Supplementation for sarcopenia in chronic kidney disease: Updated literature review

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ABSTRACT

Sarcopenia is the loss of muscle mass and strength, common in elderly patients and worsened by the presence of chronic kidney disease (CKD), which has a progressive decrease in the number of nephrons. Anaerobic physical exercise and protein supplementation are important for maintaining strength and muscle mass. Dietary interventions, such as greater protein intake, are essential to preserve and increase muscle mass. Leucine appears to be the most powerful amino acid in stimulating muscle anabolism. Testosterone and L-carnitine supplementation may also be helpful, but there is controversy regarding their use. Omega 3, vitamin D and calcium are supplements that can increase muscle mass and improve muscle function in patients with sarcopenia associated with CKD, but their dosages are still debatable. This review article aims to describe oral supplementation for sarcopenia and the kidney changes that they may cause. In summary, physical activity and protein supplementation are fundamental in the treatment of sarcopenia in patients with CKD.

Keywords: Sarcopenia, Chronic Kidney Disease, Supplementation, Elderly.

1 INTRODUCTION

Chronic kidney disease is a pathology with a multifactorial cause, which occurs as a result of irreversible alterations in renal function and physiology1.

It occurs slowly, silently, and progressively. Incidence and prevalence are associated in the older population1.

Renal function is verified through the glomerular filtration rate, which gives us the total amount of filtrate per unit of time, so in CKD there is a decrease in this filtration2. The loss of regulatory, excretory and endocrine functions of the kidney end up evolving with several complications, among them, we highlight sarcopenia, which is a progressive loss of tissue and muscle function associated with the aging process, but which is associated with CKD, and may be present from the early stages that worsens with the progression of the disease2, 3, 4.

Because of this, it is important to diagnose and treat sarcopenia early in patients with chronic kidney disease, anticipating an unfavorable outcome. The presence of sarcopenia in individuals with CKD is associated with poor quality of life, increased likelihood of falls, cardiovascular events, and higher morbidity and mortality.

Currently, treatments available to improve sarcopenia include:

- Personalized physical activity program
- Pharmacological treatment
- Nutritional therapy (oral nutritional supplement)[3, 5].

The objective of this review is to survey the articles, mainly from the last five years, related to the non-pharmacological treatment of sarcopenia and the renal alterations that they may determine.

2 METHODOLOGY

The methodology chosen to carry out this research was a literature review with an exploratory approach.

For Marconi and Lakatos (2019), literature reviews have the purpose of putting the researcher in direct contact with everything that has been written, said or filmed on the subject. It is not a mere repetition of the subject, but provides an analysis of the theme from another point of view or approach, in order to reach new conclusions6.

The research followed the recommended methods, after choosing the theme and preliminary research. The samples, were read, selected, evaluated and analyzed. The characteristics of the research were defined and then the results were discussed, interpreted and presented.

3 MATERIAL AND METHODS

This study was based on 15 articles in national and international publications, preferably in the last 5 years, in the PubMed, Scholar Google and Scielo databases, using the following keywords: sarcopenia, CKD, supplementation and elderly.

4 RESULTS AND DISCUSSIONS

The data found in the exploration of these articles showed:

The elderly population is considered a risk group for CKD, where it has been evidenced in the presence of chronic kidney injury, where we have verified a progressive decrease in the number of nephrons with an estimated loss of about 48% up to 75 years of age7. For this, two parameters are evaluated, the serum creatinine level (CrS) and the amount of urine output, in order to diagnose chronic kidney disease[7].

Sarcopenia is common in elderly patients and is aggravated in the presence of CKD7. The parameters of loss of muscle mass and strength are used, in which they show that, over the age of 50, muscle mass decreases by 1 to 2% per year, while muscle strength decreases at a rate of 1.5% per year, increasing to 3% at age 60. In the general population, the prevalence of sarcopenia in adults, aged 60 to 70 years, ranges from 5 to 13%, increasing to 11 to 50% in those aged 80 years and older. In patients with CKD, the reported prevalence of sarcopenia ranges markedly from 3.9% to 98.5%[8].

4.1 SARCOPENIA IN CHRONIC KIDNEY DISEASE

Progressive load-bearing exercise training can induce improvements in sarcopenia and health-related quality of life. It reinforces that physical exercise and protein supplementation are essential interventions to maintain strength and skeletal mass3,8.

Sarcopenia is more common in advanced age, but in patients with CKD it is aggravated due to the prevalence of a uremic state leading to metabolic acidosis, reduced protein synthesis and increased protein degradation, producing a positive nitrogen balance8,9. In CKD, in addition to the development of metabolic acidosis, this persistent catabolic state causes an increase in insulin resistance and a decrease in anabolic hormones, for example: Gh; IGF1; testosterone, in addition to vitamin deficiency7[,8,9,10].

