Chapter 6

Diagnosis, Prevention, and Treatment of Protein-Energy Wasting in Peritoneal Dialysis

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Additional information is available at the end of the chapter

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Abstract

Protein-energy wasting (PEW) is highly prevalent in peritoneal dialysis (PD) patients and is associated with mortality. Reduced protein and energy intake, comorbidity conditions, endocrine disorders, increased inflammatory cytokines, uremic toxins, metabolic acidosis, oxidative stress, nutrient losses into dialysate, continuous absorption of glucose from PD solutions, abdominal fullness induced by the dialysate, and peritonitis contribute to PEW. Assessment of nutritional status for the detection and management of PEW includes the PEW definition criteria, subjective global assessment (SGA), malnutrition-inflammation score (MIS), and geriatric nutritional risk index (GNRI). Diverse factors can affect nutritional and metabolic status in these patients so multiple strategies may be required to prevent or reverse PEW. Preventive measures include continuous nutritional counseling, optimizing dietary nutrient intake, and managing comorbidities. To treat PEW, the following may be used: administration of oral, intraperitoneal, enteral, or parenteral nutritional supplementation and adjunct therapies such as anabolic agents, appetite stimulants, anti-inflammatory interventions, and exercise. Diagnosis, prevention, and treatment of PEW in PD patients may favorably impact the prognosis and course of the disease.

Keywords: protein-energy wasting, peritoneal dialysis, nutritional assessment, protein-energy wasting definition criteria, subjective global assessment, malnutrition-inflammation score, geriatric nutritional risk index

1. Introduction

End-stage renal disease (ESRD) represents a serious public health problem in Mexico. It has been reported among the ten primary causes of death in the country with an annual mortality of 12.3 deaths per 100,000 people and is the second cause of years of life lost. The annual incidence is 421 persons per million population (pmp) with a prevalence of 1568 pmp. It is estimated that 8.5% of the Mexican population has chronic kidney disease (CKD) and almost 65,000 patients undergo dialysis. Peritoneal dialysis (PD) was introduced in Mexico in the early 1980s, and it became the renal replacement therapy of choice that rapidly extended to the population with social security coverage, as well as the uninsured population: the use of PD is the first choice in treatment when there is inadequate access to other methods like hemodialysis and renal transplant, and so the number of PD patients continues to rise [1, 2]. Despite the progressive rise in the use of hemodialysis in Mexico for some years now [1], when compared to other countries, Mexico continues to be one of the countries in the world where more PD is used [2, 3]. One of the most serious complications of CKD is protein-energy wasting (PEW), and this has an important therapeutic challenge because of its frequency in patients with ESRD who receive dialysis [4]. Therefore, from an integrated standpoint, this chapter reviews the diagnosis, prevention, and treatment of PEW in PD patients.

2. Protein-energy wasting

A variety of terms and definitions have been used to describe the conditions associated with loss of the muscle and fat tissue, malnutrition, and inflammation in patients with CKD, which have been denominated: uremic malnutrition, uremic (renal) cachexia, protein-energy malnutrition, malnutrition-inflammation-atherosclerosis syndrome, or malnutrition-inflammation complex (or cachexia) syndrome. The use of nonuniform and ill-defined terminologies may lead to both conceptual errors and malinterpretation of the data [5]. Therefore, the panel of experts of the International Society of Renal Nutrition and Metabolism (ISRNM) proposed the term "protein-energy wasting" as the state in which a decline in the body stores of protein

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1. Decreased protein and energy intake

a. Anorexia

i. Dysregulation in circulating appetite mediators

ii. Hypothalamic amino acid sensing

iii. Nitrogen-based uremic toxins

b. Dietary restrictions

c. Alterations in organs involved in nutrient intake

d. Depression

e. Inability to obtain or prepare food

2. Hypermetabolism

- **a.** Increased energy expenditure
  - **i.** Inflammation
  - **ii.** Increased circulating proinflammatory cytokines
  - **iii.** Insulin resistance secondary to obesity
  - **iv.** Altered adiponectin and resistin metabolism
- **b.** Hormonal disorders
  - **i.** Insulin resistance of CKD
  - **ii.** Increased glucocorticoid activity

3. Metabolic acidosis

4. Decreased physical activity

5. Decreased anabolism

- **a.** Decreased nutrient intake
- **b.** Resistance to growth hormone/insulin-like growth factor-1
- **c.** Testosterone deficiency
- **d.** Low thyroid hormone levels

6. Comorbidities and lifestyle

- **a.** Comorbidities (diabetes mellitus, congestive heart failure, depression, coronary artery disease, peripheral vascular disease)

7. Dialysis

- **a.** Nutrient losses into dialysate
- **b.** Dialysis-related inflammation
- **c.** Dialysis-related hypermetabolism
- **d.** Loss of residual renal function

