A Patient with CKD and Poor Nutritional Status

T. Alp Ikizler

Summary

Protein energy wasting is common in patients with CKD and ESRD and is associated with adverse clinical outcomes, such as increased rates of hospitalization and death, in these patients. A multitude of factors can affect the nutritional and metabolic status of patients with CKD, including decreased dietary nutrient intake, catabolic effects of renal replacement therapy, systemic inflammation, metabolic and hormonal derangements, and comorbid conditions (such as diabetes and depression). Unique aspects of CKD also confound reliable assessment of nutritional status, further complicating management of this comorbid condition. In patients in whom preventive measures and oral dietary intake from regular meals cannot help them maintain adequate nutritional status, nutritional supplementation, administered orally, enterally, or parenterally, is effective in replenishing protein and energy stores. The advantages of oral nutritional supplements include proven efficacy, safety, and compliance. Anabolic steroids and exercise, with nutritional supplementation or alone, improve protein stores and represent potential additional approaches for the treatment of PEW. There are several emerging novel therapies, such as appetite stimulants, anti-inflammatory interventions, and anabolic agents.

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Department of Medicine, Division of Nephrology, Vanderbilt University School of Medicine, Nashville, Tennessee

Correspondence: Dr. T. Alp Ikizler, Division of Nephrology, Vanderbilt University Medical Center, 1161 21st Avenue South, S-3223 Medical Center North, Nashville, TN 37232-2372. alp.ikizler@vanderbilt.edu

Case Presentation

First Encounter

A 74-year-old woman was admitted to the hospital with nausea and vomiting for several weeks, which she had attributed to a gastrointestinal viral disease. She reported no fever, chills, diarrhea, or abdominal pain. She was known to have had CKD for >10 years, attributed to diabetic kidney disease. Her kidney function has been deteriorating slowly over the past few years. For the past few months, she reported poor appetite, some taste changes, sleepiness, and decreased physical activity. She had lost 7 kg in the last 6 months. She had become less able to care for herself and was having difficulty maintaining her regular activities.

In addition to type 2 diabetes mellitus for 15 years and CKD, she has hypertension, hypercholesterolemia, and osteoarthritis. She is retired. Her husband died 9 months ago. Her son and grandchildren visit once a month. Medications include metoprolol tartrate, lisinopril, furosemide, atorvastatin, sodium bicarbonate tablets, calcitriol, and glyburide.

Physical examination on admission showed weight of 68.5 kg, body mass index of 28.5 kg/m^2, BP of 115/65 mmHg, and heart rate of 65 beats/min. She was in no apparent distress. There was mild to moderate muscle and fat wasting. Her skin and mucous membranes were dry. Lungs were clear and her cardiac examination was unremarkable. Her abdomen was soft and nondistended. She had 1+ edema of the feet and ankles. Neurologic examination was unremarkable. Her admission laboratory findings are depicted in Table 1, showing that her serum creatinine had risen compared with 6 months earlier.

During this hospitalization, she was treated with intravenous fluids and her kidney function improved. Diabetic gastroparesis was diagnosed, and she began receiving metoclopramide. She was evaluated by a dietitian, with the dietary assessment revealing daily intake of 1200 kcal, 40 g (0.6 g/kg) protein, 80 mmol potassium, and 800 mg phosphorus. She was discharged home in stable condition with appointments to see her primary care physician in 2 weeks and a nephrologist in 1 month. She missed both appointments because she could not get to their offices.

Second Encounter

Four months after discharge, the patient was brought to the emergency department with failure to thrive and shortness of breath on exertion. Her laboratory findings are listed in Table 1. On the basis of her clinical presentation and laboratory findings, she was initiated on maintenance hemodialysis (HD) *via* a newly placed cuffed HD catheter. She was discharged home after three HD sessions and was referred to a dialysis clinic for continuation of her outpatient maintenance HD.

