which can aggravate the effect of poorly controlled glycemia. Thus, excessive glucose absorption can lead to higher hyperglycemia, which can directly suppress appetite (39,40).

Tzamaloukas et al (41) found that the frequency of hypoglycemia was higher during HD than during CAPD, whereas the frequencies of hyperglycemia and euglycemia did not differ between the two modalities. Furthermore, hypoglycemia was severe during HD and was associated with two deaths, while no deaths were linked to abnormalities in blood glucose concentration during CAPD.

Dialysate Protein Losses, Peritoneal Permeability and Amino-Acid Solutions: Daily protein and amino acid losses in peritoneal effluent are important factors in malnutrition of CAPD patients. Peritoneal protein losses vary, with large inter-individual differences (3 -20 g/24 h). During peritonitis, protein losses increase considerably -by about 50% to 100% -for several weeks. Also, the reported average dialysate losses of free amino acids during CAPD vary between 1.2 g/24 h and 3.4 g/24 h, of which 30% are essential amino acids (EM). Such losses can be replaced easily by increased protein intake.

Increased peritoneal protein losses over time have been observed more frequently in diabetic patients than in non diabetic patients (22,42), although some workers report no difference between the two groups of CAPD patients at any given time of the treatment (43).

Harty et al (44), who examined the relationship between peritoneal permeability, protein loss, and nutritional status, found that DIP creatinine is the only significant predictor of serum albumin that is independent of PD protein loss. They could demonstrate no significant relationship between DIP creatinine and body fat, lean muscle mass, and dietary protein intake. Besides, Nolph et al (45) found that high peritoneal transporters had significantly lower
mean serum albumin, net npNA, lean body mass calculated from creatinine kinetics, and daily creatinine production, and higher albumin clearances compared to lower transport groups. They therefore hypothesized that the higher transporters among CAPD patients are prone to protein malnutrition related to increased dialysate protein losses, and perhaps suppression of appetite, with increased use of hypertonic exchanges. Also, it has been reported (46) that a high peritoneal equilibration rate (PER) is a powerful and independent predictor of clinical morbidity, which paradoxically predicts a poor clinical outcome, owing to increased loss of protein in the dialysate, poor ultrafiltration, and appetite suppression secondary to increased glucose absorption.

However, peritoneal clearance and peritoneal ultrafiltration characteristics are similar between diabetic patients and non diabetic patients on CAPD (9). Diabetic patients have a higher D/P creatinine ratio than non diabetic patients at the beginning of CAPD (1-3 months); while, after 7 months, glucose and creatinine transport rates were lower in diabetic patients (47). Comparing normoglycemic with hyperglycemic diabetic patients, normoglycemic patients have a higher creatinine clearance and an increased net ultrafiltration (47). Therefore, because diabetes has no particular effect on peritoneal solute transport rates, it may be postulated that protein intake, underdialysis, and other CAPD-related factors are responsible for the more frequent development of malnutrition in diabetic CAPD patients (6-10).

Protein and Energy Requirements in CAPD: Protein requirements in CAPD patients appear to be increased as compared to normal individuals, in whom about 0.75 g/kg body weight per day is the safe requirement for nitrogen equilibrium or positive nitrogen balance (48). For CAPD patients, a daily dietary protein intake of 1.2 g/kg body weight is generally recommended, while intercurrent illness and peritonitis will increase this requirement to 1.5 g/kg body weight. However, in most CAPD patients, protein intake is considerably lower than 1.2 g/kg body weight per day, and this lower intake has been associated with signs of protein malnutrition. In such patients, the reduced nutritional intake seems to be due to anorexia, probably because of underdialysis.

In CAPD patients, the nitrogen balance is strongly correlated with total energy intake (49) and, if the diet was prescribed or designed specifically for a protein intake < 0.8 g/kg/day, caloric intake should exceed 35 kcal/kg/day. However, despite the increased glucose uptake, total energy intake is below 35 kcal/kg body weight per day in many CAPD patients (8,49,50), which may contribute to poor utilization of dietary protein. Therefore, caloric intake must be controlled and adjusted to produce a neutral nitrogen balance if the patient’s body weight equals ideal body weight.

Recurrent Peritonitis: No good evidence exists about the catabolic effect of peritonitis on malnutrition in CAPD diabetic patients. Peritonitis rates do not differ substantially between diabetic patients and non diabetic patients. However, diabetes appears to be associated with higher incidences of tunnel infections (9).