Table 1. Causes of PEW in CKD patients.

and energy fuels (i.e., body protein and fat masses) presents due to the multiple nutritional and catabolic alterations that occur in CKD [5, 6]. These alterations include a decrease in the protein and energy intake, comorbidity conditions, endocrine disorders, an increase in the production of inflammatory cytokines, uremic toxins, metabolic acidosis, oxidative stress, and the nutrient losses into dialysate, among others (**Table 1**) [5, 6]. PD itself can lead to PEW due to the continuous absorption of glucose from PD solutions, the abdominal fullness induced by the dialysate, and peritonitis that can suppress the appetite [7]. Cachexia occurs infrequently in kidney disease, and it is the most severe form of PEW since the latter can refer to mild degrees of depleted protein and energy mass [5].

3. Prevalence of protein-energy wasting

PEW has been reported in PD patients in a wide range that goes from 23 to 90%, and the prevalence of PEW varies depending on the definitions used and the origin of the population [8–15]. In Mexico, the prevalence fluctuates between 49 and 92% in the prevalent as well as the incidental population in distinct PD programs [16]. This is a serious problem since PEW is associated with mortality in these patients [8].

4. Assessment of protein-energy wasting

Assessment and monitoring of the nutritional status is important to diagnose, prevent, and treat PEW [17]. Nutritional tools like the PEW definition criteria, subjective global assessment (SGA), malnutrition-inflammation score (MIS), and geriatric nutritional risk index (GNRI) have been widely recommended [18].

4.1. Protein-energy wasting definition criteria

The expert panel of the ISRNM has recommended diagnostic criteria for PEW that include (1) serum chemistry (albumin, prealbumin, cholesterol), (2) body mass (body mass index-BMI), unintentional weight loss, total body fat percentage), (3) muscle mass (muscle wasting, reduced mid-arm muscle circumference-MAMC, creatinine appearance), and (4) dietary intake (low protein or energy intake) (**Table 2**). At least three out of the four listed categories (and at least one test in each of the selected category) must be satisfied for the diagnosis of PEW. Optimally, each criterion should be documented on at least three occasions, preferably 2–4 weeks apart [5].

4.1.1. Serum chemistry

The reduction in serum albumin levels is a strong predictor of mortality in PD patients [8, 19, 20]. Also, it is one of the most used biochemical criteria in the diagnosis of PEW [21]. However, as a nutritional parameter, it should be interpreted with caution because its half-life is approximately 20 days and can be affected by inflammation, losses into dialysate, and the volume state [7]. Our research group has reported that serum albumin levels are not associated between patients with and without incidents of PEW in PD [21]. On the other hand, the half-life of approximately 2 days makes the prealbumin or transthyretin a more sensitive marker for nutritional status than serum albumin [7]. The levels of prealbumin of <30 mg/dL have been observed to increase the risk of mortality [22, 23]. The value of the prealbumin as a nutritional biochemical predictor of greater survival has been confirmed [22–24]. Another proposed biochemical marker is cholesterol. Low levels of cholesterol have been associated with worse results in this population [25, 26], and this diagnostic criterion is among the most controversial for PEW because the low level as a result of diet and exercise might not reflect PEW [27].

4.1.2. Body mass

Among the indicators of body mass, the BMI is the most commonly used measurement of weight-for-height and can be applied to assess PEW. However, this can be influenced by diet,

Criteria
Serum chemistry
Serum albumin (<3.8 g/dL (bromocresol green)[a])
Serum prealbumin (transthyretin) (<30 mg/dL (for maintenance dialysis)[a])
Serum cholesterol (<100 mg/dL[a])
Body mass
BMI (<23[b])
Unintentional weight loss over time (5% over 3 months or 10% over 6 months)
Total body fat percentage (<10%)
Muscle mass
Muscle wasting: reduced muscle mass (5% over 3 months or 10% over 6 months)
Reduced MAMC[c] (reduction >10% in relation to 50th percentile of reference population)
Creatinine appearance[d]
Dietary intake
Unintentional low dietary protein intake (<0.80 g/kg/day for at least 2 months[e] for dialysis patients)
Unintentional low dietary energy intake (<25 kcal/kg/day for at least 2 months[e])

At least three out of the four listed categories (and at least one test in each of the selected categories) must be satisfied for the diagnosis of kidney disease-related PEW.

Optimally, each criterion should be documented on at least three occasions, preferably 2–4 weeks apart.

[a]Not valid if low concentrations are due to abnormally great urinary or gastrointestinal protein losses, liver disease, or cholesterol-lowering medicines.

[b]A lower BMI might be desirable for certain Asian populations; weight must be edema-free mass.

[c]Measurement must be performed by a trained anthropometrist.

[d]Creatinine appearance is influenced by both muscle mass and meat intake.

