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A short-term arm-crank exercise program improved testosterone deficiency in adults with chronic spinal cord injury

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ABSTRACT

Purpose: To determine the influence of arm-crank exercise in reproductive hormone levels in adults with chronic SCI. Further objectives were to assess the influence of arm-crank exercise on muscle strength and body composition.
Materials and Methods: Seventeen male adults with complete SCI at or below the 5th thoracic level (T5) volunteered for this study. Participants were randomly allocated to the intervention (n = 9) or control group (n = 8) using a concealed method. The participants in the intervention group performed a 12-week arm-crank exercise program, 3 sessions/week, consisting of warming-up (10-15 min) followed by a main part in arm--crank (20-30 min [increasing 2 min and 30 seconds each three weeks]) at a moderate work intensity of 50-65% of heart rate reserve (HRR) (starting at 50% and increasing 5% each three weeks) and by a cooling-down period (5-10 min). Serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone and estradiol were determined by ELISA. Muscle strength (handgrip) and body composition (waist circumference [WC]) were assessed.
Results: After the completion of the training program, testosterone level was significantly increased (p = 0.0166;d = 1.14). Furthermore, maximal handgrip and WC were significantly improved. Lastly, a significant inverse correlation was found between WC and testosterone (r =- 0.35; p = 0.0377).
Conclusion: The arm-crank exercise improved reproductive hormone profile by increasing testosterone levels in adults with chronic SCI. A secondary finding was that it also significantly improved muscle strength and body composition in this group.

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INTRODUCTION

Several studies have reported that measuring serum total testosterone levels should be included in standard screenings for patients with SCI, particularly those with motor complete injuries, given their high prevalence of testosterone deficiency (1,2).

In fact, low levels of testosterone may further adversely affect metabolism and body composition in this group (3). Similarly, a recent review reported it may also contribute to the impairment of semen quality in spinal cord injured men (4).

Therefore, testosterone deficiency has been reported as a target in the therapeutic approach of this entity. In this respect, results achieved by using testosterone replacement therapy both in animal research (5) and human studies (3) have been promising. To date, no studies have been focused on improving testosterone levels by performing an intervention program based on regular exercise in individuals with chronic SCI. However, a recent published trial has demonstrated that aerobic training at moderate intensity increased testosterone levels in abdominally obese, sedentary adults without SCI (6).

For the reasons already mentioned, this was the first study conducted to determine the influence of arm-crank exercise in reproductive hormone levels in adults with chronic SCI. Further objectives were to determine the influence of arm-crank exercise on muscle strength and body composition.

MATERIALS AND METHODS

Study population

A total of 17 male adults with complete SCI at or below the 5th thoracic level (T5) volunteered for this study from the community. The rationale of this sampling was that the work capacity of individuals with spinal cord injury at or above the 4th thoracic level (T4) is limited by reductions in cardiac output and circulation to the exercising musculature (7).

Injury level was determined from a motor and sensory physical examination using the International Standards for Neurological Classification of Spinal Injury written by the American Spinal Injury Association (ASIA) (8).

Inclusion criteria were defined as follows: man; aged 20-35 years-old; SCI below T5; all lesions were traumatic; 4-5 years post-injury; 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 their metabolism; participation in a training program in the 6 months prior to their participation in the trial; not-completing at least 90% of the training sessions; a concurrent medical condition that might impact on their ability to participate in an exercise program.

Ethics

This research has been conducted in full accordance with ethical principles, including 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.

Subjects assigned to the intervention group performed a 12-week arm-crank exercise program 3 sessions per week, consisting of warming-up (10-15 min) followed by a main part in arm-crank (20-30 min [increasing 2 min and 30 seconds each three weeks]) at a moderate work intensity of 50-65% of heart rate reserve (HRR) (starting at 50% and increasing 5% each three weeks) and by a cooling-down period (5-10 min).

Heart rate reserve was obtained according to the following equation by Wilmore et al. (9):

$$HRR = ((HRact - HRrest) \times (HR\ peak - HRrest)^{-1}) \times 100\%.$$

The resting heart rate (HRrest) was measured on one occasion during rest early in the morning before the training program had started. The peak heart rate (HRpeak) was derived from the pre-test arm-cranking maximal ergometry.

Exercise duration and intensity were carefully monitored and gradually increased in order to guarantee long-term compliance and injury avoidance (7). In this respect, each training session was supervised by researchers to ensure training workload was appropriate. In addition, participants wore a wireless wearable heart rate monitor (Sport Tester PE3000, Polar Electro, Kempele, Finland).

Prior to testing, participants were asked to desist from eating for 4h. To perform each training

Table 1 - Participant´s characteristics at baseline in the intervention (n = 9) and control (n = 8) groups.

