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Editorial

The Nephrology-Nutrition Binomial in Hemodialysis Patients. A Multidisciplinary Puzzle to be Solved in the Clinical Practice

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Editoral

Malnutrition and Protein-Energy Wasting (PEW) are common conditions which prevalence is up to 80% in HD patients [1]. Several contributing factors as advanced age, dialysis procedure, inflammation and comorbid related-conditions (cardiovascular disease, diabetes, metabolic derangements, anorexia etc.), intervene on nutritional status. Additionally, nutrient loss during dialysis such as amino acids, some peptides, blood, vitamins, trace elements, and glucose may further carry these patients to an increased risk of PEW.

Emerging evidences [1,2] suggest that nutritional management is a mandatory procedure in patients receiving HD treatment. Malnutrition, one of the main criteria for initiating dialysis, is considered an independent predictor of morbidity and mortality during the first two years in renal replacement therapy in HD patients [3], as well as an exclusion criterion in kidney transplantation list. As malnutrition, PEW appears to be a significant prognostic factor in HD patients. Improving nutritional status through dialysis adequacy and nutritional assessment could improve clinical outcomes. Therefore, management of nephron-nutritional binomial might be an approach in clinical practice of a complex-disease puzzle in HD. The potential aims of the management nephron-nutrition binomial are classified into four consecutive steps in HD patients: a) to prevent malnutrition and deliver adequate dialysis dose; b) precocious assessment and early diagnosis of malnutrition, inflammation and dialysis associated factors; c) to guarantee an adequate medical-nutritional treatment as many of responsible causative factors as on adverse clinical effects and, d) to provide nutrition support and the therapeutic strategies required at any time.

Dialysis adequacy and vascular access are major pre-requisites in well–nourished patients and/or wasted patients for achieving and/or maintaining nutritional status [4]. The use of central venous catheter as potential foci of inflammation should be avoided. Minimum adequacy of the delivered dose (Kt/V urea single pool ≥ 1.2) has been recommended to maintain optimal dietary nutrient intake and nutritional status. Several studies [5,6] showed that protein nitrogen appearance is dependent on the type and the dose of dialysis, suggesting a relationship between under dialysis and anorexia. Epidemiological data [5,7] showed that improving the efficiency of HD, and increasing frequency and duration of HD treatment, had better volume control and clearance efficiency of uremic toxins, middle molecular weight compounds and improved nutritional status and quality of life. Currently, the doses of dialysis that can improve nutritional status are still unknown. However, a low systemic inflammatory response, maximum biocompatibility of the dialysis membranes and, control of chronic foci of infection should be achieved. As the dialysis procedure promotes a catabolic inflammatory stimulus *per se,* the effects of dialysis membranes related with middle molecules clearance as a source of inflammation and the type of daily sate using with ultrapure water should also be taken into account.

Recent studies [8,9] on HD techniques have attracted much attention as promising optimum modalities to maintain or improve the nutritional status on HD patients. Patients in on-line Hemodiafiltration (HDF) showed fewer requirements of phosphate binders, better control of hypertension with fewer use of antihypertensive drugs, less doses of erythropoietin stimulating agents, and iron supplements as a result of abolishing or reducing the inflammatory response [8]. Conversely, a recent study [9] showed that treatment with HDF did not reduce all causes of mortality compared with treatment with low-flux membranes in conventional HD therapy as non-significant differences in serum albumin, C-reactive protein and serum cholesterol during follow-up. Short daily dialysis, as compared with conventional HD, was associated with improved inflammatory status, and lower levels of interleukin-6 were observed following on-line HDF as compared with conventional HD [10]. Daily dialysis results in less fluid overload, fewer medications and dietary restrictions, better blood pressure and phosphate binder compared with conventional HD therapy. Clinical nutrition guideline [11], recommends daily short or long-nocturnal HD in malnourished or PEW patients as adjunctive therapy for 6-12 months. Exclusive hemodialysis technique factors to point out could be in clinical practice: a) increased of resting energy expenditure related with HD technique; b) ultrapure dialysis water as an essential requisite in on-line HDF, and whenever retro-filtration is presented. Previous points are highly increased with convective clearance therapies; c) vascular access, explicitly with regard to catheter as an external inflammation source; d) metabolic acidosis correction by using bicarbonate as buffer in HD session as well as for diminishing the oxidation of aminoacids and provide adequate protein intake in

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HD patients [12]. Daily HD or on-line HDF as adjuvant techniques can be also prescribed. Hemodialysis tailored to patient needs should be taken into account.

