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Effects of resistance training and vibration on hormonal changes in female patients with multiple sclerosis

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Abstract

Background & Objective: Resistance training is deemed to be beneficial for multiple sclerosis patients. The aim of this study was to determine whether a program of RT and whole body vibration has any effect on the pattern of hormonal changes in female MS patients. *Methods:* Twenty-four female MS patients were enrolled in this study. They were aged between 20-40 years and ranged from 2-4 on the Expanded Disability Status Scale (EDSS). Twelve patients took part in this protocole. The duration of the program was eight weeks, each sessions were held three times per week. The twelve controls did not take part in this program. Serum levels of follicle-stimulating hormone, luteinizing-hormone, estradiol, progesterone, testosterone, prolactin and cortisol were measured before and after the protocole between the 8th and 10th day of the follicular phase of the patients' menstrual cycle. Descriptive statistics and co-variance analysis were adapted for evaluating the data. *Results:* Significant increases in levels of testosterone and prolaction, whereas a significant decrease in levels of cortisol were detected. *Conclusion:* The results provide clues as to the involvement of testosterone, prolactin and cortisol as possible mediators of the beneficial effects of resistance training and whole body vibration in multiple sclerosis.

INTRODUCTION

Multiple sclerosis (MS) is one of the most common debilitating neurological diseases to affect young adults. Clinical manifestations include focal or multifocal and transient or persistent signs and symptoms which result in disability and a reduction in patients' quality of life.[1] Sex steroid hormones and pregnancy are thought to have an impact on the course of MS, and the possible role of sex hormones in modulating disease activity and brain damage has been proposed.[2,3] Studies have shown that levels of follicle-stimulating hormone (FSH), luteinizing-hormone (LH), testosterone and prolactin (PRL) are significantly lower than average in female MS patients.[4,5] However, Nabavi *et al*. have reported that LH and PRL levels in MS patients are higher than in healthy women.[6] In female MS patients with severe demyelination and brain atrophy, progesterone and beta-estradiol levels, during the luteal phase of the menstrual cycle, were related to both the number and volume of the patients' MRI enhancing lesions.[7,8] There is increasing evidence that estrogen[9,10], progesterone[5,11] and testosterone[5,12], influence damage repair in the nervous system and PRL is being explored for its possible immunomodulatory and directly neuroprotective effects that may influence diseases such as multiple sclerosis.[5]

Physical activity is an effective way of increasing anabolic hormone levels.[13] Exercise stimulates the endocrine system and heavy exercise has been shown to alter serum levels of progesterone and estradiol.[13,14] Exercise-induced hormonal responses are significant for acute adaptation.[13] In addition, whole body vibration (WBV) significantly increases levels of testosterone and at the same time decreases cortisol levels.[15] WBV by mechanical multidimensional oscillations of the muscle-nervous system can lead to physiological changes on numerous levels.[16] Changes of hormonal concentrations such as increases in growth hormone and testosterone and a decrease in cortisol have been described.[5,15,17]

Therefore, this study was designed to further investigate hormonal changes during resistance training and WBV among female MS patients.

METHODS

This study was carried out from November until December 2010 at the Islamic Azad University,

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Najafabad Branch. The local ethics committee approved the study protocol and each patient was asked to sign an informed consent form prior to enrollment.

Twenty-four patients aged 20-40 years took part in this quasi-experimental study. The inclusion criteria were MS patients, with a relapsing-remitting (RR) form of the disease and an Expanded Disability Status Scale (EDSS) in the range two to four were enrolled.[1] The exclusion criteria were hormonal problems, infertility, abnormal pituitary, the existence of orthopedic, cardiovascular or pulmonary disease, pregnancy, cancer, bone fracture during the previous six months, use of prosthetics, participating in any regular exercise program, a relapse, the administration of corticosteroids within the previous 6 months, any special diets, and any serious health problems which could potentially prevent the patient from following the training program.

Patients were allocated randomly to groups, divided in the exercise group (n=12) and the control group (n=12). The body height of each subject was measured with a portable wall-mounted ruler in the upright position (accuracy 0.1 cm), body mass was recorded using a portable scale (Seca Vogel & Halke German model: 760 1029009) and body mass index [BMI (Kg/m^2)] was calculated. Maximal voluntary contraction (MVC) of the isotonic strength of the knee extensor, abduction scapula, and downward rotation scapula muscle groups was calculated using Brzycki formula.[18]

Venous blood samples were obtained from the antecubital vein of the patient whilst they were in a seated position. Blood (twenty milliliters in two stages within 30 minutes) was collected during the follicular phase of the patients' menstrual cycle at eight AM, after 10 hours fasting, before and after the end of the protocol, to determine serum levels of FSH, LH, estradiol, progesterone, testosterone, PRL, and cortisol. These hormones were measured using commercially available kits (Beckman Coulter, Inc. Diagnostic Systems Laboratories/DSL/Immunotech).

