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Protein and Vitamin D Supplementation in Sarcopenia: A Review

ABSTRACT:

RESEARCH OBJECTIVE: Perform a review of protein and vitamin D supplementation in Sarcopenia.

THE RESEARCH PROBLEM AND METHODS: Demographic change implies new demands for public health, with health promotion and prevention activities seeking to delay the appearance of common diseases in elderly population. We performed a review of protein and vitamin D supplementation in Sarcopenia.

THE PROCESS OF ARGUMENTATION: Changes in body composition occur during the aging process, resulting in increased body fat and reduced muscle mass and also bone mass. Sarcopenia is defined by a syndrome characterized by generalized and progressive loss of muscle mass and strength. After 50 years, there is a reduction between approximately 1% and 2% of muscle mass per year.

RESEARCH RESULTS: Currently progressive resistance training is the most well-established intervention, and dietary interventions such as protein and vitamin D also mentioned in literature. Leucine is a branched chain amino acid knows as key role in muscle protein synthesis. The consumption of leucine-enriched amino acids showed beneficial effects in the elderly contributing to the conservation of skeletal muscle mass. Vitamin D has pre-hormone functions, vitamin D deficiency is related with diffuse musculoskeletal pain, myopathy, sarcopenia and falls. Vitamin D supplementation of 800 to 1000 IU/day is associated with increased muscle strength in the elderly.

CONCLUSIONS, INNOVATIONS AND RECOMMENDATIONS: The protein and vitamin D supplementation are strategies that are proving to be important for the prevention and treatment of sarcopenia, especially when associated with resistance training.

→ **KEYWORDS:** **AGING, SARCOPENIA, VITAMIN D, DIETARY SUPPLEMENTS**

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Aging world population

The World Health Organization (2015) estimates grow in elderly population from 12% to 22% of the world's population between 2015 and 2050, this 900 million to two Billion people in this age group. It is estimated that by the year 2020 the number of people over 60 years of age will be higher than children under five years old. This population growth occurring more expressively in developing countries. European countries have had more than a century to adapt to this ongoing population growth, countries like Brazil, China and India have a little over two decades to make the same adjustment.[1] This demographic change implies new demands for public health, with health promotion and prevention activities seeking to delay the appearance of common diseases in this population (WHO, 2015).

Aging, changes in body composition and sarcopenia

Aging is the major cause and risk of developing diseases in different systems as cardiovascular, neurodegenerative, endocrine system (Ehninger, Neff, & Xie, 2014). Changes in body composition occur during the aging process, resulting in increased body fat and reduced muscle mass and also bone mass (Miljkovic et al., 2015). According to the European Working Group on Sarcopenia in Older People (EWGSOP), sarcopenia is defined by a syndrome characterized by generalized and progressive loss of muscle mass and strength. After 50 years, there is a reduction between approximately 1% and 2% of muscle mass per year (Cruz-Jentoft et al., 2010). In sarcopenia, there is a decline of type II muscle fibers and replacement of lean mass by different types of tissues that have a reduced ability to synthesize proteins resulting in reduced muscle strength (Clark & Manini, 2008). The elderly with sarcopenia have difficulties in performing daily activities, poor quality of life, increased risk of falls and fractures, disability, dependence, periodic hospitalizations and increased mortality (Masanes et al., 2012; Janssen et al., 2004). Brown, Harhay, & Harhay (2015) evaluate the relationship between sarcopenia and mortality in 4425 elderly individuals during the years 1988 to 1994. The prevalence of sarcopenia was 36.5%. The mean survival of the elderly without sarcopenia was 16.3 years, compared with 10.3 years for those with sarcopenia, sarcopenia was related to increased mortality in this population. Tyrovolas et al. (2015) in a multicenter study (China, France, Ghana, India, Mexico, Russia, South Africa and Spain) analyzed factors associated with sarcopenia and reduction of muscle mass.

The prevalence of sarcopenia was 15.2%, ranging from 12.6% to 17.5%, higher in females. Other factors associated to the higher prevalence of sarcopenia in this study were the low socioeconomic status and reduced physical activity. The prevalence of sarcopenia in hospitalized elderly increase to 67.4% (Maeda & Akagi, 2016). The authors also found a relationship with greater cognitive impairment in elderly with sarcopenia.

During the aging process the reduction of muscle mass is related to the reduction in the number of muscle fibers, principally in type II. This reduction implies a decrease in the number and the response of satellite cells, whose function is to maintain skeletal muscle homeostasis and its regeneration (Miljkovic et al., 2015; Nilwik et al., 2013). Nilwik et al. (2013) observed after six months of resistance training intervention, hypertrophy of type II muscle fibers. Liu and Latham (2009) after three and six months of resistance training in the elderly showed an increase of muscle strength between 20 and 40%.