[e]Can be assessed by dietary diaries and interviews or for protein intake by calculation of normalized protein equivalent of total nitrogen appearance (nPNA or nPCR) as determined by urea kinetic measurements.

Table 2. Criteria for the clinical diagnosis of PEW in CKD.

exercise, fat mass, and hydration status and may not be pathological in certain racial-ethnic groups [5, 27]. In a recent meta-analysis, it was confirmed that patients with PD who presented with low weight compared to the ranges of overweight and obesity had an increased risk of mortality [28]. The expert panel also recommends that the unintentional loss of 5% of non-edematous weight within 3 months or an unintentional loss of 10% of non-edematous weight over the past 6 months should be considered an indicator of PEW [5]. Even still, the majority of PD patient cases experience a significant gain in body weight [29]. The presence of weight loss in the first year is associated with adverse results [30, 31]. One limitation for the assessment of this parameter is the fluid gain that can mask weight loss [27]. The third measure that can be considered for the diagnosis of PEW is a low percentage of body fat, but the specificity of this criterion is questionable in persons who are very muscular and athletic [5, 27].

4.1.3. Muscle mass

The reduction of muscle mass appears to be the most valid criterion for the presence of PEW [5]. Methods like the dual-energy X-ray absorptiometry and bioelectrical impedance analysis have

been used to assess the loss of muscle mass in PD patients [32–34]. The increase in risk of mortality has been observed with the loss of muscle mass assessed through these types of methods [35, 36]. The reduction in MAMC is another recommended criterion for the diagnosis of PEW [5], and the anthropometric parameters, including the MAMC, have been demonstrated to identify low muscle mass in these patients [37]. However, this method can be insensitive since it is associated with a substantial interobserver error and the volume state [7]. Equations based on the MAMC and handgrip strength have been favorably correlated with muscle mass [38].

4.1.4. Dietary intake

A decrease in appetite (anorexia) can be associated with PEW. Therefore, the unintentional reduction of protein intake <0.80 g per kg of body weight per day and an unintentional reduction in energy intake of <25 kcal per kg of body weight per day for at least 2 months have been proposed as an indicator of PEW [5]. Dietary intake can be assessed by dietary diaries and interviews or for protein intake by calculation of normalized protein equivalent of total nitrogen appearance (nPNA or nPCR) as determined by urea kinetic measurements [5]. One important aspect to consider is the obligatory absorption of glucose with PD, since it can result in an absorption of carbohydrates on average of approximately 400 kcal of energy intake every day, and so estimating the total daily energy intake derived from the sum of the diet and the dialysate could be adequate for the diagnosis of PEW [39].

4.2. Subjective global assessment

The SGA is a tool that is used to assess the nutritional status, and it has been validated for use in PD patients [18, 40–42]. The increase in risk of mortality has been confirmed with the presence of PEW assessed by this tool [12, 43]. The SGA is composed of a medical history and a physical examination (**Figure 1**). In each component a score is assigned based on a scale from 1 to 7, with lower values representing worse nutritional status. The medical history includes weight change (the last 2 weeks, as well as the previous 6 months), dietary intake, gastrointestinal symptoms, functional capacity, and the disease state and comorbidities. The physical exam includes the loss of subcutaneous fat (below the eye, triceps, biceps, chest), muscle wasting (temple, clavicle, scapula, ribs, quadriceps, calf, knee, interosseous), and edema. When this examination has been completed, an overall SGA rating is assigned to the patient and ranges from a rating of 1–2 for severe PEW, 3–5 for mild-moderate PEW, and 6–7 for very mild PEW to well-nourished [17, 40].

4.3. Malnutrition-inflammation score

Upon recognizing the role that inflammation plays in the pathogenesis of PEW, a more comprehensive, quantitative scoring system was created called the MIS, which utilizes a revised form of the SGA scoring system and adds BMI, serum albumin, and the binding capacity of iron or transferrin [17, 18, 44]. The MIS has 10 components, each one with four levels of severity, from 0 (normal) to 3 (severely abnormal) (**Figure 2**). The sum of all 10 MIS components ranges from 0 (normal) to 30 (severe PEW); a higher score reflects a more severe degree of PEW and inflammation [44]. The MIS assessment has been identified as a predictor of morbidity and mortality in PD patients [45, 46]. Also, diverse authors have observed a reasonable correlation of the MIS with the SGA in this population [47, 48].