	Intervention group	Control group	p Value
Age (year)	29.6 ± 3.6	30.2 ± 3.8	> 0.05
Duration of injury (months)	54.8 ± 3.4	55.7 ± 3.6	> 0.05
WC (cm)	98.1 ± 6.6	98.4 ± 6.7	> 0.05
Maximal handgrip (Kg)	45.7 ± 7.2	46.3 ± 7.5	> 0.05

Note: Results expressed as mean ± sd; **WC =** Waist circumference.

session, they were placed on a chair that was connected to the arm-crank ergometer (Ergometrics 900 SH) with their legs and their hips fixed with belts for optimal stability. It should be pointed out the pedal axis was aligned with the participant's shoulder, and participants were positioned such that their elbows were slightly flexed at maximal reach. Their feet were placed on the floor such that the knees were bent at an angle of approximately 90º. Control group included 8 age, sex and injury level matched individuals who did not take part in any training program. Further, it should be pointed out that all participants underwent a pre-training 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.

Muscle strength

The Jamar handgrip electronic dynamometer (Bolingbrook, Illinois, US) was used to assess maximal handgrip strength of the dominant hand, defined as the one preferred for daily activities. The standard testing position, approved by the American Society of Hand Therapists, was used (10). Three maximal attempts, separated each one by 90 second (maximal handgrip) and 20 min (peak torque) resting periods, were given by each subject. The highest value was considered for further analysis. Verbal encouragement was afforded to ensure maximal efforts. Furthermore, all participants included in the intervention and control group underwent a preliminary session to be familiar with the correct use of the dynamometer as well as to determine the handle position at which they achieved maximal grip strength (11).

Biochemical outcomes

Blood samples were collected from the antecubital vein puncture after a 12h fast and collected by using an evacuated tube containing EDTA. The whole blood was centrifuged at 3000 rpm for 10 minutes in a clinical centrifuge.

The plasma was separated and stored at -80º C until further analysis. Serum levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol and testosterone were determined by ELISA (Diagnostics Systems Laboratories Inc., Texas, USA).

Abdominal fat mass

Waist circumference (WC) was determined at minimal waist after normal expiration using an anthropometric measuring tape. It should be pointed out participants were placed in a sitting position.

Statistical analyses

The results were expressed as a mean (SD) and 95% confidence intervals (95%CI). The Shapiro-Wilk test was used to assess whether data were normally distributed. To compare the mean values, a one-way analysis of variance (ANOVA) with post-hoc Bonferroni correction to account for multiple tests was used. Pearson´s correlation coefficient (r) was used to determine potential associations among tested parameters. For all tests, statistical significance was set at an alpha level of 0.05. Finally, Cohen's d statistics were used for determining mean effect sizes that were considered to be small $d \geq 0.2$ and < 0.5, medium $d \geq 0.5$ and <0.8 or large $d \geq 0.8$ respectively.

RESULTS

After the completion of the training program, testosterone level had significantly increased ($p = 0.0166$; $d = 1.14$). Conversely, changes in levels of FSH and LH were not statistically significant in the intervention group. These results are detailed in Table-2.

Regarding muscle strength assessment, the maximal handgrip strength was significantly improved after the completion of the training program (45.7 ± 7.2 vs. 50.1 ± 6.9 Kg; $p = 0.027$; $d = 0.76$). Similarly, body composition was improved as WC was significantly reduced (97.7 ± 6.3 vs. 94.2 ± 6.2cm; $p = 0.044$; $d = 0.82$).

Lastly, a significant, negative, correlation was found between WC and testosterone levels ($r = -0.35$; $p = 0.0377$) after being exercised. Similarly, testosterone concentration was significantly associated with handgrip strength ($r = 0.31$; $p = 0.0412$).

With respect to the control group, no significant changes in any of the tested parameters were found. Finally, neither sports-related injuries nor withdrawals from the program were reported during the entire study period in the intervention group.

DISCUSSION

To the best of our knowledge, this was the first study that demonstrated arm-crank exercise improved reproductive hormone profile, by increasing testosterone levels, in adults with chronic SCI. Our results are consistent with a previous study that reported aerobic training at moderate intensity increased testosterone levels in abdominally obese, sedentary adults without SCI (6). Similarly, a 12-week resistance training significantly increased sex hormone-binding globulin (SHBG) in overweight/obese, sedentary young men (12).

These findings are of particular interest given that considerable evidence had emphasized the role of testosterone in increasing and maintaining muscle mass leading to a better metabolic control and basal energy expenditure (13). Furthermore, low levels of androgens have been associated with cardiovascular disease progression, especially coronary artery disease, and increased mortality (14). The clinical relevance of the present study seem even more relevant given that morbidity and mortality from cardiovascular disease are greater and occur earlier among individuals with chronic SCI compared to able-bodied population (15).