One of the signals involved in the process of protein synthesis in response to exercise is stimulated by Mammalian Target of Rapamycin (mTOR) through three main regulatory proteins: the ribosomal protein kinase S6 70 KDa (p70S6k); the eukaryotic initiation factor binding protein 1 4E (4E-BP1); and the eukaryotic initiation factor 4G (eIF4G) (Drummond et al., 2009). It is suggested that ally the TR it is necessary adequally concentrations of amino acids in plasma and muscle to stimulate muscle protein synthesis (Wolfe & Miller, 1999). Currently progressive resistance training is the most well-established intervention, and dietary interventions such as protein and vitamin D also mentioned in literature (Dodds & Sayer, 2014).

Sarcopenia: Diagnostic and social aspects

Although well defined in the literature what is sarcopenia, in clinical practice this is still an underdiagnosed disease due to the lack of a standard protocol for its diagnosis. Currently SARC-F is the most recommended and used, however according to the population may be necessary to associate different tools for its diagnosis. SARC-F has excellent specificity but poor sensitivity for sarcopenia classification (Ali & Garcia, 2014; Barbosa-Silva et al., 2016; Woo, Leung, & Morley, 2014).

Sometimes mistaken classifications may occur between sarcopenia and Cachexia. Cachexia is defined as multifactorial syndrome characterized by severe reduction of body weight, with or without fat loss and muscle loss due to an underlying disease (Evans et al., 2008). Usually, Cachexia is associated with increased catabolism that cannot be reversed by nutritional therapy alone (Ali & Garcia, 2014).

Dorosty et al. (2016) investigate the prevalence of sarcopenia and its association with socioeconomic status among the elderly in Tehran. The prevalence of sarcopenia found among the 644 participants varied between 16.5% by the Asian Working Group classification and 32.5% by the European Working Group classification. The authors found a higher prevalence of sarcopenia in the elderly of low income (20.5%) than in those of higher income (12.8%). It was also found an association of sarcopenia in relation to educational level, where the proportion of sarcopenia in illiterates, elementary school and diploma was 18.6%, 16.2% and 12.3%, respectively.

Recently a systematic review and meta-analysis performed by Beaudart et al. (2017) listed the main consequences of Sarcopenia in the elderly. We included in the review 17 studies where the main outcomes found in relation to Sarcopenia were: mortality, funcional decline, falls, fractures, length of hospital stay and hospitalization. Regarding mortality, the authors assessed by meta-analysis an overall OR of 3.596 (95% CI 2.96-4.37), indicating a higher risk of mortality for sarcopenic subjects compared with non-sarcopenic. A higher risk was found in the elderly older than 79 years (OR 4.42; 95% CI 3.60-5.42).

New perspectives of supplementation in the elderly for Sarcopenia

Protein supplementation and sarcopenia

Proteins are macronutrient formed by a succession of amino acids. Amino acids represent the basic structural unit of proteins. With regard to nutritional aspects these are divided: essential, conditionally essential and non-essential. Amino acids are present in foods of animal or vegetable origin, however animal origin have a greater amount of essential amino acids and are considered complete proteins (Cozzolino, 2007). One essential amino acids present in animal foods is leucine. Leucine is a branched chain amino acid knows as key role in muscle protein synthesis (Volpi et al., 2003). Branched-chain amino acids, especially leucine, practice a primary effect on mTOR signaling, thereby stimulating muscle protein synthesis (Kim et al., 2010). According to Bolster et al., 2004 the amino acid leucine directly stimulates in the skeletal muscle the synthesis of proteins through the activation of signaling pathways related to the initiation of the mRNA translation. The consumption of leucine-enriched amino acids showed beneficial effects in the elderly contributing to the conservation of skeletal muscle mass (Katsanos et al., 2006).

The quality and quantity of ingested amino acids has a direct influence on the muscular synthesis of proteins (Pasiakos, 2012). For the elderly, the daily protein intake recommendation ranges from 1.2g/kg to 1.5g/kg/day (Bauer, 2013).Another factor that should be considered is the absorption time of the proteins in the diet, and some sources take longer to be digested and absorbed. Rapid absorption of amino acids may favor the synthesis of postprandial protein and consequently protein reserves (Boire et al., 1997; Landi et al., 2016). Aging is also accompanied by the gradual reduction of food consumption (Budui et al., 2015). According to Nieuwenhuizen et al. (2010) with aging, there is a reduction in food intake of 25% between 40 and 70 years old. One of the causes this reduction is the reduction of appetite (physiological anorexia resulting from the aging process due to changes hormonal), smell, and satiety precocious (Wilson & Morley, 2003). A study with elderly individuals older than 70 years, Tarantino et al. (2007) found that approximately 40% of the population studied presented lower than recommended protein intake. The authors attributed this to dental problems, chewing difficulties, difficulties during digestion and also related to the absorption of proteins. Malnutrition is related to the development and progression of sarcopenia, so strategies related to nutritional interventions can be an important contributing factor in preventing and reducing the sarcopenia progression (Yanai, 2015). The most studied nutritional interventions of the increase the muscular protein synthesis are creatine, casein, essential amino acids and whey protein, but there contradictory results about the efficacy (Xu et al., 2014). The hypothesis of these studies is around the mechanisms of muscle protein synthesis by the mTOR pathway. Branched-chain amino acids, especially leucine, increase the activation of mTORC1 through TSC1 / 2 inhibition mechanisms or by Rheb (enriched homologue enriched in the brain) Rheb stimulation, which is a small GTPase required for Activation of mTOR (Proud, 2004). Leucine leads to a 50% increase in mTORC1 activation (Close et al., 2016). The study by Dickinson et al. (2011) sought to evaluate whether muscle protein synthesis after consumption of essential amino acids provide positive effects and the authors suggest the use of nutritional therapies reduce muscle loss and decrease muscle function.