The pro-inflammatory state is probably the most common cause of muscle tissue depletion. Cytokines activate the transcription of nuclear factor NF Kapa-B, which results in decreased muscle protein synthesis, TNF-alpha is highly specific for stimulating the proteolysis of heavy-chain myosin. In addition, cytokines stimulate the release of cortisol and catecholamines from the adrenal gland. As a result, it results in muscle loss and atrophy7,8,9.

4.2 NUTRITIONAL SUPPLEMENTATION

Dietary interventions are essential to preserve muscle mass and promote its elevation, providing an energy and protein load to recover the adequate nutritional status for the health of patients who already have established CKD, especially when the processes of mass and strength reduction are already taking place1,9. The recommended daily requirement of protein intake for CKD patients is twice as high as that of the general elderly population8.

Authors recommend a protein intake of 0.6 to 0.8 g/kg body weight per day (in stages III-V) without presenting a deficit for glomerular filtration rate1,9,10 and the introduction of 2 servings of WP-MND (21g of protein, 3g of leucine, 10 µg of vitamin D and 500 mg of calcium) for a period of 6 months. did not result in deterioration of renal function and no vitamin D or calcium toxicity, the product was overall well tolerated[2].

The use of leucine as a supplement stimulates muscle protein synthesis in older patients, being considered the most potent amino acid in stimulating muscle anabolism and inhibiting catabolism10.

As for testosterone, its use is indicated from the weekly dosage of 100mg of Nandrolone for a period of 24 weeks, there will be an increase in appendicular lean mass in two times. But we should look at testosterone replacement, especially in women [11, 12].

On the other hand, according *to Sabatino et al* (2021), protein supplementation in elderly patients with stage III to V CKD is still a subject to be debated due to controversies10.

A co-ingestion of leucine with a bolus of dietary protein for a supplementation period of 16 weeks will stimulate protein synthesis. 2.5g – 3.0g of leucine associated with about 25 to 30g of protein was analyzed to increase anabolism, through the mTOR signaling pathway: ribosomal kinase of 70 kDA - p70S6k; eukaryotic initiation factor 4E - 4E-BP1 and eukaryotic initiation factor 4G - eIF4G have been shown to increase muscle mass[10,11,13].

Although L-carnitine supplementation significantly increases muscle area in CKD patients, exercise seems to be the therapeutic action with the highest result in the population with sarcopenia associated with advanced kidney disease, and nutritional and pharmacological interventions lack effective proof[14,15].

Reports mention that large protein supplementations tend to decline renal function, generating renal hyperfiltration and hyperemia, accelerating chronic kidney disease, associated with several metabolic alterations16.

The use of omega-3 fatty acids in elderly patients with CKD-associated sarcopenia increases muscle mass, reduces oxygen demand during physical activity, and prevents muscle catabolism4,11. Anabolism occurs through the ingestion of 1g - 2 g of omega 3 at intervals of up to 150 days (acting on the mTOR-p70s6k signaling pathway) concomitantly with anaerobic physical exercise[11].

Vitamin D supplementation, which is essential for calcium absorption, resulted in the improvement of muscle trophism and minimizing falls, at a dosage of 1,200mg – 1,500mg/day11,12.

The association of calcium with vitamin D strengthens musculoskeletal function (calcium carbonate 1,200mg - 1,500mg/day), which is essential to meet the deficiency of sarcopenic patients with CKD17,18.

From the analysis of the various opinions, we noticed that the less recent articles recommended the need for a double dose of protein supplements, but that they would cause worsening of renal function8,15. Current studies show that leucine supplementation is more effective in preserving renal function2,10,11.

Anaerobic physical activity is a consensus, and it is necessary for the effectiveness of protein supplementation3,7,8,11,12,13,15.

Vitamin D, omega-3 and calcium supplementation are important as adjuvants in the treatment of sarcopenia in CKD4,11,12,17,18.

5 CONCLUSION

After analyzing the articles dealing with the non-pharmacological treatment of sarcopenia in CKD, we found a consensus on the indication of anaerobic physical activities associated with supplementation.

The emphasis was on protein supplementation based on leucine, due to its efficacy in stimulating muscle trophism, in addition to being the one that least harms renal function.

The use of other supplements, omega 3, vitamin D and calcium are also effective when administered adjunctly, however, more studies are still needed focusing on their doses and mechanism of action.

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