Third Encounter

The patient was again admitted to the hospital 5 months after starting maintenance HD with low-grade fever and chills. She stated that she did not tolerate meals well (usually less than half consumed) and had a very poor appetite. She felt sick toward the end of her HD treatments, usually after the third hour, and often signed off early because of cramps. Her dialysis prescription was 4 hours with a biocompatible high-flux membrane, 350 ml/min blood flow,

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Table 1. Selected laboratory values for different encounters with the patient

Variable	6 mo before First Encounter	First Encounter	Discharge	Second Encounter	Third Encounter
TCO_2 (mEq/L)	24	21	24	17	24
BUN (mg/dl)	36	52	36	42	24
Creatinine (mg/dl)	2.5	3.6	3.1	4.7	4.5
Glucose (mg/dl)	145	265	135	185	165
Albumin (g/dl)	3.4	3.2	3.3	3.1	2.9
Calcium (mg/dl)	8.2	8.4	9.1	8.6	9.3
Phosphorus (mg/dl)	4.0	5.2	4.2	5.1	5.3
Hemoglobin A1c	9.2	9.4	ND	ND	ND
Urine spot ACR	3.5	2.4	ND	2.0	ND
Hemoglobin (g/dl)	11.2	11.8	10.8	9.8	9.4
Estimated GFR (ml/min per 1.73 m^2)	19	12	15	9	ND

tCO_2, total serum bicarbonate; ND, not done; ACR, albumin-to-creatinine ratio.

800 ml/min dialysate flow, and Kt/V of 1.6. She was dialyzed with ultrapure dialysate and 2 mEq/L potassium and 2.5 mg/dl calcium dialysate concentrations. She continued to be dialyzed through the dialysis catheter. An arteriovenous fistula (AVF) of the upper left arm had been created 3 months earlier but was not being used. Her urine output had dropped to less than 200 ml/d.

Her physical exam on admission revealed weight of 59 kg, body mass index of 24.6 kg/m^2, BP of 110/60 mmHg, and heart rate of 95 beats/min. Her skin and mucous membranes were dry. She had decreased lung sounds at the bases bilaterally. Cardiac examination was unremarkable other than sinus tachycardia. Her abdomen was soft and nondistended. She had trace edema of the feet and ankles. A bruit was audible at the AVF site without any palpable veins. Her catheter exit site was clean. Admission laboratory findings are depicted in Table 1. Blood cultures were positive for gram-positive cocci in clusters. The HD catheter was removed and she was started on intravenous antibiotics. She became afebrile and a new cuffed HD catheter was placed. She was discharged to a skilled nursing facility.

Case Discussion

This case illustrates a common scenario in which a patient with CKD progressed to ESRD, was initiated on maintenance HD, and endured several complications during this transition and the initial 6 months of ESRD, including a subtle but clinically important progressive deterioration of her nutritional status. CKD leads to a state of metabolic and nutritional derangements, more aptly called protein energy wasting (PEW) (1,2). PEW is closely associated with major adverse clinical outcomes, such as increased rates of hospitalization and death, in patients with ESRD (3,4).

Screening and Assessment of Nutritional Status in CKD

A clinically meaningful assessment of nutritional status should be able to identify and risk-stratify patients with PEW, distinguishing the causes and consequences of both PEW and the underlying disease states, and to determine whether there is potential benefit from nutritional interventions (5). No single nutritional marker can adequately phenotype this comorbid state, and a comprehensive assessment of protein and energy nutritional status requires several different measurements (6).

Table 2 lists screening and assessment tools that can be used to identify patients at risk for or with PEW. Although several considerations must be accounted for given the unique situation of patients with CKD upon screening and assessing their nutritional status (Table 3), most of these tests are easy to perform, readily available, and inexpensive. Screening variables can be collected routinely in clinical practice by any health professional and mostly provide a trigger to conduct more extensive assessment, to confirm or establish the diagnosis and determine best course of treatment, if needed. Any of these tests is adequate to initiate a more thorough work-up. On the other hand, a thorough nutritional assessment that provides comprehensive information to make a nutritional diagnosis and aids in intervention and monitoring plan should be performed by qualified individuals, preferably trained dietitians. These tests should also be used for guiding nutritional therapies once initiated.