The current results have also demonstrated that arm-crank exercise improved body composition, by reducing WC, in adults with SCI. Similarly, a 12-week mixed protocol based on resistance training using neuromuscular electrical stimulation (FES) + diet significantly reduced visceral adipose tissue in men with chronic SCI (15). It should be emphasized our protocol was based only on exercise so that it may facilitate participants´ compliance with the intervention. These findings are of particular interest given that abdominal obesity has a negative impact on reproductive hormone levels such as testosterone (17).

Table 2 - Reproductive hormone profiles in sedentary adults with chronic SCI enrolled in the intervention (n = 9) and control (n = 8) groups.

	INTERVENTION GROUP		CONTROL GROUP		
	Pre-test	Post-test	Baseline	Final	Cohen´s d
FSH	6.26 ± 1.76	6.45 ± 1.68	6.18 ± 1.72	6.17 ± 1.70	0.17
LH	4.62 ± 1.41	4.82 ± 1.37	4.54 ± 1.43	4.55 ± 1.43	0.19
Testosterone	216.6 ± 17.4	238.4 ± 15.7 [a,b]	212.2 ± 16.9	214.6 ± 17.0	1.4
Estradiol	59.0 ± 6.2	57.4 ± 5.7	58.2 ± 5.9	58.3 ± 6.0	0.15

Note: Results expressed as mean ± sd. FSH and LH expressed mIU/mL. Testosterone expressed as ng/dL. Estradiol expressed as pg/mL. **Ratio T/E:** Ratio testosterone/estradiol. [a]p < 0.05 versus pre-test; [b]p < 0.05 versus final

In a more detailed way, current evidence suggests excess adipose tissue results in increased conversion of testosterone to estradiol, which may lead to secondary hypogonadism through reproductive axis suppression (18).

Another challenge of the present trail was to identify significant associations between testosterone and abdominal obesity in order to provide an easier, quicker, cheaper and non-invasive assessment of this reproductive hormone. In this respect, a significant but negative correlation was found between WC and testosterone. Similarly, the significant inverse association between plasma levels of cytokines and testosterone suggests an important role of low-grade visceral fat inflammation in the testosterone deficiency (19).

Regarding muscle strength, a recent systematic review of the literature concluded that handgrip dynamometry has a great potential, and could be used more often in clinical practice in a wide range of medical conditions (20), including SCI (21). In the present study, it was shown that arm-crank exercise significantly improved handgrip strength in sedentary adults with chronic SCI. Despite functional outcomes were not included in the study, Larson et al. (22) reported that the use of hand-held dynamometry to predict postural muscle strength for maintaining upright sitting in individuals with SCI has high intrarater and interrater reliability.

In spite of individuals with SCI have to face many obstacles to exercise (23), the current results are strong arguments for strengthening the role of exercise as a preventive strategy. It may also reduce healthcare costs associated to secondary conditions in this group, given the longer life expectancy observed in the last decades (24).

Finally, despite our significant results, the present study had some limitations that should be considered. Since all patients volunteered for this study from the community, a selection bias might be considered given that participants were highly motivated to undergo and follow through the program. The short sample size may also limit the generalization of the results. Lastly, a major weakness was the relatively short duration of the exercise intervention so that testosterone levels still remain below normality limit in spite of they were significantly increased. Furthermore, there is a clear need for long-term, well-conducted studies to determine whether correction of reproductive hormone profile improves clinical outcomes of individuals with SCI.

On the other hand, strengths of the current study included the homogeneous sample size in contrast to previous studies that included males and females, tetra- and paraplegia, different etiologies for SCI, years since injury, etc... Furthermore, the presence of a control group consisting of age, sex and injury-level matched individuals may reduce the recruitment bias of able-bodied controls. Lastly, the excellent adherence rate suggested the training program was effective and easy to follow-up. In fact, testosterone may improve motivation and decrease fatigue and may therefore enable participants to better adhere to exercise (25). Furthermore, it may also give them the confidence to continue exercising after the trial finishes. It should be pointed out that erring on the conservative side of selected exercise durations and intensities are prudent and even more important for persons training with a disability than those without (7). Mainly, if we take into consideration that overuse injuries, joint dislocations and fractures have been reported as common and may ultimately compromise performance of essential daily activities, including wheelchair propulsion, weight relief, etc. in this group (26).

CONCLUSIONS

A short-term intervention program based on arm-crank exercise improved reproductive hormone profile by increasing testosterone levels in adults with chronic SCI. A secondary finding was that arm-crank exercise significantly improved muscle strength and body composition. In order to confirm and extend these preliminary findings, larger, randomized, controlled clinical trials are required.

CONFLICT OF INTEREST

None declared.

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