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ORIGINAL ARTICLE

Low-Grade Systemic Inflammation and Leptin Levels Were Improved by Arm Cranking Exercise in Adults With Chronic Spinal Cord Injury

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Abstract

Objective: To ascertain the effect of arm cranking exercise on improving plasma levels of inflammatory cytokines and adipokines in untrained adults with chronic spinal cord injury (SCI).

Design: Longitudinal study.

Setting: Community-based supervised intervention.

Participants: Men (N=17) with complete SCI at or below T5 volunteered for this study. Participants were randomly allocated to the intervention (n=9) or control group (n=8) using a concealed method.

Intervention: A 12-week arm cranking exercise program of 3 sessions per week consisted of warm-up (10−15min), arm crank (20−30min; increasing 2min and 30s every 3wk) at a moderate work intensity of 50% to 65% of heart rate reserve (starting at 50% and increasing 5% every 3wk), and cool-down (5−10min).

Main Outcome Measures: Plasma levels of leptin, adiponectin, plasminogen activator inhibitor-1, tumor necrosis factor-alpha, and interleukin-6 were determined. Furthermore, physical fitness (maximum oxygen consumption [$\dot{V}O_2$max]) and body composition (anthropometric index, waist circumference, and body mass index) were also assessed.

Results: Plasma levels of leptin, tumor necrosis factor-alpha, and interleukin-6 were significantly decreased after the completion of the training program. Similarly, the anthropometric index and waist circumference were diminished too. A moderate correlation was found between leptin and the anthropometric index. Finally, $\dot{V}O_2$max was significantly increased, suggesting an improvement of physical fitness in the intervention group. No changes were found in the control group.

Conclusions: Arm cranking exercise improved low-grade systemic inflammation by decreasing plasma levels of inflammatory cytokines. Furthermore, it also reduced plasma leptin levels. Long-term, well-conducted studies are still required to determine whether these changes may improve clinical outcomes of adults with chronic SCI.

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Recent studies have reported that morbidity and mortality from cardiovascular disease are greater and occur earlier among individuals with chronic spinal cord injury (SCI) compared with the able-bodied population.[1]

As a consequence of physical inactivity, body composition alterations, and metabolic disturbances, individuals with SCI are predisposed to excessive abdominal obesity and, consequently, low-grade systemic chronic inflammation.[2,3] Additionally, the decrease in sympathetic activity leads to an attenuation of lipolysis and increased macrophage infiltration in adipose tissue, which contributes to chronic inflammation.[4] In fact, previous studies

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have reported SCI subjects exhibited serum concentrations of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein that were greater than their age-, sex- and race-matched able-bodied counterparts, which may help to explain the accelerated atherogenesis observed in this group.[3,5,6] In addition, plasma levels of leptin were also significantly increased in adults with SCI.[2]

All of these findings should be useful for prioritizing preventive health strategies and planning long-term care for people with chronic SCI,[7] which may help to improve not only low-grade systemic inflammation but also body composition in this group.

Fortunately, a recent systematic and integrative review concluded that exercise could be an interesting nonpharmacologic therapy to decrease chronic low-grade inflammation in SCI.[4] In this respect, data previously found in able-bodied individuals are promising.[8-10] However, the available evidence does not support the findings from studies conducted in able-bodied adults that evaluating efficacy and harm of interventions to prevent obesity-linked metabolic and cardiovascular diseases can be extrapolated to individuals with SCI.[11]

Therefore, the rationale for conducting this study was to ascertain the effect of a 12-week arm cranking exercise program on reducing inflammatory cytokines in untrained adults with chronic SCI. Further objectives were to determine the influence of arm cranking exercise on plasma adipokines (leptin and adiponectin), body composition, and physical fitness.

