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Original research

Identification of high responders for interleukin-6 and creatine kinase following acute eccentric resistance exercise in elderly obese women

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ABSTRACT

Objectives: Resistance exercise is used as a non-pharmacological tool to elicit both gains in and maintenance of physical function in the elderly. Thus, the present study examined the acute response of creatine kinase and interleukin-6 following an eccentric resistance exercise session in elderly obese women classified as high responders or normal responders.
Design: Cross-sectional field study.
Methods: Ninety elderly obese women (69.4 ± 6.01 years) were tested for a 10 repetition maximum on the leg extension exercise and then completed an acute eccentric resistance exercise session consisting of seven sets of 10 repetitions at 110% of 10 repetition maximum with a rest of 3 min between sets. Subjects were divided into normal response or high response on the basis of the peak serum interleukin-6 (NR = 59 and HR = 7) and creatine kinase (NR = 81 and HR = 9) concentration being greater than (HR) or less than (NR) the 90th percentile.
Results: Creatine kinase was higher at 0 h, 3 h, 24 h and 48 h following the ERE for the HR group. The peak creatine kinase was significantly higher in HR group versus the normal response group. The average increase in the serum interleukin-6Δ for the HR group (~850%) was significantly higher versus the normal response group (~55%). Serum interleukin-6 was significantly higher at 0 h and 24 h following eccentric resistance exercise only for the high response group, while peak levels were significantly higher in high response group versus the normal response group ($p \leq 0.005$). Only one subject met the criteria to be classified as high response for both creatine kinase and interleukin-6 responsiveness.
Conclusions: Elderly individuals classified as high response experienced greater creatine kinase and interleukin-6 responses to ERE. Thus, a prudent approach for eccentric resistance exercise prescription might be programming additional recovery days and/or lower intensity training, especially in the beginning stages of a program.

1. Introduction

Resistance exercise (RE) is used as a non-pharmacological tool to elicit both gains in and maintenance of physical function in the elderly; specific RE training methods need further exploration to determine the best application and the risks for this population.[1] It is well known that RE can lead to muscle microtrauma, which is an important stimulus for muscular growth.[2,3] Creatine kinase (CK) concentration has been measured to assess the extent of muscle microtrauma following RE.[4,5] It was noted in previous research that some individuals expressed disproportionately greater CK concentration following the same volume of RE and were categorized as high responders (HR).[4,5]

It has been shown that eccentric exercise can induce greater muscle damage as indicated by greater CK concentration.[6] Moreover, there is an association between the acute inflammatory response and the muscle damage induced by eccentric exercise.[7] It is known that myofibers express interleukin-6 (IL-6), a key cytokine expressed in the inflammatory response, which is involved with satellite cell proliferation, differentiation and muscle repair.[8,9]

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Considering this, it would be of great interest to investigate whether individuals may express different IL-6 responsiveness following a given RE stimulus, as was previously demonstrated for CK concentration.[4,5]

Interestingly, elderly individuals preserve eccentric strength more readily than concentric strength.[10] Evidence suggests that eccentric resistance exercise (ERE) can be an excellent method to utilize during the initial stages of a resistance training program in the elderly[10,11]; due to the lower perceived exertion versus conventional resistance exercise.[12] The higher efficiency of eccentric resistance exercise (i.e. intense muscle work is achieved at a lower metabolic expense),[13] renders it as a powerful tool for restoring muscle strength in people with a limited capacity to train at high intensities such as older adults.[14] Thus, investigating the acute CK and IL-6 responses to eccentric resistance exercise in older adults, and the potential for individuals to express different levels of responsiveness for these markers, could provide valuable information for the prescription of RE training for this population.

To the best of our knowledge, no study has investigated CK concentration and IL-6 responses following eccentric resistance exercise in older obese individuals, and further assessed the possible existence of differing responsiveness in the IL-6 marker. Thus, the purpose of the present study was to examine CK and IL-6 concentration responses following eccentric resistance exercise in elderly obese women, and to assess the existence of high responders and normal responders (NR) for these markers. Our hypothesis was that serum CK and IL-6 would be higher following eccentric resistance exercise for those individuals classified as high responders, and there would be no significant increase in CK and IL-6 in elderly individuals classified as normal responders.

2. Methods

Ninety elderly women from a local community (69.4 ± 6.01 years of age, 152.6 ± 6.2 cm in height, body mass of 64.6 ± 12.1 kg, lean mass of 58.8 ± 5.5%, and body fat of 41.2 ± 5.5%) were recruited to participate in the present study on a voluntary basis. Individuals were included according to the following criteria: age ≥60 years, sedentary elderly females, body fat percentage >32% and completion of all testing procedures. The list of medications used by the individuals included omeprazole (gastrointestinal tract/metabolism), losartan (cardiovascular system), levotiroxin, furosemide (diuretic) and simvastatin (cholesterol control). Obesity was determined as recommended by the National Institute of Diabetes and Digestive and Kidney Diseases,[15] assuming a cut-off point of 32% for women. Sedentary state was evaluated by the International Physical Activity Questionnaire. Women with inflammatory, rheumatic, or autoimmune conditions or use of medications (i.e., beta blockers, hormone replacement therapy, selective estrogen receptor modulators, anti-inflammatory, insulin, fish oil and multivitamin supplements) that could modulate the biochemical response to RE were excluded. The study was approved by the Institutional Research Ethics Committee (protocol#035/2011), and all subjects gave written, informed consent.