SUBJECTIVE GLOBAL ASSESSMENT RATING FORM

Patient Name: **ID #:** **Date:**

HISTORY

Rate 1-7

WEIGHT/WEIGHT CHANGE: ***(Included in K/DOQI SGA)***

1. Baseline Wt: _____ (Dry weight from 6 months ago)
Current Wt: _____ (Dry weight today)
Actual Wt loss/past 6 mo: _____ **% loss:** _____ (actual loss from baseline or last SGA)

2. Weight change over past two weeks: _____ No change _____ Increase _____ Decrease

DIETARY INTAKE No Change _____ (Adequate) No Change _____ (Inadequate)
1. Change: Sub optimal Intake: _____ Protein _____ Kcal _____ Duration _____
Full Liquid: _____ Hypocaloric Liquid _____ Starvation _____

GASTROINTESTINAL SYMPTOMS ***(included in K/DOQI SGA-anorexia or causes of anorexia)***

Symptom:	**Frequency:***	**Duration:⁺**
_____ None	_____	_____
_____ Anorexia	_____	_____
_____ Nausea	_____	_____
_____ Vomiting	_____	_____
_____ Diarrhea	_____	_____
	Never, daily, 2-3 times/wk, 1-2 times/wk	>2 weeks, <2 weeks

b

FUNCTIONAL CAPACITY

Description	**Duration:**
_____ No dysfunction	_____
_____ Change in function	_____
_____ Difficulty with ambulation	_____
_____ Difficulty with activity (patient specific "normal")	_____
_____ Light activity	_____
_____ Bed/chair ridden with little or no activity	_____
_____ Improvement in function	_____

DISEASE STATE/COMORBIDITIES AS RELATED TO NUTRITIONAL NEEDS
Primary Diagnosis _____ Comorbidities _____
Normal requirements _____ Increased requirements _____ Decreased requirements _____
Acute Metabolic Stress ____ None ____ Low ____ Moderate ____ High

PHYSICAL EXAM

_____ Loss of subcutaneous fat (Below eye, triceps, biceps, chest) ***(Included in K/DOQI SGA)*** _____ Some areas _____ All areas
_____ Muscle wasting (Temple, clavicle, scapula, ribs, quadriceps, calf, knee, interosseous) ***(incluided in K/DOQI SGA)*** _____ Some areas _____ All areas
_____ Edema (Related to undernutrition/use to assess weight change)

OVERALL SGA RATING

Very mild risk to well-nourished= 6 or 7 most categories or significant, continued improvement.
Mild-moderate= 3, 4, or 5 ratings. No clear sign of normal status or severe malnutrition.
Severely Malnourished= 1 or 2 ratings in most categories/significant physical signs of malnutrition.

Figure 1. Seven-point scale SGA.

4.4. Geriatric nutritional risk index

The GNRI was proposed using the argument that because current methods of nutritional assessment use several subjective assessments and judgments, assessment by a well-trained staff is necessary to obtain consistent results between the different examiners and institutions. Furthermore,

(A) Patients´ related medical history:			
1- Change in end dialysis dry weight (overall change in past 3–6 months):			
0	1	2	3
No decrease in dry weight or weight loss < 0.5 kg	Minor weight loss (≥ 0.5 kg but < 1 kg)	Weight loss more than one kg but < 5%	Weight loss > 5%
2- Dietary intake:			
0	1	2	3
Good appetite and no deterioration of the dietary intake pattern	Somewhat sub-optimal solid diet intake	Moderate overall decrease to full liquid diet	Hypo-caloric liquid to starvation
3- Gastrointestinal (GI) symptoms:			
0	1	2	3
No symptoms with good appetite	Mild symptoms, poor appetite or nauseated occasionally	Occasional vomiting or moderate GI symptoms	Frequent diarrea or vomiting or severe anorexia
4- Functional capacity (nutritionally related functional impairment):			
0	1	2	3
Normal to improved functional capacity, feeling fine	Occasional difficulty with baseline ambulation, or feeling tired frequently	Difficulty with otherwise independent activities (e.g. going to bathroom)	Bed/chair-ridden, or little to no physical activity
5- Co-morbidity including number of years on dialysis:			
0	1	2	3
On dialysis less than one year and healthy otherwise	Dialyzed for 1–4 years, or mild co-morbidity (excluding MCC*)	Dialyzed > 4 years, or moderate co-morbidity (including one MCC*)	Any severe, multiple co-morbidity (2 or more MCC*)
(B) Physical Exam (according to SGA criteria):			
6- Decreased fat stores or loss of subcutaneous fat (below eyes, triceps, chest):			
0	1	2	3
Normal (no change)	Mild	Moderate	Severe
7- Signs of muscle wasting (temple, clavicle, scapula, ribs, quadriceps, knee, interosseous):			
0	1	2	3
Normal (no change)	Mild	Moderate	Severe
(C) Body mass index:			
8- Body mass index: BMI = Wt(kg) / Ht^2(m)			
0	1	2	3
BMI ≥ 20 kg/m^2	BMI: 18–19.99 kg/m^2	BMI: 16–17.99 kg/m^2	BMI: < 16 kg/m^2
(D) Laboratory parameters:			
9- Serum albumin:			
0	1	2	3
Albumin ≥ 4.0 g/dL	Albumin: 3.5–3.9 g/dL	Albumin: 3.0–3.4 g/dL	Albumin: < 3.0 g/dL
10- Serum TIBC (total Iron Binding Capacity): ♣			
0	1	2	3
TIBC ≥ 250 mg/dL	TIBC: 200–249 mg/dL	TIBC: 150–199 mg/dL	TIBC: < 150 mg/dL
Total Score = sum of above 10 components (0–30):			