All the subjects were tested between eight to nine AM. Prior to testing, subjects were allowed to familiarize themselves with the multi-purpose machine) Rain Co. 9026, Iran) and vibration procedures (Crazy Fit Massage, Fitness Vibration Machine, Power Plate (TQ908) e, China). The protocol of training was always carried out at the same time of day. The case group participated in the resistance training and WBV program three times a week, with at least 48-hours' rest between exercise sessions, for a period of eight weeks. Subjects completed the protocol under the supervision of an exercise physiologist and a physician.

All subjects performed a 10 minute warm-up at the beginning of each training session consisting of five minutes cycling on a cycle Ergometer (Cross sport U325. China). The protocol of training consisted of three sets of 5-12 repetitions at 50-70% of MVC in the position of Knee Extension, Pec Deck Flies, and Back Lat Pull-downs. Patients had five minutes rest after completing three sets.

In order to compensate for the low intensity of this protocol, we performed whole body vibration after resistance training. After a 5-10 minute rest, patients were asked to maintain five postures on the vibration platform, including: a deep squat (with a 90 degree knee angle), a deep lunge (one foot forward with a 90 degree knee angle), a sitting forward bend, a gentle push-up, and a calf massage, each one maintained for 30 seconds. The vibration frequency and amplitude were set at 2-20 Hz and 0.1-2 mm respectively. At first, the vibration frequency was set at 2-5Hz and this was gradually increased to 20Hz by the end of the protocol.

Statistical analysis:

Descriptive analyses were adopted for the demographic and clinical characteristics reporting the variables as a mean ± SD. The Kolmogorov - Smirnov's test was used to find the normal distribution of the data. A parametric independent T-test was used for the normality distributed variables (age, weight, height and EDSS). Levene`s test was used to show any significant variance between the two groups before starting the protocol. To compare the hormone levels after the intervention/ no intervention, we used ANCOVA with hormone level before and the intervention as covariate. LSD test was used as a post hoc test to show the differences between the groups. The p-value of less than 0.05 was considered statistically significant.

RESULTS

The clinical and demographic characteristics of the 24 subjects who completed the study protocol are displayed in Table 1. No significant differences were observed in the baseline between the case group and the control group in terms of age, weight, height, and EDSS ($p<0.05$). There were

Table 1: Characteristics of the patients in the exercise and control groups and T-Independent test

Variables	Exercise group (n=12) Mean ± SD	Control group (n=12) Mean ± SD	*T*	*Sig (2-tailed)*
Age (yr)	35.08 ± 6.89	33.75 ±5.32	0.53	0.60
Weight (Kg)	61.91 ± 10.30	58.20 ± 5.54	1.09	0.28
Height (cm)	157.08 ± 6.97	158.83 ± 4.80	-0.71	0.48
EDSS	2.87 ±0.82	2.79 ± 0.65	0.27	0.87

Values are means ± SD, and T-test for equality of means of the characteristics of the subjects in the study, ($p<0.05$), and df=22.
EDSS, Expanded Disability Status Scale

no reports of any adverse events in any groups. During the time in which the study was carried out none of the cases or controls showed disease exacerbation.

Mean concentrations of FSH, LH, estradiol, progesterone, testosterone, PRL, and cortisol in plasma were assessed before and after the study for both the case and control groups and these have been recorded in Table 2. After the eight week training program, testosterone, cortisol and PRL concentrations had changed significantly. However, no significant changes were detected in plasma FSH, LH, estradiol, and progesterone concentrations after the training program.

Table 2: Before and after intervention values of hormones in the studied patients (values expressed as a mean ±SD), and ANCOVA test.

Variables	Exercise group (n=12) mean ±SD		Control group (n=12) mean ±SD		*F*	*P*	*η*	*Observed Power*
	Before	After	Before	After				
FSH (mUl/ml)	6.79 ± 2.87	6.00 ± 0.64	5.01 ± 2.27	5.55 ± 0.64	0.23	0.63	0.01	0.07
LH (IU/L)	11.00 ± 4.98	8.62 ± 1.27	10.06 ± 7.09	10.64 ± 1.27	1.25	0.27	0.05	0.19
Estradiol (Pmol/l)	113.00±69.82	141.79±23.95	195.25±125.7	148.87±23.95	1.88	0.18	0.08	0.25
Progesterone (ng/ml)	0.56 ± 0.54	0.42 ± 0.11	0.50 ± 0.36	0.72 ± 0.11	3.37	0.08	0.13	0.41
Testosterone (ng/ml)	0.27 ± 0.17	0.41 ± 0.13	0.41 ± 0.18	0.41 ± 0.18	4.56	0.04*	0.17	0.53
Prolactin (ng/ml)	8.18 ± 3.29	10.03 ± 0.58	8.73 ± 3.69	8.01 ± 0.58	5.96	0.02*	0.22	0.64
Cortisol (ng/ml)	12.32 ± 4.10	9.92 ± 0.87	9.51 ± 3.40	15.82 ± 0.87	21.05	0.00*	0.50	0.99

P= Significance. η = partial eta-squared, demonstrated the changes of variable had concluded of protocol of training., Observed Power = indicating an adequate of number of subjects.

