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Inflammatory mediators, muscle and functional performance of community-dwelling elderly women

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ABSTRACT

The purpose of this study was to investigate the correlation and association between inflammatory mediators and muscle and functional performance in elderly women. We conducted a cross-sectional study. Plasma concentrations of interleukin-6 (IL-6) and soluble receptor for tumor necrosis factor alpha (sTNFR1) were determined by enzyme-linked immune sorbent assay. The muscle performance was measured using a isokinetic dynamometer and assessment of handgrip strength was performed using a Jamar® dynamometer. Functional performance was assessed through a walking speed test. Statistical analysis was performed using the Pearson or Spearman correlation. The association between the variables was determined by multiple regression analysis. 221 volunteers (71.07 ± 4.93 years) participated in the study. Plasma levels of IL-6 (0.87 pg/mL) correlated with the power of the knee extensors ($r = 0.14$; $p = 0.03$) and the power of the knee flexors ($r = 0.16$; $p = 0.01$); the plasma levels of sTNFR1 (1051.70 pg/mL) did not correlate with any dependent variable. The regression models showed that the variables IL-6, level of physical activity and depressive status explained 5.5% ($R^2 = 0.055$, $p < 0.01$) of average power of knee extensors variability. For the average power of knee flexors, the final model showed that the factors IL-6 and level of physical activity explained 4.1% ($R^2 = 0.041$, $p < 0.01$). There was no negative correlation between inflammatory mediators and muscle or physical performance in elderly women. These results may be explained by the fact that the cytokine levels did not reach the threshold needed to influence the muscle tissue and functionality of the participants.

1. Introduction

Aging populations are a worldwide phenomenon, and the World Health Organization has stated that Brazil will have the sixth oldest population in the world by 2025. Like other countries, there is a predominance of women among the elderly population (55%) in Brazil, and there is growing interest in gerontological research on the "feminization of old age" phenomenon (IBGE, 2010).

The presence of an aging population leads to a greater prevalence of functional disability (Raiche, Hebert, Dubois, Gueye, & Dubuc, 2012). Several clinical measurements can be applied as predictors of function and disability in the elderly; gait speed, for example, has been noted to be a feasible, reliable, and valid measure (Fritz & Lusardi, 2009) as well as a predictor of adverse effects such as disability, risk for falls, and mortality (Studenski et al., 2009). According to Fried, Ferrucci, Darer, Williamson, & Anderson (2004) sarcopenia is one of the factors that influence performance on gait speed tests.

Based on a European consensus achieved in 2010, Cruz-Jentoft et al. proposed that sarcopenia is a geriatric syndrome characterized by loss of muscle mass and function without the need for the occurrence of disease for its appearance, although this process could be enhanced due to some chronic conditions. There is a high prevalence of sarcopenia among the elderly (Arango-Lopera, Arroyo, Gutierrez-Robledo, & Perez-Zepeda, 2012), and instruments such as isokinetic dynamometers and handgrip dynamometers can be used to assess muscle function (Aquino et al., 2002; Mathiovetz, Weber, Volland, & Kashman, 1984).

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Hormonal, metabolic, and neural factors, as well as level of physical activity and immunosenescence contribute to the development and progression of sarcopenia. For example, plasma levels of acute inflammation-phase proteins and cytokines such as IL-6, tumor necrosis factor alpha (TNF-α) are increased 2–4 times because of immunosenescence in aging (Krabbe, Pedersen, & Bruunsgaard, 2004).

Most studies on cytokines focus on IL-6, which has been called "the cytokine of the gerontologists" (Ershler, 1993). Its physiological role has been studied within the context of the acute inflammatory-phase response. Other authors report that IL-6 is a multifunctional cytokine, acting as both a pro-inflammatory and anti-inflammatory cytokine depending on the conditions (Pedersen, Steenberg, & Schjering, 2001). It is also suggested that an isoform of IL-6 produced during proper muscle contraction (myokine) would be capable of inhibiting pro-inflammatory cytokines. Another cytokine related to the pro-inflammatory condition in the elderly is TNF-α, which, like IL-6, participates in the inflammatory cascade event during the acute phase of a tissue injury (Pedersen et al., 2001).

Natural induction of cytokines during inflammation seems to have a positive effect; however, overproduction of cytokines and maintenance of an inflammatory state for an extended period would probably be harmful. High levels of pro-inflammatory cytokines have been shown to be negatively related to muscle strength and mass as well as to functional performance in the elderly (Haddad, Zaldivar, Cooper, & Adanis, 2005). However, there is no consensus in the literature on a cutoff point to predict adverse physical and functional outcomes; the data in the literature are conflicting and studies are scarce in Brazil.

