NUTRITIONAL ASSESSMENT IN DIALYSIS PATIENT: PREALBUMIN, A MARKER FOR NUTRITIONAL EVALUATION

Thesis

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Introduction

Malnutrition is an important problem in patients treated with hemodialysis or peritoneal dialysis. It's reported prevalence varies between 18% and 75% among dialysis patients according to type of dialysis modality, nutritional assessment tools and origin of patient population ***(Mehrotra et al., 2001, Kalanter Zadeh et al., 2001)***.

As a result of the frequency of malnutrition, periodic assessment of nutritional status should be part of the routine care of dialysis patients to permit early recognition and the institution of appropriate therapy ***(Marsha Wolfson, 2010)***.

There is no single measurement which can be used to determine the presence of malnutrition. Therefore, a panel of measurements is recommended, including a measure of body composition, a measure of dietary protein intake, and at least one measure of serum protein status ***(Tattersall et al., 2007)***.

Subjective global assessment (SGA) is a reproducible and useful instrument for assessing the nutritional status of maintenance dialysis patients. It's a simple technique that is based on subjective and objective aspects of the medical history and physical examination ***(Chauveau et al., 1996)***.

Prealbumin is the earliest laboratory indicator of nutritional status and has emerged as the preferred marker for nutrition because it correlates with patients outcomes in a wide variety of clinical conditions ***(Beck et al., 2002)***.

It has been suggested that serum prealbumin may be more sensitive than albumin as an indicator of nutritional status, since it has a shorter half- life than albumin (~2 to 3 days versus 20 days, respectively) ***(Avram et al., 1995)***.

However, similar to albumin, inflammation can lead to a reduction in serum prealbumin ***(Rambod et al., 2008)***.

Aim of the work

1-To determine the frequency and severity of malnutrition in dialysis patients.

2-To determine the correlations among prealbumin and other nutritional parameters including biochemical markers and anthropometric measurements.

3-To determine the correlation between subjective global assessment and serum prealbumin and other nutritional parameters.

Protein-Energy Wasting (PEW) in maintenance dialysis

Introduction

An array of terms has been used to describe conditions associated with loss of adequate nutrient intake, decreased body protein (often assessed by the individual's muscle mass), and/or reduced body energy reserves (often assessed by the patient's fat mass). Arguably the 2 major causes of these conditions are malnutrition and inflammation. The terms for these conditions include protein-energy malnutrition, malnutrition–inflammation complex syndrome, malnutrition–inflammation atherosclerosis syndrome, kidney disease wasting, and uremic cachexia ***(Kalanter-Zadeh et al., 2004)***.

To arrive at a consensus in applying a uniform terminology for the diagnosis of this syndrome and to avoid the use of misleading terms, the International Society of Renal Nutrition and Metabolism convened an expert panel that proposed the following term for these conditions: protein-energy wasting (PEW), that is to define the loss of somatic and circulating body protein mass and energy reserves ***(Kalanter-Zadeh et al., 2004)***.

Several studies have evidenced malnutrition in 23%-76% of patients on hemodialysis (HD) and in 18%-50% of patients on peritoneal dialysis.The prevalence of severe PEW has been estimated to be 6% to 8% ***(Dukkipati and Kopple, 2009)***.

The wide variation in malnutrition prevalence in patients on HD may be attributed to the different assessment methods, and to the multiple factors contributing to its development ***(Kalanter-Zadeh et al., 2004)***.

Currently, with the use of modern technology in dialysis, malnutrition is less prevalent in those patients undergoing maintenance dialysis. However, there is evidence suggesting that many factors that promote malnutrition in renal failure persist even with modern methods of dialysis treatment ***(Al-Saran et al., 2009)***.

There have not been any rigorously conducted epidemiologic studies that have examined the comparative incidence of PEW over the past few decades. Therefore, it is unclear whether the prevalence of PEW is increasing or decreasing or has remained the same in maintenance dialysis patients ***(Dukkipati and Kopple, 2009)***.

PEW and mortality

Protein-energy malnutrition is one of the major factors adversely affecting the prognosis of patients with chronic kidney disease, being associated with an increase in morbidity and mortality in those patients ***(Dukkipati and Kopple, 2009)***.