*MCC (Major Comorbid Conditions) include hearth failure class III or IV, full blown AIDS, severe coronary artery disease, moderate to severe chronic obstructive pulmonary disease, major neurological sequelae, and metastatic malignancies or s/p recent chemotherapy.
♣Suggested equivalent increments for serum transferrin are: > 200 (0), 170–200 (1), 140–169 (2), and < 140 mg/dL.

Figure 2. Components of the malnutrition-inflammation score (MIS).

these methods are somewhat time-consuming and cumbersome. The GNRI was developed with the intention of being the simpler method to assess nutritional status in which only three objective parameters are used: body weight, height, and serum albumin levels (**Table 3**) [18]. It has been observed that the GNRI is related to diverse nutritional parameters including the MIS, SGA,

Formula
GNRI = [14.89 × albumin (g/dL)] + [41.7 × (body weight/ideal body weight)]

Table 3. Geriatric nutritional risk index (GNRI).

BMI, creatinine, albumin, arm circumference, and fat mass index, as well as being associated with greater mortality in PD patients [9, 49]. This makes the GNRI a simple method to predict nutritional status and the clinical results in these patients [49].

4.5. Clinical scenario for the diagnosis of protein-energy wasting in peritoneal dialysis

4.5.1. Case 1

A 27-year-old male with PD for 36 months who attending to the nephrology service in order to perform a peritoneal equilibrium test, wich results in a low-average transport.

Baseline weight 64.5 kg, current weight 64.5 kg, height 1.75 m, BMI 21.06 kg/m^2, ideal body weight 70.5 kg, MAMC 21.51 cm (reduction >10%), percentage of body fat 13.52, energy intake 742 kcal (10.52 kcal/kg per day), and protein intake 28 g (0.39 g/kg per day).

Laboratory measurements: hemoglobin 7.64 g/dL, total lymphocyte count 900 cells/mm^3, glucose 85 mg/dL, creatinine 18.75 mg/dL, BUN 79.80 mg/dL, P 8.10 mg/dL, Ca 8.7 mg/dL, Cl 100 mmol/L, K 4.90 mmol/L, Na 140 mmol/L, Mg 3.30 mg/dL, albumin 3.00 g/dL, total proteins 5.7 g/dL, cholesterol 139 mg/dL, and transferrin 256.5 mg/dL.

Based on these data, which of the following diagnostic criteria meet for PEW (**Table 2**)?

(A) Cholesterol, percentage of body fat, and MAMC

(B) Albumin, BMI, and MAMC or protein/energy intake

(C) Albumin, unintentional weight loss, and percentage of body fat

4.5.2. Case 2

An 18-year-old male with PD for 13 months who is hospitalized in our service for the presence of abdominal pain at the time of the replacement dialysis solutions is diagnosed with peritonitis and *Pseudomonas aeruginosa*, which were isolated.

Baseline weight 55 kg, current weight 44.7 kg, height 1.60 m, BMI 17.46 kg/m^2, ideal body weight 59 kg, MAMC 19.61 cm, and percentage of body fat 8.3. The medical history shows an unintentional weight loss of 18.73% in the last 6 months, as well as an inadequate calorie intake of 1075 kcal (18.22 kcal/kg per day) and a protein intake of 56.5 (0.95 g/kg per day). Anorexia, nausea, vomiting, and diarrhea were not present. In terms of functional capacity with loss, rarely gets out of bed and does so with help for <2 weeks and in the state of the disease and comorbidities, presents an increase in nutritional requirements and high metabolic stress due to the presence of peritonitis. The physical exam shows a severe loss of subcutaneous fat and muscle wasting in all areas, without the presence of edema.

Laboratory measurements: hemoglobin 6.48 g/dL, total lymphocyte count 670 cells/mm^3, glucose 65 mg/dL, creatinine 9.91 mg/dL, BUN 53.30 mg/dL, P 3.90 mg/dL, Ca 9.92 mg/dL, Cl 92 mmol/L, K 3.90 mmol/L, Na 132 mmol/L, Mg 1.90 mg/dL, albumin 2.10 g/dL, total proteins 4.7 g/dL, cholesterol 115 mg/dL, and transferrin 98.4 mg/dL.

Based on these data, what overall SGA rating presents this patient (**Figure 1**)?

(A) 6–7 Very mild PEW to well-nourished

(B) 3–5 Mild–moderate PEW

(C) 1–2 Severe PEW

4.5.3. Case 3

A 36-year-old female with PD for 60 months who is hospitalized for the presence of abdominal pain, constipation, nausea and vomiting is diagnosed with peritonitis and *Staphylococcus haemolyticus*, which were isolated.