Therefore, the purpose of this study was to investigate the correlation between the inflammatory mediators IL-6 and sTNFR1 and muscle and physical performance in community-dwelling elderly women and association between the variables.

2. Materials and methods

2.1. Study design and ethical aspects

This was a cross-sectional study. The Universidade Federal de Minas Gerais Ethics Committee approved the research protocol (ETIC 038/2010). We informed the participants of the characteristics of the study and they signed an informed consent form.

2.2. Sample

Sample selection was performed by convenience, and 221 community-dwelling elderly women aged 65 years or older were included in the study. Exclusion criteria were cognitive dysfunction as detected by Mini-Mental State Examination (MMSE) score, was considered indicative of the presence of cognitive impairment a score less than 18 for illiterates and 24 for participants with one or more years of study (Bertolucci, Brucki, Campacci, & Juliano, 1994), and self-report of acute inflammatory conditions; uncontrolled cardiovascular and metabolic conditions; history of cancer in the past 5 years; intake of anti-inflammatory, calcium blocker, or other drugs that could alter the immune system; presence of neurological deficits; fractures or history of osteosynthesis of the lower limbs in the past 6 months; and severe visual or hearing loss.

2.3. Instruments and procedures

2.3.1. Sample sociodemographic and clinical characterization

Information on sample characteristics in terms of sociodemographic data as well as the clinical condition of the participants, such as education, age, number of co-morbidities, and body mass index (BMI), was obtained using a standardized multidimensional questionnaire. The short version of the Geriatric Depression Scale (GDS-15) (Paradela, Lourenço, & Veras, 2005) was used to quantify depressive symptoms, and the Human Activity Profile (HAP) (Souza, Magalhães, & Teixeira-Salmela, 2006) was used to investigate the participants' level of physical activity. Depressive symptoms, level of physical activity, and BMI were measured due to their influence on the investigated variables. All questionnaires were administered by previously trained assessors.

2.3.2. IL-6 and sTNFR1 levels (independent variables)

Plasma levels of IL-6 and sTNFR1 mediators were measured by the enzyme-linked immunosorbent assay method using high-sensitivity kits for quantifying IL-6 and economy pack kits for quantifying sTNFR1 (Quantikine® HS, R&D Systems, Minneapolis, MN, USA). Measurements were duplicated, and assays were performed according to the manufacturer's instructions. Samples were read using a microplate reader capable of measuring absorbance at 490 nm, with the correction wavelength set at 650 nm.

2.3.3. Muscle performance of knee extensors and flexors (dependent variables)

Due to the relevance of knee muscles to the performance of daily activities, quadriceps and hamstring muscles were selected for the muscle function assessment, which was performed using a Biodex System 3 Pro® isokinetic dynamometer (Biodex Medical System Inc., Shirley, NY, USA). Participants performed a 5-min lower limb warm-up by walking on a flat surface before being positioned in the dynamometer chair. The selected range of motion for assessment was 90°, starting from 90° of knee flexion. Verbal feedback was provided during the assessment so participants would move the dynamometer lever as fast and as vigorously as possible (Perrin, 1993, Chapter 2).

Data analysis was performed using only the results obtained from the dominant lower limb, which was assessed with the question "If you were about to kick a ball, with which leg would you kick it?" (Dean, Kuo, & Alexander, 2004). The concentric–concentric mode was selected for assessment. The following isokinetic variables were chosen for analysis: peak torque/body weight, total work/body weight, agonist/antagonist ratio at the angular velocity of 60°/s with 5 repetitions, and average power at 180°/s with 15 repetitions. These variables were selected for their direct influence on physical performance. Angular velocities of 60°/s and 180°/s were chosen for most functional activities, being related to the ability to generate power at low speed (Ferri et al., 2003).

2.3.4. Handgrip strength (dependent variable)

Handgrip strength (HGS) in the dominant upper limb was isometrically measured using the Jamar® PC5030JI dynamometer (Sammons Preston, IL, USA). Participants were positioned according to the recommendations of the American Society of Hand Therapy (Crosby, Wehbe, & Mawr, 1994). For standardization, the dynamometer was set at the second or third handle position as deemed more suitable by the participant; the mean of 3 trials was obtained to derive the final score, with a 60-s rest between trials.

2.3.5. Gait speed test (dependent variable)

We used a Q & Q (Japan CBM Corp) stopwatch to measure habitual and fast gait velocity. In 2008, Graham, Osti, Fisher, & Ottenbacher performed a systematic review of assessment of gait speed and concluded that methodological differences in the literature made it difficult to compare results, and suggested that a distance of 10 meters should be used to standardize methods. Therefore, this was the distance selected for the estimation of gait