The illustrated case provides insight into the clinical steps that can be taken to prevent some of the nutritional complications associated with CKD. The most striking finding that indicated development of PEW in this patient is the progressive weight loss combined with a lower than expected dietary protein and calorie intake. Serum creatinine concentration, while a marker of kidney function, is also markedly influenced by muscle mass. The relatively low serum creatinine in a patient such as this with low muscle mass complicates the assessment of residual kidney function and can delay timely initiation of maintenance HD. The patient also has low serum albumin and obvious loss of subcutaneous fat tissue; even in the absence of a formal nutritional assessment, it is obvious that she has passed the risk status and has PEW, even defined by the most stringent criteria (7).

Prevention of PEW: A Cause-Specific Approach

Many factors affect nutritional and metabolic status in patients with CKD, leading to multiple adverse consequences (8). Accordingly, prevention and treatment of

Table 2. Suggested strategies to screen and assess nutritional status in advanced CKD

Variable	Threshold for Detailed Assessment/Intervention	Relevant to Case?
Screening		
Body weight	Continuous decline or <85% IBW	Yes
Dietary nutrient intake		
DEI (kcal/kg IBW/d)	<25	Yes
DPI (g/kg IBW/d)	<0.8	Yes
Serum albumin (g/dl)	<4.0	Yes
Serum creatinine	Relatively low value	Yes but subtle
MST	>2	Yes
Assessment		
Serum prealbumin (mg/dl)	<28	ND
hsCRP (mg/dl)	>10	ND
Anthropometrics	Deviation from norms	ND
SGA	B or C (moderately or severely malnourished)	ND (presumed score B or C)
MIS	>5	ND
Diagnosis (2 of the 4)		
Serum chemistry		
Albumin (g/dl)	<3.8	Yes
Prealbumin (mg/dl)	<28a	ND
Cholesterol (mg/dl)	<100	ND
Body mass		
BMI (kg/m^2)	<23	No
Weight loss	>5% over 3 mo or 10% over 6 mo	Yes
Total body fat (%)	<10	ND
Muscle mass		
Muscle wasting	>5% over 3 mo or 10% over 6 mo	ND
Reduced MAMC	>10% reduction compared with norms	ND
Creatinine appearance (g/kg IBW)	<1	ND
Dietary intake		
Low DPI (g/kg IBW per d)	<0.8	Yes
Low DEI (kcal/kg IBW per d)	<25	Yes

IBW, ideal body weight; DEI, dietary energy intake; DPI, dietary protein intake; MST, Malnutrition Screening Tool; hsCRP, high-sensitivity C-reactive protein; SGA, subjective global assessment; MIS: malnutrition inflammation score; MAMC, mid-arm muscle circumference; ND, not done.
[a]Influenced by kidney function.

PEW of CKD should involve an integrated approach to reduce protein and energy depletion, avoid further losses, and replenish already wasted stores (Figure 1). The illustrated case exemplifies several factors that can be identified and prevented before development of PEW, including but not limited to decreased dietary nutrient intake, catabolic effects of renal replacement therapy, systemic inflammation, and comorbid conditions, such as diabetes mellitus and depression.

Dietary Nutrient Intake in Patients with CKD. A frequent and important cause of PEW in patients with advanced CKD is inadequate dietary protein and energy intake relative to their needs (9,10), which is primarily due to uremic anorexia. Anorexia has long been considered the hallmark of advanced CKD. Patients with CKD spontaneously restrict their dietary protein intake often to levels <0.6 g/kg per day when estimated GFR falls to <15 ml/min (11). Anorexia in CKD may develop because of retention of uremic toxins (12), intercurrent illness and inflammation (3,13), comorbid illness that affects gastrointestinal function, depression, and poor socioeconomic situations (14,15). In clinically stable patients with stage 3–5 CKD not undergoing dialysis, daily dietary protein and energy intake of 0.6–0.8 g/kg ideal body weight and 30–35 kcal/kg ideal body weight, respectively, are sufficient to preserve protein stores (16–18). However, these levels should be increased when hypermetabolic conditions, such as acute illness and hospitalizations, occur. Another important implication of anorexia in advanced CKD is its use as an indication for initiation of maintenance dialysis. Data available from a randomized clinical trial (RCT) indicate that patient symptoms (19), including anorexia accompanied with significant weight loss, is often used as an indication for initiation of maintenance dialysis, which can be readily applicable to the present case.