Multiple pathophysiologic mechanisms have been suggested to explain the link between PEW and mortality in CKD, including derangements in muscle, adipose tissue, and the gastrointestinal, hematopoietic, and immune systems; complications related to deficiencies of multiple micronutrients; and the maladaptive activation of the inflammatory cascade. In addition to well-described pathophysiologic mechanisms involved in the higher mortality seen with PEW, also there is the potential role of novel factors such as circulating actin, gelsolin, and proinflammatory high-density lipoprotein ***(Dukkipati and Kopple, 2009)***.

In contrast to PEM, however, the effect of obesity, visceral obesity or the metabolic syndrome on morbidity and mortality is uncertain in HD patients. Fleischmann et al. and Kopple et al. have demonstrated that obesity was not associated with increased mortality over 1 year in HD patients. This phenomenon is in contrast to the general population, in which there is a significantly positive association between obesity and increased mortality.

Such a dialysis related change in the relationship between obesity and mortality is referred to as ‘reverse epidemiology’ ***(Kalantar-Zadeh and Kopple, 2006)***.

Causes of PEW

There are many causes of PEW in maintenance dialysis patients. Some of the most common causes are listed in Table (1).

- **Inflammation**

Inflammation may induce any degree of severity of PEW, and it may be associated with the most severe forms of PEW encountered in chronic dialysis patients. Indeed, although protein-energy malnutrition per se may reduce serum albumin levels, a serum albumin of less than 3.0 g/dL generally is associated with an inflammatory process ***(Stenvinkel, 2006)***.

Table (1) Causes of PEW

*A possible minor cause of PEW, •A theoretically possible cause of PEW

Inflammation	-Associated with clinically apparent diseases (eg, infected vascular access sites, systemic infectious illnesses including tuberculosis, diabetes mellitus, myocardial infarction, stroke, peripheral vascular ischemia, vasculitis) -Unassociated with clinically apparent diseases (eg, inflammatory reaction to vascular access catheters or grafts, peritoneal dialysis catheters, dialysis tubing, impure dialysate, old nonfunctioning transplant kidneys, kidney failure per se)
Decreased food intake	-Anorexia (eg, caused by uremic toxicity, emotional depression, medications, inflammatory disorders) -Non anorexic causes (financial constraints, medical or surgical illnesses—particularly but not exclusively of the gastrointestinal tract, impaired cognitive function, other mental disability, physical disability, loss of dentures)
Dialysate nutrient losses	Losses of amino acids, peptides, and proteins into dialysate. Losses of water-soluble vitamins and minerals during dialysis
Metabolic academia	
Hormonal disorders	Resistance to anabolic hormones such as insulin, growth hormone, insulin-like growth factor-I Increased levels of counter regulatory hormones, such as glucagon and parathyroid hormone
Increased fecal excretion of nitrogen *	
Decreased levels of anti-oxidants†	such as vitamin E, C, selenium, reduced glutathione (GSH)
Physical deconditioning •	
Carbonyl stress •	

(Fouque et al., 2008)

Inflammatory disorders engender PEW by several mechanisms such as the elaboration of inflammatory cytokines that promote catabolism, baseline energy expenditure and may suppress protein synthesis. Several inflammatory cytokines, such as tumor necrosis factor and interleukin-6, also promote anorexia, reduced appetite and food intake ***(Fouque et al., 2008)***.

In inflammatory states, serum levels of positive acute phase reactants increase and negative acute phase reactants decrease. Assessment of inflammatory markers is useful for distinguishing between both types of malnutrition in CRF: type 1 or pure malnutrition and type 2 or inflammatory malnutrition. The prognosis of patients with type 1 malnutrition and no inflammation is usually more favorable **(*Fouque et al., 2008)***.

- **Anorexia/Decreased Food Intake**

Nutrient intake, which does not meet a given patient's nutritional requirements, a common complication of end-stage renal disease (ESRD), often is caused by anorexia.

Anorexia can be caused by uremic toxins, inflammatory conditions with anorexigenic cytokines, superimposed illnesses including diabetes mellitus, possibly altered serum hormone levels, and psychiatric disorders, particularly depression ***(Dukkipati and Kopple, 2009)***.