DISCUSSION

There is evidence suggesting that major stress response systems, such as the hypothalamus-pituitary adrenal (HPA) axis and the autonomic nervous system, influence immune function and that the stress induced by exercise can inhibit gonadal function[19], and may thereby influence MS disease activity.[7,20]

The results of our study indicate that training significantly alters testosterone, PRL and cortisol concentrations, but has no significant effect on FSH, LH, estrogen and progesterone.

In our study, testosterone levels increased significantly in the exercise group. Our results are in line with previous observations that suggest exercise can contribute to anabolic hormonal response.[20,21] WBV carried out as an acute exercise in men induced higher blood concentrations of testosterone.[15] Another study has reported an increase of testosterone levels after resistance training and WBV in healthy young men, which support the results obtained in this study.[22] Testosterone has also been shown to have beneficial effects in men with multiple sclerosis[17], though testosterone may be only one of the mediators of beneficial effects of training in MS. In our study the beneficial effects and progesterone were not significantly changed, which might be due to the small sample size and/or the short duration of the protocol.

PRL has been shown to have proinflammatory properties and its presence has been proven to be critical in the development of a number of experimental autoimmune diseases. Moreover, PRL is thought to play a role in the pathogenesis of MS.[23] In our study, PRL levels significantly increased in the exercise group. Exercise is thought to stimulate PRL release[14,24,25], and the magnitude of the PRL release appears to depend on the intensity of exercise.[26] However, studies on male recreational athletes indicated PRL hormone levels had no dependence on training.[27]

It has been shown that cortisol serum levels are dependent on the duration and severity of training.[19,28,29] It is possible that a physical stressor such as exercise may influence the disease progression of MS through stress-mediated mechanisms.[19,29] Physical activity and exercise training have been shown to modulate immune function in both health and disease, whereas during acute exercise there is also a marked increase in cortisol, which is known to have immunomodulatory effects.[19,24,25] However, after prolonged exercise a decrease in cortisol levels has been shown.[30] A decrease in cortisol levels may be linked to adaptation to exercise. Exercise increases the production and catabolism of cortisol. The level rises transiently during exercise of both moderate and severe intensity, and falls rapidly to basal level or below within a few hours of cessation of exercise. The magnitude of the response is proportional to the relative intensity of the exercise but is independent of the level of fitness of the trainee.[28,29] However, our findings do not support those of Lehmann's study which indicate no influence on base or exercise-induced serum cortisol hormone levels in male recreational athletes.[27]

In this study, there were no significant differences between two groups in respect of changes in levels of FSH and LH. This is in line with other studies reporting no changes in FSH and LH in healthy individuals after training.[27,30] However, it must be taken into account that the methods of training employed in the two studies were different; our subjects were MS patients, whereas subjects of Bonen's study were healthy females. Another study on male recreational athletes indicated no influence on base or exercise-induced serum hormone levels of FSH and LH.[27] However, Safarinejad showed that in the long term moderate-intensity exercise (~60% VO_2max] and high-intensity exercise (~80% VO_2max) decreased male LH and FSH serum concentrations below the baseline level in both test groups.[31] The protocols of these studies were moderate to high-intensity exercise, and their subjects were trained at higher VO_2Max intensities compared with our MS patients. So the intensity of training percentage of VO_2max was different with the same percentage of VO_2max in untrained subjects, specially MS patients. Another significant factor that must be taken into consideration is the sex of the subjects, as this has an effect on the levels of plasma sex hormones.

The serum levels of estradiol and progesterone remained unchanged in our study, however it has been shown that heavy exercise in untrained subjects can provoke significant increments in ovarian hormones (estradiol and progesterone).[13] Steroid hormones have a complex role in MS, and both estrogen and progesterone are interesting in terms of their remyelinating and immunomodulating effects.[32] Estradiol and progesterone might be beneficial for MS patients[32,33], but these studies used the hormones exogenously, so even though strenuous training may increase levels of these hormones the changes might not be therapeutic. Moreover, although, mild to moderate training in these subjects had effects on disease activity, this degree of exercise is clearly not going to be possible for MS patients to undertake.

In conclusion, since the exercise-induced HPA axis activation has not been studied extensively in individuals with MS, further investigation could yield potentially important information about physical activity and disease status.

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