Renal Replacement Therapy as a Catabolic Stimulus. Provision of an adequate dialysis dose has long been considered as a cornerstone among measures to prevent and treat PEW in maintenance dialysis patients to avoid uremic anorexia and maintain optimal dietary nutrient intake,

Table 3. Factors that affect interpretation of nutritional markers in CKD

Fluid status: altered body composition and biochemical markers
Systemic inflammation: increased (hsCRP) or decreased (albumin, prealbumin, cholesterol) acute phase protein synthesis
Proteinuria: major determinant of serum albumin levels
Residual renal function: some biochemical markers, such as prealbumin, are cleared by the kidneys

hsCRP, high-sensitivity C-reactive protein.

with a minimum dose of dialysis generally recommended (20–22). Data from RCTs in patients receiving maintenance HD (HEMO [Hemodialysis] study) (23) and peritoneal dialysis (PD; ADEMEX [ADEquacy of PD in MEXico] trial) (24) indicate that what is currently considered adequate dialysis in various guidelines is sufficient to preserve nutritional status, although the HEMO study showed that maintenance HD patients lose weight over time regardless of "adequate" dialysis dose (23). Increasing dialysis dose beyond these targets does not further improve the nutritional status. Further, most nutritional measures did not differ among patients exposed to high-flux compared with low-flux HD membranes (25). The Frequent Hemodialysis Networks trial found no appreciable difference in nutritional markers between patients randomly assigned to in-center HD six times per week versus standard in-center HD three times per week (26).

In patients with ESRD receiving maintenance dialysis, there are additional protein catabolic processes, such as the unavoidable loss of amino acids (6–8 g per HD session) and albumin into the dialysate and the inflammatory stimulus associated with the dialysis procedure or other components of ESRD (*i.e.*, HD catheters) (27). An important caveat is the need to increase dietary protein intake targets once the patient begins undergoing maintenance dialysis, especially in those who were instructed to reduce protein intake to slow progression of CKD. Accordingly, minimum daily protein and energy requirements for maintenance HD and PD patients are 1.2–1.3 g/kg ideal body weight and 30–35 kcal/kg ideal body weight, respectively. The energy intake should be adjusted according to physical activity levels. Furthermore, it is important that at least 50% of the protein intake should be of high biologic value. An important consideration regarding strategies to improve dietary protein intake in patients with ESRD is the potential increase in the intake of several potentially harmful elements, especially phosphorus (28). Dietary recommendations to improve protein intake should take into account the phosphorus content of the specific protein sources (*i.e.*, vegetarian diets tend to be low in phosphorus) and other phosphorus sources, such as additives and preservatives in processed food (29,30).

Systemic Inflammation. Inflammation is a major driving force for many uremic complications, including PEW. Systemic levels of proinflammatory cytokines are elevated in CKD and ESRD (31) and are thought to play an integral role in the muscle catabolism of patients with ESRD. For example, elevated levels of IL-6 are associated with increased muscle proteolysis, an effect that can be blocked with administration of IL-6 receptor antibodies (32). IL-1 and TNF-α cause anorexia through effects on the satiety center in the central nervous system (33).

The initial step in treatment of inflammation should be elimination of etiologic factors, such as central venous HD catheters, which is directly applicable to the present case (34). Because the dialysis procedure *per se* might stimulate the immune system, proinflammatory effects of dialysis membranes and fluids should also be taken into account. Many uremic toxins are known to be proinflammatory (35) and are inadequately removed with standard dialysis methods; alternative removal techniques, such as strategies to modify intestinal generation or absorption, may have a role in this regard (36). Appropriate management of fluid status might improve systemic inflammation in patients with ESRD because volume overload leads to immunoactivation and increased cytokine production *via* bacterial or endotoxin translocation (37).