Baseline weight 62 kg, current weight 51.2 kg, height 1.55 m, ideal body weight 55 kg, MAMC 21.95 cm, and percentage of body fat 21.39.

In the medical history component, there is evidence of an unintentional weight loss of 17.42% in the last 6 months, as well as an inadequate calorie intake of 630 kcal (11.45 kcal/kg per day) and a protein intake of 21.1 gr (0.38 g/kg per day). Also presenting gastrointestinal symptoms like nausea every day >2 weeks and vomiting every day <2 weeks. In the functional capacity, presents difficulty with independent activities, and as the only comorbidity, the time in dialysis of 5 years. The physical exam shows a moderate loss of subcutaneous fat in the triceps and biceps, as well as a moderate muscle wasting in the interosseous, temples, clavicles, and quadriceps. With a calculated BMI of 21.31 kg/m^2 and laboratory parameters with albumin 2.00 g/dL and transferrin 128 mg/dL.

Other laboratory measurements: hemoglobin 9.41 g/dL, total lymphocyte count 670 cells/mm^3, glucose 78 mg/dL, creatinine 9.41 mg/dL, BUN 27.57 mg/dL, P 4.60 mg/dL, Ca 9.42 mg/dL, Cl 91 mmol/L, K 3.50 mmol/L, Na 130 mmol/L, Mg 1.60 mg/dL, total proteins 5.1 g/dL, and cholesterol 152 mg/dL.

Based on the 10 components of the MIS, what score does this patient present (**Figure 2**)?

(A) 22

(B) 29

(C) 15

4.5.4. Case 4

A 32-year-old male with PD for 74 months who attending to the nephrology service in order to perform a peritoneal equilibrium test, wich results in a high-average transport.

Baseline weight 55 kg, current weight 55 kg, height 1.62 m, BMI 20.95 kg/m^2, ideal body weight 60.5 kg (ideal body weight = ([BMI = 23 kg/m^2] x height^2), MAMC 19.68 cm, percentage of body

fat 21.07, energy intake 1380 kcal (22.80 kcal/kg per day), and protein intake 52 g (0.85 g/kg per day).

Laboratory measurements: hemoglobin 7.63 g/dL, total lymphocyte count 1460 cells/mm^3, glucose 97 mg/dL, creatinine 10.27 mg/dL, BUN 40.90 mg/dL, P 3.30 mg/dL, Ca 8.7 mg/dL, Cl 101 mmol/L, K 4.40 mmol/L, Na 139 mmol/L, Mg 1.90 mg/dL, albumin 2.00 g/dL, total proteins 5.6 g/dL, cholesterol 135 mg/dL, and transferrin 138.1 mg/dL.

Based on this data, which of the following ranges of IRNG does this patient present (**Table 3**)?

(A) 92.91

(B) 67.68

(C) 72.93

5. Prevention of protein-energy wasting

Diverse factors can affect the nutritional and metabolic status of patients with CKD, for which they require interventions to prevent or reverse protein and energy depletion. Preventive measures include continuous nutritional counseling, optimizing dietary nutrient intake, renal replacement therapy, and management of the different comorbidities (metabolic acidosis, diabetes mellitus, congestive heart failure, depression) [50].

5.1. Nutritional counseling

Nutritional counseling can be a useful tool in PD patients in order to improve compliance with nutritional recommendations [51]. The minimum recommendations in order to prevent inadequate nutrient intake in these patients is presented in **Table 4** [50]. In a prospective study with 258 PD patients, individualized nutritional counseling significantly improved calorie and protein intake, the BMI, and the PEW [14]. However, despite this type of intervention, it has been observed that not all patients achieve an optimal nutrient intake [14, 52]. In our population, although nutritional counseling has been shown to not significantly improve all of the nutritional parameters, it is capable of maintaining the nutritional status despite the decrease in residual kidney function and the presence of systemic inflammation [53]. The Kidney Disease Outcomes Quality Initiative (K/DOQI) Guidelines recommend that nutritional counseling should be intensive initially and provided thereafter every 1 or 2 months and more frequently if inadequate nutrient intake or PEW is present or if adverse events or illnesses occur that may cause deterioration in nutritional status [54].

