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Intradialytic parenteral nutrition in malnourished patients with chronic kidney disease: a systematic review

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Abstract

Introduction: Malnutrition is a prevalent condition among patients with chronic kidney disease (CKD). **Objective**: To answer the question of the effect of intradialytic parenteral nutrition (IPN) on malnourished CKD patients undergoing dialysis, a systematic review of clinical trials was performed. **Methods**: The systematic review was performed according with PRISMA. The review was carried out between September and October 2022. The search strategy included PubMed, Web of Science and LILACS databases. The selection of articles was carried out using the Rayyan platform and to assess the chance of bias, the Rob2 instrument recommended by Cochrane was employed. **Results and Conclusions**: From 762 article retrieved in the initial strategy only 4 articles were included in the review. In a general view, the use of IPN increased the levels of prealbumin and albumin in the participants. Studies evaluating this topic are sparse. More studies are needed to recommend the use of IPN universally in the context of malnourished patients with CKD.

Keywords: Parenteral Nutrition. Chronic kidney Disease. Renal Dialysis. Malnutrition. Albumins. Prealbumin.

Introduction

Malnutrition is a prevalent condition in individuals with Chronic Kidney Disease (CKD) **[1-6]**. Malnutrition in this group of patients is considered a multifactorial condition **[2]** and is considered a poor prognostic factor, especially in the elderly **[7]**. It is expected that some patients with CKD will undergo renal replacement therapy through hemodialysis **[7]**. The hemodialysis process consists of pumping heparinized blood through the dialyzer at a flow rate of 250 to 450 mL/min, while the dialysate flows in an opposite direction in countercurrent 500-800 ml/min **[8]**. In this procedure, it has been described that in each hemodialysis session about 12 g of amino acids **[1]** and around 200 to 480 kcal of energy is withdrawn.

The intradialytic supply of nutrients and proteins has been highlighted as an intervention that could be performed early in patients with CKD and malnourished **[2]**. This caloric protein support does not favor uremia **[9]**. It has been reported that circulating urea and phosphate concentrations were not affected by protein intake or by intradialytic exercise **[9]**. In recent decades, with the development of parenteral nutrition in the most dissimilar clinical settings, the use of this intradialytic parenteral nutrition (IPN) has been gaining ground in the context of patients with CKD and severe malnutrition, especially after the failure of oral and enteral nutrition **[2]**.

The objective of the present study was to survey the existing evidence regarding the benefits that the use of IPN may have on the state of malnutrition through a systematic review of the literature.

Methods

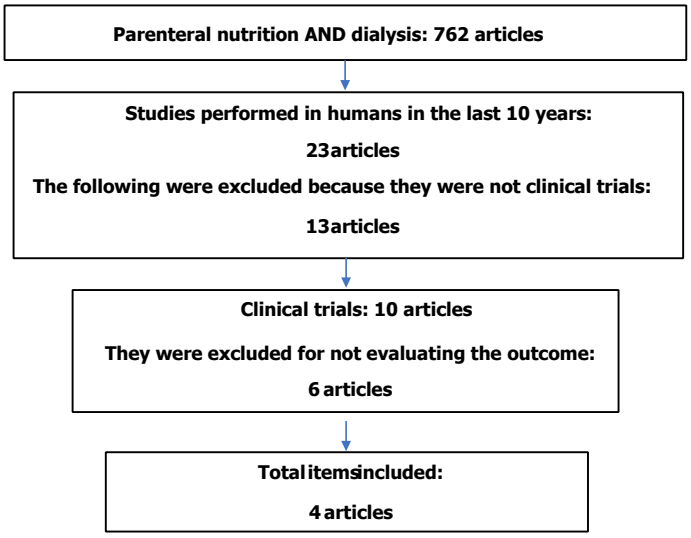
The present study is a systematic review of the literature, which, according to Cochrane, can be understood as research that seeks to gather evidence that fits prespecified eligibility criteria to answer a specific research question **[10]**. The review was conducted based on the following guiding question: What is the effect of prealbumin and/or albumin of IPN use in malnourished adults with CKD undergoing dialysis treatment?

Inclusion criteria were defined as being clinical trials, published in the last 10 years, having been carried out in humans, in individuals over 18 years of age, undergoing dialysis treatment for chronic renal failure, and having evaluated the effect of IPN on albumin levels and /or prealbumin. Those studies with observational, review, theoretical, carried out in animals, pregnant women, or children would be excluded. Articles that still met the inclusion criteria and had evidence of bias in their methodology would also be excluded.

