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Can we Avoid the Dialytic Emergency using Ketoanalogues Until We Create Definitive Vascular access that Improve the Survival of the Kidney Patient?

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Abbreviations: KD: Chronic Kidney Disease; PEW: Protein Energy Wasting; ESRD: End-stage renal disease; IGF: Insulin-like Growth Factor; CVC: Central Venous Catheter

Introduction

One of the most difficult circumstances in a doctor's life is making decisions, especially when the patient's life depends on it. Renal replacement therapy in its hemodialysis support modality allows compensation for body parameters that may be potentially critical in a patient with renal failure and includes the placement of a vascular access, extracorporeal circulation of the blood component through a polysulfone filter and the return of this already purified. There are already defined criteria by which we can schedule admission to dialysis, such as: uremia, hyperkalemia, metabolic acidosis and hypervolemia. As chronic kidney disease (CKD) progresses until reaching stage 5, the probability of reaching dialysis support increases. Likewise, each of the stages requires an action plan that allows avoiding the progression of damage and managing the treatment of complications of the disease. CKD such as anemia, malnutrition, bone disease, neuropathy and decreased quality of life of the patient.

Protein Energy Wasting (PEW) is defined as a pathological state where there is a decrease or continued wear and tear of both protein deposits and energy reserves, including loss of fat and muscle [1]. Patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD) in particular have muscle wasting, sarcopenia, and cachexia that contribute to frailty and morbidity. DPE is characterized by the simultaneous loss of systemic body energy and protein stores that occurs due to the hypercatabolic state induced by uremia, acidosis, anorexia due to lack of appetite, resistance to insulin and insulin-like growth factor (IGF). -1), hyperparathyroidism, low testosterone levels and abnormalities in the thyroid profile, which drive hypermetabolism and low anabolism [2]. It is estimated that between 28% and 54% of dialysis patients are malnourished. However, nutritional deterioration usually begins before the patient enters ESRD, being 11-54% in stages 3-5 [2].To avoid a deterioration in nutritional status in these patients, early and effective nutritional intervention is desirable, with clinical follow-up that is maintained throughout the different phases of kidney disease. Nutrition is especially important in all groups of patients with renal failure (CRF), whether they are with or without hypercatabolia, both on dialytic support (hemodialysis or peritoneal dialysis) and in the pre-dialysis stage.

In fact, patients in the predialysis stage who are uremic and may constitute a potential dialysis emergency are of special importance. Here a great possibility arises of approaching the patient through a strategy that allows avoiding the uremic and inflammatory state and having vascular access that allows better survival. Alphafacetoanalogues are nitrogen-free ketoanalogues,

which provide a sufficient amount of essential amino acids and reduce the formation of endogenous urea, toxic ions and metabolic products [3]. Alpha ketoanalogues (Ketosteril) is a preparation that contains the essential amino acids: L-lysine, L-threonine, L-tryptophan, L-histidine and L-tyrosine; and alpha-keto or alpha- hydroxy acids: keto-leucine, keto-isoleucine, keto-phenylalanine, keto-valine, as well as hydroxymethionine, all as calcium salts. These keto or alpha-hydroxy acids are enzymatically transaminated to the corresponding L-amino acids. It is argued that Ketosteril would produce a set of metabolic effects that would in turn induce an improvement in uremic symptoms and signs, and a delay in the deterioration of glomerular function, allowing dialysis to be deferred in some cases [4] .

In a meta-analysis done by Sanchez in 2016, he found that most studies presented positive results using mainly very low protein diets (0.3 g/kg/d) supplemented with alpha ketoanalogues (3780 to 7560 mg/d) in CKD stage 4 and 5, showing an improvement in the levels of serum creatinine, urea, glucose, serum albumin, nutritional status, weight gain mainly in lean body mass, metabolic and endocrine control. Likewise, uremic signs were controlled, as well as toxicity and progression of renal failure [5]. Duenhas M, in 2013 demonstrated that a very low protein diet plus keto analogues is safe for maintaining the nutritional status of patients with ESRD until the creation and maturation of the Arteriovenous Fistula or placement of a peritoneal Dialysis catheter, even in diabetic patients. It was found that 62% achieve the creation of permanent access to initiate renal replacement therapy and reduce uremic symptoms and morbidity related to emergency vascular access without deterioration of nutritional status [6]. Maggiani -Aguilera also reports that the central venous catheter (CVC) as vascular access in hemodialysis is associated with adverse events, and that patients who do not have a CVC at the beginning of dialysis have lower mortality than those who have a CVC, in the same way the Conversion to permanent access reduces the risk of hospitalization [7].

Mocanu et al, demonstrate in 10 years of follow-up that renal survival and survival of non-diabetic patients is better with a very low protein diet supplemented with ketoanalogues (0.3g/kg-day supplemented with ketoanalogues 1tb /5kg- dry weight , during meals) than with a low protein diet (0.6g/Kg-day) supplemented with them (78 vs 26% and 83 vs 58%) (Figure 1 & 2). Likewise, it showed that with a low protein diet supplemented with keto analogs (0.6g/kg-day supplemented with keto analogs 1 tb /10 kg-dry weight) there is a 70% decrease in proteinuria (5.2 vs 1.6 g/g creatininuria) , as well as significant improvement in nutritional markers: BMI (26 versus 27.1 kg/m^2), serum albumin (4.1 versus 3.9 g/dl), C-reactive protein (9 versus 14 mg/L) [8]. For its part, the Core Curriculum 2022 and the KDIGO 2024 Guidelines points out that according to various meta-analyses, a very low protein diet supplemented with keto analogues delays the start of dialytic therapy and significantly reduces urea production, as well as improves insulin resistance and oxidative stress. They also recommend that the diet be planned by a nutritionist who is an expert on the subject and that it be administered to an adherent and motivated patient. Finally, they suggest giving between 0.3-0.4 g/kg per day and adding ketoanalogs in patients at risk of kidney failure until obtaining a protein requirement of 0.60 g/kg per day [3,9]. Recently, Chang and Rhee consider dietary intervention as the cornerstone of clinical treatment to delay or avoid admission to dialysis; and that despite concerns about the consequences of decreased protein and energy intake, it is nutritionally adequate [10]. Finally, Garneata L demonstrates that a low-protein diet supplemented with ketoanalogs appears effective in safely postponing renal replacement therapy by reducing proteinuria and decreased renal function in advanced diabetic kidney disease [11].

We can conclude then that there is clear evidence that diets very low in protein and supplemented with ketoanalogues delay admission to dialysis and improve nutritional parameters, allowing dialysis urgency to be avoided and the patient to have safe vascular access.

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