Comorbid Conditions in CKD. Patients with CKD secondary to diabetes mellitus have a higher incidence of PEW than those without diabetes (38). The degree of insulin resistance and/or insulin deprivation seems to play the most critical role in this process (39–42). Patients with CKD also often have protein depletion because of gastrointestinal disturbances (*e.g.*, diabetic gastroparesis, nausea and vomiting, bacterial overgrowth in the gut, pancreatic insufficiency, and impaired intestinal protein absorption). Polypharmacy can worsen these gastrointestinal problems. Appropriate management of these disturbances, along with an emphasis on oral health, especially in the elderly, is critical to maintain optimal oral nutrient intake. Uncontrolled hyperparathyroidism and cardiac cachexia are associated with systemic inflammation and increased energy expenditure, so their appropriate management is also necessary to prevent PEW (43,44). Depressive symptoms, which are common in patients with CKD and ESRD and were quite evident in the illustrated case, are linked to fatigue, lack of appetite (45), and weight loss. Early recognition and treatment are important components in the prevention of PEW (46).

Metabolic Acidosis. Metabolic acidosis is associated with increased muscle protein catabolism and promotes PEW in patients with advanced CKD (47). Metabolic acidosis stimulates oxidation of essential amino acids and further raises protein requirements for maintenance HD patients. Oral bicarbonate supplementation can improve nutritional status in patients with CKD (48,49). In an RCT of 134 patients with stage 4 CKD in whom serum bicarbonate was increased to 24 mmol/L, dietary protein and energy intake, mid-arm muscle circumference, and serum albumin improved and progression of CKD was slowed over 2 years compared with patients with a serum bicarbonate level of 20 mmol/L. Accordingly, a steady-state serum bicarbonate level should be ≥24 mmol/L in patients with CKD not yet undergoing maintenance HD and patients receiving PD. Recent epidemiologic data indicate adverse outcomes with high predialysis serum bicarbonate levels in maintenance HD patients, with a target of 22–24 mmol/L in these patients to avoid alkalosis after HD (50,51).