Uremia may engender anorexia by the accumulation of toxic metabolites that normally are excreted in the urine or degraded by the kidney. One of the more recent exciting developments in understanding the link between anorexia and uremia has been the discovery of the protein leptin. Increased levels of serum leptin occur in chronic renal failure may be due to increased serum insulin and the acute phase inflammatory response which can stimulate leptin synthesis or may be secondary to impaired leptin degradation ***(Dukkipati and Kopple, 2009)***.

It is important to appreciate that there are causes for reduced food intake in persons with chronic renal failure that are not related to appetite. These causes can be financial, medical, surgical, mechanical, or caused by mental or physical debility (Table 1). ***(Kalantar-Zadeh and Kopple, 2006)***.

- **Dialysis Nutrient Losses**

Dialysis removes amino acids, peptides, and proteins, as well as many water-soluble vitamins and minerals. The extent and pattern of nutrient losses depends on whether the patient is receiving hemodialysis or peritoneal dialysis and the character of the dialysis procedure. For example, a single hemodialysis using a low-flux hemodialyzer removes about 6 to 8 g of free amino acids

if patients are in postabsorptive state and about 8 to 10 g when patients are postprandial ***(Foque et al., 2008)***.

An often overlooked cause of protein loss is the protein in the blood sequestered in the hemodialyzer and the blood lost with occult gastrointestinal bleeding or blood testing. A patient with a blood hemoglobin level of 12.0 g/dL and a serum protein of 7.0 g/dL loses about 16.5 g of protein in each 100 mL of blood removed ***(Foque et al., 2008)***.

Water-soluble vitamins and other bioactive compounds are removed by both hemodialysis and peritoneal dialysis. In patients with an adequate food intake these vitamin losses usually can be replaced by their diet. However, because the dietary vitamin requirements are increased for some vitamins, and because ESRD patients often are anorexic, it has been suggested that, as a precautionary matter, patients undergoing maintenance dialysis therapy should routinely take a vitamin supplement. The vitamin supplements in the appropriate and recommended amounts appear to be safe ***(Baily and Franch, 2010)***.

- **Acidemia**

Acidemia engenders protein catabolism and negative protein balance. Mehrotra et al have shown that an arterial blood pH of 7.43 to 7.45 is associated with a more positive protein nitrogen

balance than an arterial blood pH of 7.36 to 7.38. In maintenance hemodialysis and peritoneal dialysis patients who still have substantial residual renal function urinary bicarbonate losses also may contribute to metabolic acidosis ***(Mehrotra et al., 2004)***.

- **Hormonal Disorders**

Resistance to insulin, growth hormone, and insulin-like growth factor-I occurs in kidney failure and may promote PEW. On the other hand, increased serum levels of the catabolic hormones glucagon and parathyroid hormone in kidney failure also may contribute to PEW. Deficiency of 1, 25-dihydroxycholecalciferol, a common sequelae of kidney failure, may induce muscle wasting ***(Feldt-Rasmussen et al., 2007)***.

- **Miscellaneous**

There is evidence for a slight increase in fecal nitrogen excretion in maintenance dialysis and chronic peritoneal dialysis patients from about 1.3 g/d normally to roughly 1.5 g/d.

Reduced levels of such anti-oxidants as vitamin E, vitamin C, selenium, and reduced glutathione also are found in ESRD. It is not known whether these disorders may promote PEW.

Decreased physical conditioning often is profound in ESRD patients because of a combination of their comorbidity and

lack of physical exercise. It has been suggested, without any clear evidence, that physical deconditioning, as well as carbonyl stress, may contribute to PEW in chronic renal failure patients ***(Dukkipati and Kopple, 2009)***.

Prevention and treatment of PEW

- **Early initiation of renal replacement therapy**

Because the prevalence and severity of PEW often diminishes during the months after the commencement of maintenance dialysis therapy, it has been suggested that patients should be started on maintenance dialysis therapy earlier in the course of their renal failure. A number of nonrandomized retrospective studies have indicated that earlier initiation of renal replacement therapy is associated with greater survival ***(Mehrotra et al., 2002)***.

However, a variety of study designs, populations and health care delivery systems supports the conclusion that early initiation confers no survival benefit and argues against pre-emptive initiation of dialysis in asymptomatic patients ***(Friedma and Fadem, 2010)***.