The search strategy included PubMed, Web of Science and LILACS databases. The open search terms were used: parenteral nutrition AND dialysis. The review was carried out between September and October 2022. Figure 1 shows the flowchart referring to the search strategy, as well as the selection of articles. The selection of articles was carried out by the authors JMM, VA and RC, using the Rayyan platform **[11]**. Data extraction was performed by the authors JMM and YRH. To assess the chance of bias in the clinical trials selected for the review, the Rob2 instrument recommended by Cochrane **[12]** was used, indicating a low chance of bias in the selected studies.

Results

In the search strategy (Figure 1) 762 results were identified. After restricting the search to humans, over 18 years old and published in the last 10 years, 23 articles remained. After restricting to clinical trials, only 10 articles remained. After reading them in full, 6 articles were excluded because they did not assess the outcome of interest. Finally, 4 clinical trials were included in the review. The bibliography sections of the selected articles were also reviewed. No new publications have been incorporated.



Source: Own Authorship.

Figure 1. Flowchart of search and sampling of articles evaluating the association between intradialytic parenteral therapy and protein-calorie malnutrition in patients with chronic renal failure on dialysis through hemodialysis.

The characteristics extracted from the articles are shown in Table 1. It can be seen in the table that the years of publication of the works varied between 2016 and 2022. Of the four articles, three were published in journals in the field of nutrition, two in Clinical Nutrition and one in the Asian Pacific Journal of Clinical Nutrition. The other work was published in Science Reports, from the Nature group, all with an excellent concept and impact factor, given that it would be important for the quality of the productions. After evaluation by the Cochrane Rob2 instrument **[12]**, a low chance of bias was concluded in the selected studies. All included studies were randomized trials and had a control group.

Table 1. Summary of sampled articles evaluating the association between intradialytic parenteral therapy and protein-calorie malnutrition in patients with chronic renal failure on dialysis through hemodialysis.

Author Year Journal	*Study design*	*Sample size and characteristics*	*Intervention*	*Results*
Kittiskulnam [13] 2022 Sci Rep	A randomized clinical trial, controlled, open-label	N = 38 Participants > 18 years old, on maintenance hemodialysis for at least 3 months The presence of protein-calorie deficit is defined as at least two of the following: serum albumin level ≤ 3.5 g/dL, serum prealbumin ≤ 30 mg/dL, subjective global assessment (7 points)	Intervention: parental nutrition based on fish oil 3 in 1, infused for 3 months. Control group: intensive dietary counseling once a week for 3 months	After 3 months: Serum albumin was higher in the intervention group. Serum prealbumin was not statistically different. Other results: Spontaneous dietary intake, body weight, and inflammation score were improved in the intervention group. Muscle mass, strength, interleukin-6, high sensitivity c-reactive protein, and ghrelin were not significantly different between groups. Leptin levels increased in the control group. At 6 months: Serum albumin in the intervention group was persistently higher than the baseline.

Suryantoro [14] 2021 Asia Pac J Clin Nutr	A randomized clinical trial, controlled	N = 63 On hemodialysis, malnourished, assessed by global subjective assessment. They were evaluated at 0, 1, and 3 months	counseling group oral therapy group Intradialytic parenteral nutrition group	At months 1 and 3, nutritional therapy was associated with improvements in all 3 study groups. Increases in serum albumin. Other results: Arm circumference and triceps and biceps skinfolds were improved in the counseling group and the intradialytic parenteral nutrition group.
Marsen [15] 2017 Clinical Nutrition	A multicenter clinical trial, randomized, open, controlled, of parallel groups	N= 107 Moderate or severe malnutrition (SGA score B or C), maintenance hemodialysis therapy (3 times a week) for more than six months, and presence of two of the following three criteria: albumin <3.5 g/L, prealbumin <250 mg/L, alpha phase angle <4.5 as assessed by bioelectrical impedance (BIA)..	Intervention group: standardized nutritional counseling plus intradialytic nutritional therapy, three times a week for 16 weeks, followed by a 12-week treatment-free period. Control group: standardized nutritional counseling only.	Intradialytic parenteral nutrition significantly increased prealbumin after 16 weeks of treatment showing sustained response thereafter. The intervention had greater effects on patients suffering from moderate malnutrition (SGA B score) compared to patients with severe malnutrition (SGA score C).
Liu [16] 2016 Nutrients	A clinical trial, controlled, with 2 arms,	N=36 Non-diabetic patients on dialysis for more than 3 months were included in the study.	Non-diabetic hemodialysis patients were randomized to three treatment groups: oral supplementation, oral supplementation plus high-concentration glucose solution (250 mL containing 50% glucose), and these two interventions. plus 8.5% amino acid solution, parenteral.	The amino acid group had significantly higher albumin levels compared to the glucose group and significantly higher prealbumin levels compared to the control group Other outcomes: All three groups had improvement in hemoglobin and a decrease in transferrin. Total cholesterol was unaffected in either group. LDLc was lower in the control group. Calcium was higher in the amino acid group. Post-dialysis amino acid levels were better in the 50% glucose group.