5.2. Optimize dietary nutrient intake

Optimizing the dietary nutrient intake is one strategy that can improve calorie and protein intake [50]. The suggestion of individualized menus and the list of interchangeable foods in equivalent quantities have been demonstrated to improve the achievement of protein intake in PD patients [55]. The increased protein requirement (>1.2 g/kg/day) in these patients makes them subject to a higher phosphorus load; thus, the reduced intake of

Protein	>1.2 g/kg/day Peritonitis >1.5 g/kg/day
Energy	30–35[a] kcal/kg/day including kcal from dialysate
Sodium	80–100 mmol/day
Potassium	Not usually an issue
Phosphorus	800–1000 mg and binders if elevated

Greater than 50% of high biological value protein (i.e., complete protein sources, containing the full spectrum of essential amino acids) is recommended.[a]Based on the physical activity level. In sedentary elderly adults, recommended energy intake is 30 kcal/kg/day.
All recommendations are based on ideal body weight. Regular follow-up supports compliance.

Table 4. Recommended minimum protein, energy, and mineral intakes for peritoneal dialysis patients by the ISRNM.

phosphorus without depriving protein intake should be centered in food choices with a lower quantity of phosphorus per gram of protein (e.g., egg whites) and in those choices that have lower intestinal absorption (vegetables) [56]. The reduction in sodium intake is another commonly prescribed strategy to maintain volume state [57]. It has been observed that patients with a low sodium intake are associated with nutrient deficits, poor muscle protein stores, and worse results [58]. Therefore, measures to reduce dietary sodium through the use of flavor enhancers, and preparing a diet with 2 g of sodium (88 mM NaCl) adding 1/3 teaspoon of salt to each meal throughout the day, could help to avoid nutritional deficits [57, 59].

5.3. Renal replacement therapy

The dialysis adequacy has long been considered a measure for the prevention and treatment of PEW in patients who undergo maintenance dialysis, and a minimum dose of dialysis has been recommended to maintain optimal dietary nutrient intake [50]. A 25% increase in PD volume has been shown to improve calorie intake and stabilize the mid-arm circumference, protein nitrogen appearance, and SGA in PEW patients [60]. However, in the ADEMEX study, significant differences were not observed between the nutritional markers (nPNA, body weight, prealbumin) with the increase in the dose of PD to 60 l/week [61]. Therefore, it can be concluded that what is actually considered an adequate dialysis in different guidelines is sufficient to preserve the nutritional status [50].

5.4. Comorbidities

Diverse comorbidities associated with ESRD contribute to a catabolic milieu and the development of PEW [6]. Metabolic acidosis increases muscle protein catabolism via suppression of the insulin/insulin growth factor-1 signaling and the activation of the ubiquitin-proteasome system [50]. In PD patients, correction of the serum level of bicarbonate has demonstrated downregulation of branched-chain amino acid degradation and muscle proteolysis [62].

Other studies have reported an improvement in the nutritional status with the correction of the metabolic acidosis through an increase in the body weight, mid-arm circumference, SGA score, and the nPNA [63, 64]. Diabetes mellitus is one of the most frequent comorbidities in patients with CKD [6], and PEW is more prevalent in diabetic PD patients compared to nondiabetics [65, 66]. The degree of insulin resistance and/or insulin deprivation seems to develop this condition [50]. Therefore, the adequate management of diabetes and insulin resistance is important in preventing further loss of lean body mass in patients undergoing maintenance dialysis. This is especially relevant for PD patients because of the exposure to around 80–330 g of additional glucose from the dialysate [50]. Inflammation is frequent in PD patients and is associated with PEW, peritoneal membrane dysfunction, and cardiovascular events [67]. The increase in systemic concentrations of proinflammatory cytokines is thought to play an integral role in the muscle catabolism of patients with ESRD. Interleukin-6 causes an increase in muscle proteolysis, and the tumor necrosis factor-alpha can cause anorexia through its effects on the satiety center in the central nervous system [68]. Strategies that can reduce inflammation include the control of infectious processes, optimizing the prescription of PD (improving the volume state, biocompatible solutions), pharmacological interventions (statins, angiotensin-converting enzyme inhibitors, sevelamer), and nutritional interventions (antioxidants) [69]. Another common comorbidity is congestive heart failure [6]. In these patients the circulatory congestion has been associated with a reduction in the protein and calorie intake, greater inflammation, PEW, and the increase in resting energy expenditure [70]. Other disorders like uncontrolled hyperparathyroidism and cardiac cachexia are associated with systemic inflammation and the increase in energy expenditure [50]. The symptoms of depression, which are common in ESRD patients, are related to fatigue, the lack of appetite, and weight loss. Early recognition and treatment are important components in the prevention of PEW [68].

6. Treatment of protein-energy wasting

For patients in whom the standard preventative measures are unable to diminish the loss of protein and energy stores, nutritional supplementation should be initiated through oral, intraperitoneal, enteral, or parenteral routes. Anabolic agents, appetite stimulants, anti-inflammatory interventions, and exercise can be utilized as adjuvant therapies [50].