Residual Renal Function: In an international cross-sectional study of 224 CAPD patients, the majority of those who had severe malnutrition (94%) had no residual renal function (RRF). Though patients with no RRF received more dialysis, compared with well-nourished patients who had RRF, the increased dialysis dose was not enough to compensate completely for loss of RRF (4). It is of particular interest that CAPD is associated with better preservation of renal function in diabetic patients than is hemodialysis (9).

MANAGEMENT OF MALNOURISHED CAPD DIABETIC PATIENTS

In the presence of malnutrition, the physician and dietitian should work with the patient and the family to identify preferred foods; in the presence of severe malnutrition, most or all dietary limitations may have to be removed for a short time. The primary goals of nutritional support in diabetic patients are to supply adequate energy, protein, and micro nutrients (vitamins, minerals, and electrolytes) and to provide an adequate dialysis dose.

Provide Adequate Nutrients and Protein Intake: Daily protein intake should exceed 1.2 g/kg body weight including at least 60% high biologic value (HBV) proteins. This requirement should increase to 1.5 g/kg body weight per day in the presence of intercurrent illness and peritonitis. Carbohydrates should be primary complex polysaccharides, providing approximately 35% to 40% of the daily ingested caloric intake: lipids should provide the rest of the calorie requirements with a polyunsaturated/saturated fatty acid ratio of 1.5:1.0 (Table 3).

If attention to the preceding symptoms and signs does not improve appetite and food intake, and patients are not able to achieve the prescribed protein intake, oral (enteral), parenteral, or peritoneal nutritional supplementation with essential amino acids (EMs) is necessary. EM-supplemented diets have many positive effects, including improvement in metabolic state, nitrogen-sparing effect, decrease in proteinuria and in serum parathyroid hormone (PTH) levels, and improvement in the wellbeing of patients (51). However no evidence exists that EM supplementation is able to improve nutritional status, and conflicting results have been obtained on the effects.
of oral supplementation with EM or the value of peritoneal dialysis solutions enriched with EM. Also, compliance with such supplementary diets may be poor owing to high cost, the need for careful dietary education, and decreasing family support with time.

In patients with severe anorexia who are unable to increase their oral intake, a short course of overnight supplementation via nasogastric feeding tube can improve nutritional status and overall wellbeing. Parenteral nutrition should be employed only if nourishment through the intestinal tract is not safe and practical.

Amino acid-based peritoneal dialysis solutions may provide suitable supplementation for inadequate dietary protein intake, and may lead to an improvement in nutritional status in CAPD patients (19,52). Although concern exists that using amino acids will raise urea nitrogen appearance rate and also may lead to metabolic acidosis, malnourished patients who do not tolerate oral supplements are likely to benefit from amino acid solutions.

Provide Adequate Energy Supply: Anabolism requires adequate caloric intake. Such intake must be adjusted to produce a neutral nitrogen balance if the patient’s body weight equals ideal body weight. In patients treated with continuous peritoneal dialysis, glucose absorption from the dialysate provides about 800 kcal per day, (5 20 kcal/kgbodyweight per day) and this value must be considered in calculations of total caloric requirements.

Some ESRD patients may be in a state of persistent increased catabolism caused by chronic metabolic acidosis, while resistance to anabolic factors such as growth hormone, insulin, and insulin-like growth factor 1 has also occurred (53). Preliminary studies suggest that administration of recombinant human growth hormone can reduce wasting and catabolism, improve nitrogen balance, and lower the BUN in hemodialysis patients (54,55).

Provide Adequate Dialysis Dose: For continuous ambulatory or cycling peritoneal dialysis, weekly Kt/V of≥ 2.0 (or ≥ 2.2 for intermittent peritoneal dialysis) and creatinine clearance of > 60 L/week per 1.73 m2 (or 66 L for intermittent peritoneal dialysis) are the minimal recommended target doses (18). In patients with no evidence of malnutrition and a dialysis dose below target values, a higher dose should be prescribed in the presence oflower-than-expected values for plasma albumin concentration, nPNA, or lean body mass. Generally, any patient with a low plasma albumin concentration should be closely evaluated for the possibility of underlying malnutrition, particularly if the albumin level, PNA, or lean body mass is declining. Also, patients who lose residual renal function should be monitored carefully, because underdialysis may develop gradually.

REFERENCES