Verlaan et al. (2015) in an observational case-control study, 253 volunteers with sarcopenia and 66 without sarcopenia, both older than

65 years, identified the elderly in the sarcopenia group had a higher body fat composition than the control group. In addition, the sarcopenia group had lower daily protein intakes than the non-sarcopenia group. Vitamin B12, phosphorus, selenium and vitamin D were also found to be lower in the sarcopenic elderly (Verlaan et al., 2015). Paddon-Jones and Rasmussen (2009) suggest that there is a need to consume between 25g and 30g/day of high-quality protein for the stimulation of muscle protein synthesis. Devries and Phillips (2015) in a review about the benefits of whey protein supplementation affirms the whey protein has better in amino acid quality, digestibility and bioavailability when compared other proteins supplements. Recently systematic review and meta-analysis developed by Colonetti et al. (2017) evaluated whey protein supplementation in the elderly associated a resistance training, observed an increase in total protein intake, increased concentration of leucine and mixed muscle protein fractional synthesis rate.

Supplementation of vitamin D and sarcopenia

Vitamin D has pre-hormone functions. For elderly and postmenopausal women, the recommendation in serum of 25 (OH) D above 30ng/mL (Maeda et al., 2014). The recommendation of daily intake of vitamin D for healthy population is 600 IU, for people older than 70 years old the recommendation is 800 IU/day (Ross et al., 2011). Tanner and Harwell (2015) conducted a review showing the relationship between vitamin D deficiency and muscle health. The authors related vitamin D deficiency with diffuse musculoskeletal pain, myopathy, sarcopenia and falls. The authors also point with aging, there is a reduction in vitamin D receptor expression in muscle tissue. Bischoff-Ferrari (2004) and Bischoff-Ferrari (2009) indicate the relationship between the use of vitamin D supplementation and reduction of falls in this population. Achakzai et al (2016) developed a study with 400 patients with musculoskeletal symptoms, the vitamin D deficiency was present in 80% this subjects. The authors concluded that there was a statistically significant association between low levels of vitamin D with the severity of clinical signs and musculoskeletal symptoms presented (Achakzai et al., 2016). Feng et al. (2016) analyzed the correlation between vitamin D levels of 686 individuals and quality of life, with aging the vitamin D deficiency ratios increased significantly in both sexes. The elderly with higher vitamin D deficiency had lower scores on the quality of life questionnaire, suggesting an inverse relationship between vitamin D levels and the quality of life in elderly people (Feng et al., 2016). Vitamin D deficiency has been discussed as a possible sarcopenia-related factor because of its relationship with muscle function (Tanner & Harwell, 2015). One of the interventions suggested for the treatment of patients with sarcopenia is the use of vitamin D supplements. Salles et al. (2013) suggest a positive effect of vitamin D supplementation on muscle protein metabolism. Sato et al. (2005) identified vitamin D supplementation resulted in an increase in type II muscle fibers. Muir and Montero-Odasso (2011) in their meta-analysis, concluded vitamin D supplementation of 800 to 1000 IU/day is associated with increased muscle strength in the elderly. Anagnostis et al. (2015) reviewed the use of vitamin D supplementation in postmenopausal women with sarcopenia. In their analyzes vitamin D plays an essential role in the skeletal muscle, indicating benefits in muscle strength and physical performance and in the prevention of falls. In the study the deficiency of vitamin D is related to the diagnosis of sarcopenia in elderly women (Anagnostis et al., 2015). Agergaad et al. (2015) conducted a randomized clinical trial with young and elderly men to evaluate the effects of vitamin D supplementation and resistance training on muscle function and muscle strength. After 12 weeks with daily vitamin D supplementation and training sessions three times a week, the authors observed an increase in type II muscle fibers in the elderly and in the young group. The authors associated vitamin D supplementation with increased muscle quality in elderly men (Agergaad et al., 2015).

Conclusion

Aging results in chances in body composition with increase in fat mass and reduction in muscle and bone mass. The sarcopenia is a syndrome characterized by generalized and progressive loss of muscle and strength. Currently resistance training is the most well-established strategy to avoid sarcopenia and its procession. The protein and vitamin D supplementation are strategies that are proving to be important for the prevention and treatment of sarcopenia, especially when associated with resistance training.

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