High responders for CK concentration were defined as a ΔCK ≥ 90th percentile or 96.3 U/l, according to the definition of a "rare event" as compared with normal responders. [16,17] According to Toft et al.,[18] plasma IL-6 concentrations increased approximately four-fold immediately following eccentric muscle actions in young subjects (20–27 years); whereas, the increase was much smaller in elderly subjects (67–75 years) (approximately 90% increase following eccentric exercise consisting of 60 min of opposing the rotation of cycle ergometer pedals down to 60 rpm). In this way, we assumed that the ΔIL-6 ≥ 90th percentile or 7.5 pg/ml was a valid criterion to define HR for this marker.

A ten repetition-maximum (10 RM) test was performed according to the recommendations of Tibana et al.[19]. On the first visit, subjects completed a medical form and physical questionnaire, anthropometric measures, dual-energy X-ray absorptiometry (DXA, General Electric-GE model 8548 BX1L, 2005, Lunar DPX type, software Encore 2005, Rommelsdorf, Germany) body composition analysis, and completed a familiarization session on a leg extension isoinertial machine (Righetto, Sao Paulo, Brazil) that involved performance of three sub-maximum sets of 8–10 repetitions. Three days later, subjects performed a 10 RM test and following 72 h of rest they completed the 10 RM test again to determine test-retest reliability ($R = 0.99$). The test was terminated when voluntary concentric failure occurred (inability to perform a full range repetition of the movement as a consequence of fatigue). As described previously by Tibana et al.,[19] testing errors were minimized by the following strategies: (a) standardized instructions were given concerning all data collection procedures; (b) exercise technique and leg extension machine adjustments were standardized for each subject; and (c) subjects were given verbal encouragement throughout testing. Rest intervals of 3–5 min were instituted between 10 RM trials. Moreover, subjects were asked not to ingest any stimulants (e.g. caffeine) or perform any physical activity during the week prior to testing.

Seven days following the 10 RM tests, subjects completed an eccentric resistance exercise (ERE) protocol adapted from Willoughby et al.[20] Upon arrival at the lab, subjects began with a warm-up on a cycle ergometer for 10 min at 60 rpm and 50 W, followed by 10 leg extension repetitions at 50% of the 10 RM, and then a rest interval of 3–5 min. The ERE session was performed on the bilateral knee extension isoinertial machine with a load corresponding to 110% of the 10 RM. Subjects performed only the eccentric phase of the lift (2–3 s); at the end of each eccentric repetition, the researcher moved the load through the concentric portion of the range of motion to begin the next eccentric repetition. Subjects completed seven sets of 10 repetitions with a passive rest of 3 min between sets. The 10 RM trials and ERE session were scheduled between 2:00 and 4:00 pm and were performed under standardized controlled room temperature. The knee extension exercise was chosen because the investigation of lower limb strength in the elderly is particularly important, considering that it is particularly affected by sarcopenia and loss of functionality.[21]

Blood samples were drawn from an antecubital vein by venipuncture to determine whole blood CK and IL-6 concentration pre- and 3, 24, and 48 h postexercise. CK concentration was determined by use of a commercially available Reflotron CK assay using the Reflotron system (Boehringer Mannheim GmbH, Mannheim, Germany). IL-6 concentration was measured by Quantikine or Quantikine high sensitivity commercial enzyme-linked immunosorbent assay Kit (R&D Systems, Minneapolis, MN, USA). The intra-assay coefficient of variation of the kits was 1.5–5.6% for IL-6. The interassay coefficient of variation was 4.3–6.4% for IL-6. The measures for CK and IL-6 were performed in triplicate and averaged.

The data are expressed as means (95% confidence interval). Shapiro–Wilk tests were applied to check for normality in distribution of the variables assessed. In case of non-normal distribution, the variables were log transformed to base *e* prior to analysis to approximate a normal distribution. The difference between baseline CK and peak CK concentration (the highest value achieved at 0, 3, 24, or 48 h for each subject), or ΔCK, was considered the response following exposure to the ERE. The difference between baseline IL-6 and peak IL-6 concentration (at 0, 3, 24, or 48 h), or ΔIL-6, was considered the response following exposure to the ERE. The achieved power of the sample size was determined using G*Power version 3.1.5 (Kiel, Germany), based on the differences between baseline