Methods

Participants

A total of 17 men with complete SCI at or below T5 volunteered for this study from the community. The rationale of this sampling was that the work capacity of individuals with SCI at or above T4 is limited by reductions in cardiac output and circulation to the exercising musculature.[12]

Injury level was determined from a motor and sensory physical examination using the International Standards for Neurological Classification of Spinal Injury, which is written by the American Spinal Injury Association.[13]

Inclusion criteria were defined as follows: men, aged between 20 and 35 years, SCI below T5, all lesions were traumatic, 4 to 5 years postinjury, and medical approval for physical activity participation.

On the other hand, exclusion criteria were pressure ulcers and/or coexisting infections, toxic habits (smoking or alcohol), receiving medication that may interfere with metabolism, participation in a training program in the 6 months prior to participation in the trial, not completing at least 90% of the training sessions, and a concurrent medical condition that might impact on the ability to participate in an exercise program.

List of abbreviations:

AI	**anthropometric index**
BMI	**body mass index**
IL-6	**interleukin-6**
PAI-1	**plasminogen activator inhibitor-1**
SCI	**spinal cord injury**
TNF-α	**tumor necrosis factor-alpha**
$\dot{V}o_2$max	**maximum oxygen consumption**
WC	**waist circumference**

Ethics

This research has been conducted in full accordance with ethical principles according to the World Medical Association Declaration of Helsinki (version 2002). Participants gave their written informed consent prior to study participation. Furthermore, the present protocol was approved by an institutional ethics committee.

Intervention program

Participants were randomly allocated to the intervention (n=9) or control group (n=8) using a concealed method. Characteristics of participants at baseline are summarized in table 1. The control group consisted of individuals matched for age, sex, and injury level. Control participants completed assessments but did not take part in a training program.

Subjects assigned to the intervention group performed a 12-week arm cranking exercise program for 3 sessions per week (subsequently described in detail). Main outcome measures included plasma levels of leptin, adiponectin, plasminogen activator inhibitor-1 (PAI-1), TNF-α, and IL-6. Furthermore, physical fitness (maximum oxygen consumption [$\dot{V}o_2$max]) and body composition (anthropometric index [AI], waist circumference [WC], and body mass index [BMI]) were also assessed. All outcomes at an individual level were assessed at baseline and 72 hours after the end of the intervention.

All participants, including both the intervention and control groups, performed a continuous incremental workload test until exhaustion, on the arm cranking ergometer, to assess physical fitness by measuring $\dot{V}o_2$max. All participants underwent a pretraining period to be familiarized with the correct use of the arm crank ergometer. In addition, they were also asked not to perform strenuous workouts before the testing session.

Oxygen uptake was continuously measured via open-circuit spirometry during baseline rest, exercise, and recovery. In this respect, the criteria we used to determine $\dot{V}o_2$max was the maximum oxygen value at plateau, despite increasing workload.

Each training session consisted of warm-up (10−15min), arm crank (20−30min; increasing 2min and 30s every 3wk) at a moderate work intensity of 50% to 65% of heart rate reserve (starting at 50% and increasing 5% every 3wk), and cool-down (5−10min).

Heart rate reserve (HRR) was obtained according to the following equation by Wilmore[14]:

$$HRR = \left([HRactivity - HRrest] \times [HRpeak - HRrest]^{-1}\right) \times 100\%$$

where the resting heart rate (HRrest) was measured on one occasion during rest early in the morning before the training

Table 1 Participants' characteristics at baseline in the intervention (n=9) and control (n=8) groups

Characteristic	Intervention Group	Control Group	*P*
Age (y)	29.6±3.6	30.2±3.8	>.05
Duration of injury (mo)	54.8±3.4	55.7±3.6	>.05
WC (cm)	98.1±6.6	98.4±6.7	>.05
BMI (kg/m^2)	27.6±4.1	27.8±4.4	>.05
Fitness (mL·kg^{-1}·min^{-1})	23.2±2.1	23.0±2.2	>.05

NOTE. Values are mean ± SD or as otherwise indicated.