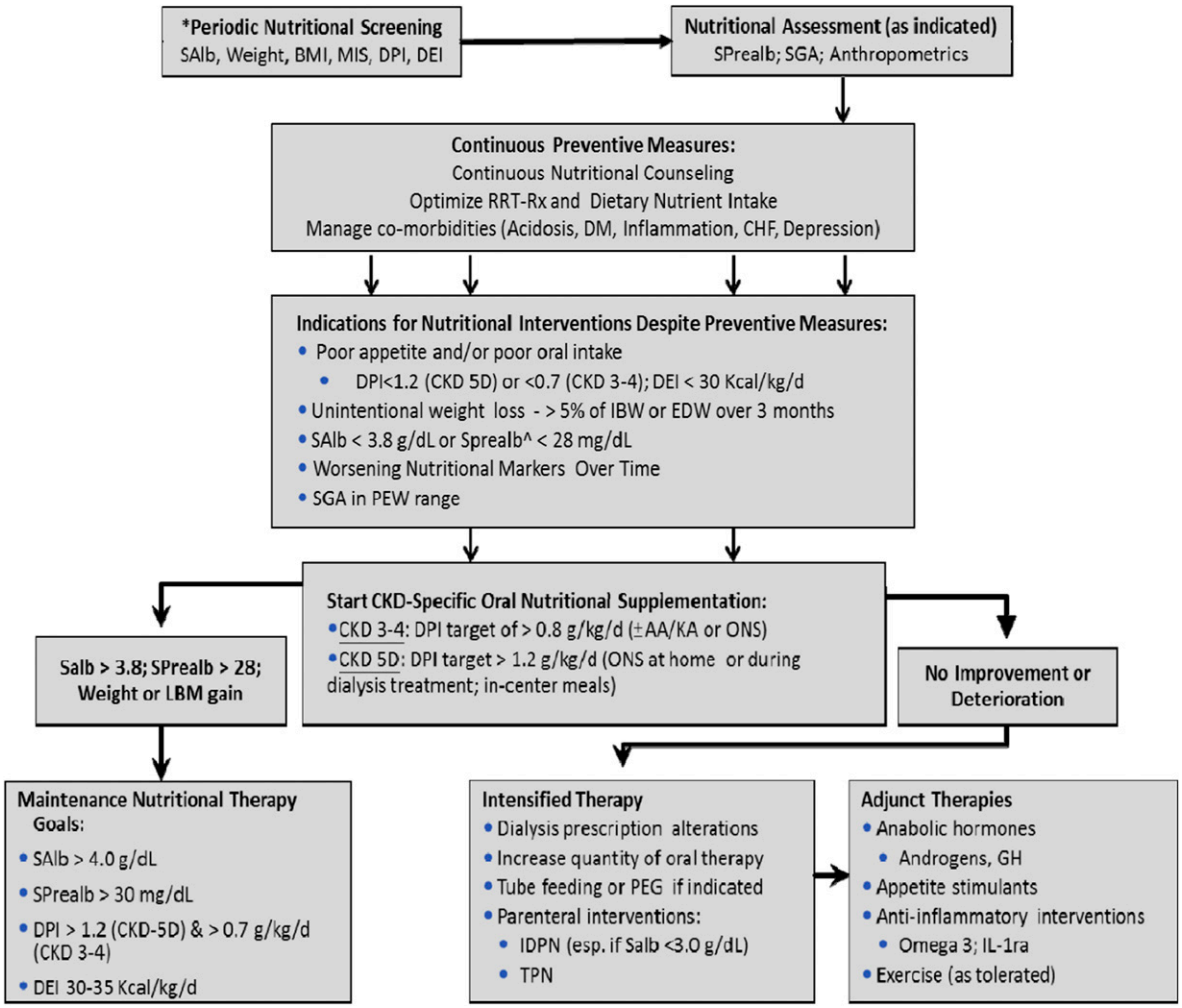

Figure 1. | Algorithm for nutritional management and support in patients with CKD. *Minimum every 3 months, monthly screening recommended. ^Only for patients with ESRD who do not have residual renal function. AA, amino acid; BMI, body mass index; CHF, congestive heart failure; DEI, dietary energy intake; DM, diabetes mellitus; DPI, dietary protein intake; EDW, estimated dry weight; GH, growth hormone; IDPN, intradialytic parenteral nutrition; IL-1ra, IL-1 receptor antagonist; KA, ketoanalogs; LBM, lean body mass; MIS, malnutrition-inflammation score; ONS, oral nutritional supplement; PEG, percutaneous endoscopic gastrostomy; PEW, protein energy wasting; RRT-Rx, renal replacement therapy prescription; SAlb, serum albumin (measured by bromocresol green); SGA, subjective global assessment; SPrealb, serum prealbumin; TPN, total parenteral nutrition. Reprinted from reference 52, with permission.

Treatment of PEW: An Integrated Approach

Oral and Enteral Nutritional Supplementation. In certain patients with CKD and ESRD, preventive measures are unable to diminish loss of protein and energy stores. As a result, nutritional supplementation may become appropriate (Figure 1). Oral supplementation should be given two to three times a day, preferably 1 hour after main meals and/or during dialysis for maintenance HD patients. This can provide an additional 7–10 kcal/kg of energy and 0.3–0.4 g/kg of protein per day. This requires a minimum spontaneous dietary intake of 20 kcal/kg energy and 0.4–0.8 g/kg protein per day in order to meet the recommended dietary energy and protein intake targets.

The efficacy of oral supplementation has been studied in multiple settings (reviewed by Ikizler *et al.* [52]). The beneficial nutritional effects of these supplements range from improvements in serum biomarkers, such as albumin, prealbumin, and transferrin, to gains in different body compartments, such as weight and lean body mass. The effects are evident as early as within a month and are generally sustained and associated with improvements in quality of life and physical functioning. In several studies, improvements in hospitalizations and death were reported, but none had the statistical power to appropriately assess these outcomes. For patients who are unable to tolerate nutritional supplementation by mouth, nasogastric tubes, percutaneous endoscopic gastroscopy, or jejunostomy tubes can be considered (17).