Source: Own Authorship.

The instrument most used by the authors of the reviewed clinical trials to assess malnutrition was the Subjective Global Assessment (SGA) **[13-15]**. Serum albumin levels were measured in two of four articles **[13,14]**, whereas serum prealbumin levels were measured in three of four articles **[13, 15,16]**. Improvements in albumin and prealbumin levels after IPN intervention were observed in all studies (Table 1). This improvement was still evident three months after the intervention **[13-15]**, and in two studies the effect on the improvement of prealbumin and albumin levels was maintained up to 6 months after the intervention **[13,15]** (Table 1).

Can also emphasize the fact that the characteristics of the substances that were infused as part of the intervention were different between the studies, therefore there is a lot of heterogeneity in the type of diet used between the articles (Table 1). In addition to the outcome of interest in this review, the articles evaluated other characteristics that were also reported in Table 1. Kittiskulnam et al. evaluated spontaneous dietary intake, body weight, and inflammation score with improvement in the intervention group, while ghrelin levels were higher in the control group **[13]**.

The work by Suryantoro et al. evaluated arm circumference and triceps and biceps skinfolds. They improved in the counseling and parenteral nutrition groups, but not in the oral therapy group **[14]**. The study by Liu et al described that there were no differences between groups in total cholesterol levels, that there were improvements in hemoglobin levels in the three groups under study, with a decrease in transferrin, and that the best levels of amino acids, in general, were found in the 50% glucose group **[16]**.

Discussion

The present review points to the fact that intradialytic parenteral nutrition in patients with protein-caloric malnutrition on hemodialysis due to CKD improves prealbumin and albumin levels. This improvement in serum levels of prealbumin and albumin markers was maintained for 3 and 6 months after the intervention. As far as we know, the present work is the first systematic review trying to raise evidence regarding the effect of intradialytic nutritional therapy using parenteral nutritional therapy in patients with CKD and malnutrition.

The importance of worrying about avoiding or reversing the state of malnutrition is evidenced by the fact that it is considered a predictor of mortality among patients with CKD in advanced stages **[5,17-19]**, as well as hospitalizations and low quality of life **[5]**. Protein-calorie malnutrition in these patients can be considered multifactorial **[2]**. Evaluating serum levels of prealbumin and albumin as markers of malnutrition in patients with CKD seems to be appropriate **[5,19]**.

The most important limitation of the present work is the scarcity of publications related to the topic of IPN in CKD. This denotes the real need for more research involving this group of patients and this type of intervention. New research addressing outcomes in patients with CKD according to a set of variables that assess nutritional, inflammatory, and oxidative status is being improved **[18]**. Despite the heterogeneity found in the types of formulas administered by the different articles during the IPN intervention, effects on albumin and prealbumin levels were identified. Studies to try to define which would be the best formula to be used are a necessity.

Conclusions

Intradialytic parenteral nutrition improves the state of protein-calorie malnutrition in patients with CRF on dialysis. More studies evaluating this topic are needed.

CRediT

Author contributions: **Conceptualization -** Jeovany Martínez-Mesa, Nádia Juliana Beraldo Goulart Borges Haubert. **Data curation -** Jeovany Martínez-Mesa, Rafaela Cabeda, Verônica Albrecht; **Formal Analysis -** Nádia Juliana Beraldo Goulart Borges Haubert; **Investigation -** Jeovany Martínez-Mesa, Nádia Juliana Beraldo Goulart Borges Haubert; **Methodology -** Verônica Albrecht, Natalia Bassani Schuch, Yudeisy Rodríguez-Hernández; **Project administration -** Jeovany Martínez-Mesa , Nádia Juliana Beraldo Goulart Borges Haubert; **Supervision -** Nádia Juliana Beraldo Goulart Borges Haubert; **Writing - original draft -** Jeovany Martínez-Mesa; **Writing-review & editing -** Jeovany Martínez-Mesa**,** Rafaela Cabeda, Verônica Albrecht, Natalia Bassani Schuch, Yudeisy Rodríguez-Hernández.

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The authors declare no conflict of interest.

Similarity check

It was applied by Ithenticate@.

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