However, how to fit together the multiple pieces of which this complex and at the same time interesting puzzle is made up?. Malnutrition is a consequence of a substantial decrease in energy and/or protein intake, while PEW is characterized by the loss of somatic stores and visceral protein levels such as a remarkable elevation of pro-inflammatory cytokines, endogenous muscle catabolism, uremic anorexia and elevation of serum CRP in dialysis patients [13]. Main differences in PEW compared to malnutrition are that the latter encompasses mainly non-inflammation forms (undernutrition or overweight), whereas PEW is referred to mild degrees of metabolic depletion, inflammation and comorbid associated conditions (table 1). Additionally, cachexia is a complex metabolic syndrome associated with underlying illness and characterized by loss or decreased of muscle strength with or without loss of fat (corrected for overload volume) [14]. Nutrition-related factors with impact on HD patients to taken into account might be: etiology of CKD as a pioneering of nephron-nutritional binomial; frequent hospital admissions as a potential cause of PEW; anorexia by retention of uremic toxins and under dialysis, and advanced age as a dynamizing element of frailty and malnutrition. The nephro-nutritional binomial is strongly associated with clinical prognosis in each one of stage disease. Malnutrition per se, is reversible by dialysis and nutritional support, whereas at the end stage of PEW or severe forms as cachexia, are not only insufficient and inadequate but, seriously increasing mortality rates [1,15]. Since the onset and throughout the course of illness, HD patients should have access to a multidisciplinary team, to take part in a rehabilitation program tailor-made to their needs and consider the adequacy of dialysis and the use of specific nutritional support. As a compromised nutritional status is still a common feature of HD patients, the periodic nutritional assessment even in well-nourished HD patients, should be a part of the clinical procedure to diagnoses and treatment as early as possible in order to improve survival. Preventive nutritional strategies include nutritional counseling adapted to each stage of CKD and type of HD, might help to reduce and/or prevent malnutrition and some of the PEW conditions. But there remains the unresolved problem of complex nephron-nutrition puzzle. The main point of the nephron-nutrition binomial that may be of interest is integrating the presence of constituents derived from malnutrition and HD technique. The management of nephron-nutrition binomial requires and active commitment to measuring and registering the appropriate outcome indicators relevant to the nutritional diagnosis' signs and symptoms as a follow: a) nutritional screening to identify patients at nutritional risk by using validated screening tools as subjective global assessment or malnutrition-inflammation score in HD patients; b) patients at risk of malnutrition or PEW should be diagnosed by a comprehensive nutritional assessment which includes serum albumin and or prealbumin concentrations, bioinflammatory markers and body composition analysis (anthropometric measures, electrical bioimpedance) and hand-grip strength. Malnutrition or PEW should be discarded, and, c) planning nutritional therapy based on multimodal-multidisciplinary strategies (nutritional counseling. nutritional support by oral nutritional supplements, enteral nutrition or intradialytic parenteral nutrition and pharmacological interventions) when required.

Table 1: Proposed classification of and types of malnutrition in hemodialysis patients.

Parameters	Malnutrition	Protein-Energy Wasting (PEW)	Cachexia
S-albumin	Normal or low	Low	Very low
Comorbidities	Uncommon	Common	Common
Inflammation	Absent	Present	Highly present
Food intake/Appetite	Insufficient/ Loss of appetite	Highly insufficient/ Anorexia	Very highly insufficient/ Anorexia
Resting energy expenditure	Normal	Increased	Highly increased
Volume Overload	Mild	High	Very high
Oxidative stress	Increased	Highly increased	Highly increased
Protein catabolism	Normal or slighty increase	Increased	Highly increased
Reversible by dialysis and nutritional support	Yes	Mild forms could be reversible No, at advanced-stage of PEW	No

Source: Modified from Stenvinkel et al [16] and Ruperto et al [17] PEW: Protein-Energy Wasting

The re-evaluation of outcomes may also involve additional data collection in order to explore why the nutritional changes have not occurred as expected. This clinical approach provides consistency in the practice. Adds value and quality and demonstrates effectiveness of nutritional care. Thus, further holistic nutrition-dialysis approaches are required.

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