Two recent large-scale observational studies reported significant survival benefit in hypoalbuminemic maintenance HD patients receiving nutritional supplementation compared with matched controls (53,54). In a retrospective cohort study of 4289 matched pairs, death rates were 30.9% versus 37.3% in the treated versus untreated groups, respectively (53). In a prospective observational study of oral nutritional supplementation (ONS) performed as part of a

disease management plan in maintenance HD patients, ONS use was associated with higher serum albumin and lower hospitalization rate at 1 year, without reduction in mortality risk, compared with patients who did not receive ONS (54). The limitations of these studies include their retrospective design, convenience sampling, and residual confounding from unmeasured variables.

Intradialytic Parenteral Nutrition. Parenteral provision of nutrients during HD (intradialytic parenteral nutrition [IDPN]) has been shown in many studies, including RCTs, to be a safe and convenient approach for individuals who cannot tolerate oral or enteral supplements, including those with overt PEW, although many studies had significant design flaws (55,56). In the largest nutritional intervention study in maintenance HD patients with PEW (FINE [French Intradialytic Nutrition Evaluation] study) (57), similar improvements of nutritional measures were observed in both the IDPN and oral nutritional supplementation groups, without differences in rates of hospitalization or death. These various studies have shown that there is a direct correlation between response to nutritional supplementation and the severity of PEW and the amount of nutrients received, with diabetic patients showing a reduced response to nutritional support, and that an inflammatory status does not significantly affect the response to nutritional support. The high cost of IDPN and regulatory concerns remain the greatest barriers for use of IDPN, which should be reserved for patients in whom oral or enteral supplements are not feasible. Other studies using amino acids in dialysate (AAD) as a nutritional intervention in PD patients with PEW have provided conflicting results (58,59). Overall, AAD remains a viable option in PD patients with PEW who cannot tolerate or are not suitable for oral and other enteral supplements. AAD is not currently available in the United States, although some compounding pharmacies prepare solutions by injection of amino acid concentrate into glucose-based dialysate for compassionate use.

Anabolic Hormones. Recombinant human growth hormone (rhGH), an approved treatment of short stature in pediatric patients with CKD (60), leads to improved growth, confirming that rhGH could overcome GH resistance associated with CKD. In adults with CKD, resistance to native GH may be responsible for the premature decline in body composition (61). In a large multicenter RCT, C-reactive protein, homocysteine, HDL cholesterol, and transferrin levels significantly improved in hypoalbuminemic patients receiving maintenance HD (62). Unfortunately, this large RCT was prematurely terminated because of slow recruitment and thus could not assess the effects of rhGH on hospitalization or death.

Testosterone deficiency is also very common in male patients undergoing maintenance HD (63) and is associated with increased mortality risk. Several RCTs performed in maintenance HD patients showed significant benefits of nandrolone decanoate treatment in both anthropometric and biochemical measures, including body weight; body mass index; skinfold; mid-arm muscle circumference; and serum levels of total protein, prealbumin, and transferrin. No consistent effect of nandrolone decanoate was demonstrated on physical functioning in several studies, and high-dose nandrolone decanoate (100 mg/week) was intolerable in women because of its virilizing effects (64,65). Anabolic steroids can be used for preventing sarcopenia, albeit under close supervision with use limited to 6 months.

Exercise. Abnormalities in muscle function, exercise performance, and physical activity begin in the early stages of CKD and progress dramatically as ESRD develops (66). In ESRD, there are metabolic and structural muscle abnormalities with reductions in oxidative capacity and type 1 fibers with associated decrease in muscle endurance (67,68). Although several studies have examined the effects of cardiopulmonary fitness training in patients with ESRD (69), few studies have examined the role of exercise training on stimulating muscle growth. Collectively, these studies indicate that beneficial effects of exercise, such as improvements in muscle quality and quantity, strength, and physical functioning, are not consistently observed in patients with ESRD (70), perhaps because of limitations of methods to assess body composition, inadequate intensity and/or duration of exercise, and lack of understanding of the actual metabolic and morphologic abnormalities related to PEW in advanced CKD.