6.1. Oral nutritional supplementation

Oral supplementation can provide an additional 7–10 kcal/kg per day of energy and 0.3–0.4 g/kg per day of protein. This requires a minimum spontaneous dietary intake of 20 kcal/kg per day of energy and 0.4–0.8 g/kg per day of protein in order to meet the recommended dietary energy intake and dietary protein intake targets [50, 68]. Oral nutritional supplements have been shown to improve protein-calorie intake and the nutritional status (body weight, prealbumin, SGA score) in PD patients [71, 72]. However, a high rate of non-compliance and intolerance has been reported with the long-term use of these types of supplements [73]. Other

studies have demonstrated that supplementation with calcium caseinate and egg albumin increases levels of serum albumin and nutrient intake [74, 75]. When considering the use of these supplements, in addition to the type and quantity to use, one must also take into consideration the baseline nutritional status, dietary intake, patient preference, acceptance, willingness to use and to purchase the supplements, tolerance and contraindications, and duration of use in the care plan [76].

6.2. Intraperitoneal nutritional supplementation

PD patients lose 3–4 g/day of amino acids (AAs) and 4–15 g/day of proteins [77, 78]. One exchange with a 1.1% AA dialysis solution has been demonstrated to be sufficient to compensate for these losses [78]. In patients with PEW, the treatment with AA in the nitrogen balance dialysate became significantly positive, and there was a significant increase in net protein anabolism, the fasting morning plasma amino acid pattern became more normal, and serum total protein and transferrin concentrations rose [79]. In another long-term study, improvements in some nutritional parameters including the nPNA, lean body mass, and handgrip strength have been observed [80]. In general, it is recommended to use one bag of AA dialysate in place of one glucose-based dialysate. Using more than one bag during a 24-h period runs the risk of increasing the level of urea nitrogen and decreasing levels of bicarbonate [39]. Overall, AA dialysate remains a viable option in PD patients with PEW who cannot tolerate or are not suitable for PO (per oral) and other enteral supplements [50].

6.3. Enteral nutritional supplementation

Enteral nutrition has been poorly investigated in PD patients [81]. Considerations for its use include the lack of improvement in nutritional status despite the use of oral nutritional supplements, the presence of severe PEW, spontaneous intake of <20 kcal/day, or conditions of stress [82]. Enteral nutrition can be administered via nasogastric feeding [51]. The use of percutaneous endoscopic gastrostomy or percutaneous endoscopic jejunostomy has been contraindicated in these patients due to the increase in the incidence of peritonitis [81]. However, there have been some reports of cases where the percutaneous endoscopic gastrostomy can be an effective nutritional strategy [83–85]. The feeding formulas with a higher protein but lower carbohydrate content are to be preferred. Products rich in proteins should be used as oral nutritional supplements [81].

6.4. Parenteral nutritional supplementation

Parenteral nutrition has also been poorly investigated in PD patients [82]. It has been suggested that its initiation should be limited to patients with PEW and those who are stressed, or in patients with severe encapsulating peritonitis, when the nutritional requirements cannot be ensured through oral or enteral routes [82]. Early parenteral nutrition has been shown to maintain a positive nitrogen balance in peritonitis [86]. As well, in patients with encapsulating

peritoneal sclerosis, the parenteral nutritional support seems to be better than enteral nutrition [87, 88]. During parenteral nutrition the energy supply should combine carbohydrate and lipid. The use of specific formulas for parenteral mixtures is not yet supported by controlled data [82].

7. Adjuvant therapies

Diverse adjunctive therapies can be used to treat PEW in these patients. The use of anabolic hormones results in a positive nitrogen balance, an increase in lean body mass, and improvement in the anthropometric parameters [89–91]. Appetite stimulants can have favorable effects on body weight, appetite, and calorie intake [92, 93]. When comorbidities and potential dialysis-related causes of inflammation have been assessed and appropriately treated, other anti-inflammatory treatment strategies such as anti-oxidative and/or bioecologic strategies or targeted anti-cytokine therapies could be considered in patients who are persistently inflamed [68]. On the other hand, PD patients have low levels of physical activity, which can be associated with PEW [94, 95]. Progressive resistance exercise induces skeletal muscle hypertrophy, increases muscular strength, and improves the health-related quality of life [96]. This is important since exercise interventions can prevent or reverse PEW [97].

8. Conclusions

PEW is very frequent in PD patients and is associated with mortality. Assessment and monitoring of the nutritional status are important to diagnose, prevent, and treat PEW. Large-scale clinical trials and international collaborations that refer to the effects of nutritional interventions on PEW are necessary in order to advance on this subject. Meanwhile, individualizing the different interventions for prevention and treatment of PEW proposed in this chapter should be employed in PD patients.

Clinical scenario responses for the diagnosis of protein-energy wasting in peritoneal dialysis:

Case 1 = (B) Albumin, BMI, and MAMC or protein/energy intake.

Case 2 = (C) 1–2 Severe PEW.

Case 3 = (A) 22.

Case 4 = (B) 67.68.

Conflict of interest

There are no conflicts of interest to report.

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