Case Follow-up

After discharge, the family elected to place the patient in a nursing home. She began receiving renal specific oral nutritional supplement, two cans a day taken between main meals. She also received one of the supplements during dialysis. The renal dietitian performed biweekly food recalls and instructed the patient and nursing home staff on increased dietary protein and calorie intake. The patient also began to take an antidepressant. She subsequently resumed more of her social activities. A procedure was performed to ligate accessory veins at the site of the AVF, with improved fistula blood flow within a few weeks and removal of the tunnelled HD catheter. The patient's weight stabilized and her serum albumin increased to 3.7 g/dl over the subsequent 3 months.

Summary and Recommendations

Because of its metabolic and functional importance in whole-body homeostasis, preservation of muscle mass is the ultimate goal in the management of PEW in patients with CKD. In patients with CKD and ESRD, in whom many catabolic signals dominate, it is critical to maintain a dietary protein and energy intake relative to needs. Treatment of concurrent conditions that contribute to catabolism, such as metabolic acidosis, insulin resistance, and systemic inflammation, is of paramount importance for the prevention of PEW. When supplemental nutrition is indicated, it is crucial to take into account all the determinants of body and muscle mass, including protein and energy content, exercise, anabolic hormones, antioxidants, anti-inflammatory nutrients and drugs, and other specific nutrients. Finally, it is important to assess the effect of nutritional supplements on nutritional measures; unfortunately, cost-effectiveness of these interventions and effects on hospitalization and mortality remain to be determined, with an absence of large, adequately powered RCTs demonstrating benefits of nutritional interventions on morbidity and mortality.

Question 1 (Dr. R. Hakim): What is the clinically recommended approach for nutritional assessment in patients with CKD?

Answer: In patients with stage 3–5 CKD not on maintenance dialysis, nutritional screening should include assessments of serum albumin, weight loss, and a malnutrition screening tool at every outpatient clinic visit. For those receiving in-center maintenance HD, this should be performed monthly. In patients deemed to be at risk for PEW, anthropometric measurements, subjective global assessment, or malnutrition-inflammation score should be performed every 6 months, in addition to periodic measurements of serum prealbumin, high-sensitivity C-reactive protein, and cholesterol. A thorough physical examination is critical for appropriate analysis of these findings. In addition to examining absolute values for certain thresholds, trends over time should be considered. For all indirect methods, such as subjective global assessment, repeated measures and technical standardization are extremely important to reduce variability of results. Regardless of the method, it is important to keep in mind that none is perfect and definitive, and the results should always be analyzed in the clinical context of each individual patient.

Question 2 (Dr. E. Siew): What are the role of appetite stimulants and other novel interventions, such as probiotics, in the treatment of PEW?

Answer: Several pharmacologic agents may stimulate appetite, including megestrol acetate, dronabinol, cyproheptadine, melatonin, thalidomide and ghrelin. Most of these drugs have not been studied systematically in maintenance HD patients. In such patients, small uncontrolled studies showed that megestrol acetate can stimulate appetite and induce small increases in serum albumin and weight (71), but large-scale prospective studies are needed. Ghrelin is an orexigenic peptide released primarily from the stomach; it increases appetite and adjusts both short- and long-term energy balance, making it a good candidate for treatment of anorexic patients with ESRD. Two pilot studies suggested improved energy intake during short-term ghrelin administration (72,73). There is also limited but supportive evidence for the effectiveness of pre- and probiotics on reducing plasma levels of some uremic toxins (74).

Question 3 (Dr. J. Berns): You mentioned depression in your discussion of the case. How common is this as a contributing factor to PEW in patients with CKD and ESRD, how should we assess for it, and are there any recommended treatment options?

Answer: Depression and anxiety obviously influence the willingness to eat, and observational reports show that appetite is poorer when patients score worse on their depression tests. A recent study showed strong associations between depression, inflammation, and serum albumin in maintenance dialysis patients (75). It is recommended that patients with ESRD be screened at the initiation of dialysis therapy, within 3–6 months after therapy initiation, and then yearly using depression screening self-report questionnaires, such as the Beck Depression Inventory. At-risk patients should then undergo a structured clinical interview to confirm the diagnosis, with subsequent consideration of treatment with a selective serotonin reuptake inhibitor or serotonergic agonist (76).

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