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Effect of aerobic exercise on dehydroepianderestrone and cortisol in in female patients with multiple sclerosis

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Abstract.

Introduction: The aim of this study was to examine the effects of 8 weeks aerobic training on dehydroepianderestrone sulfate (DHEA-S) and cortisol in female patients with multiple sclerosis disease.

Material & Methods: Twenty seven women with MS disease in a range of 20-47 year of old and EDSS lower than 5.5 participated in this study as the subject. Subjects were divided into control group (n=14) or training group (n=13) randomly. The training group performed aerobic training program, 3 days a week for 8 weeks according to 55-60 percentage of VO_{2max}. The control group was in absolute rest at the same time. Serum level of DHEA-S and cortisol were measured by ELISA kits before and after training.

Results: The results showed that cortisol and DHEA-S concentrations did not change significantly after the intervention.

Conclusions: In conclusion, the results suggest aerobic training with specific intensity and duration utilized in this study had not effects on cortisol and DHEA-S levels in female patients with MS.

Key words: Multiple sclerosis, aerobic training, Cortisol, DHEA-S.

1. Introduction

During multiple sclerosis (MS), an inflammatory demyelinating disease of the central nervous system (CNS), activation of the hypothalamo-pituitary-adrenal (HPA) axis is considered to modulate the immune system in such a way that the probability of recovery from a relapse is increased (1). Several studies indicated that HPA axis plays a crucial role in the control of the disease process in MS (2). During the time of active demyelination in the rat model of experimental allergic encephalomyelitis, there is activation of the HPA axis which is vital for recovery from the disease (3). HPA activity has also been found to be increased in other inflammatory diseases and may indeed act as a protective mechanism against an excessive immune response. In rats with adjuvant-induced arthritis the HPA axis is chronically activated and diurnal rhythms of corticotropin (ACTH) and corticosterone are lost (4). Patients with rheumatoid arthritis also have an activated HPA axis (5) with an impaired cortisol rhythm and a poor response to stress (5,6). Cortisol, the end product of HPA axis, has immune modulatory effects and synthetic glucococorticoids are used to treat relapses of MS (7,8).

Dehydroepiandrosterone sulfate (DHEA-S) is the most abundant steroid hormone in the circulation; almost all is secreted by the zona reticularis of the adrenal cortex. DHEA-S secretion is mediated by the trophic effect of ACTH (9). Dehydroepiandrosterone (DHEA) is an androgenic steroidal hormone produced by the adrenal gland and DHEA-S is a metabolite of DHEA. Its specific physiological functions, other than serving as a precursor to other steroid hormones (such as testosterone), are not yet established. Recent evidence has suggested that DHEA-S level is a good predictive marker of HPA impairment (10,11). Previous studies demonstrated that the persons with MS have low levels of DHEA-S (12) and elevated resting cortisol level also more common in MS patients (13).

Although previous studies demonstrated that exercise training increases the levels of DHEA-S in healthy subjects (14), athletics (15) and in bipolar patients (16), but a little data on exercise-induced changes of DHEA-S and cotrisol in patients with MS have been reported. Rashidfar et al. (2014) noted that DHEA-S increased after 8 weeks resistance training in female patients with MS (17). Najafi and Moghadasi (2016) indicated that cortisol level was decreased after 8 weeks yoga training in female patients with MS (18); however Hejazi et al. (2013) and Schulz et al. (2004) were found no significant changes in cortisol level after the exercise in patients with MS (19,20). As the effect of aerobic exercise on DHEA-S and cortisol is still unclear, this study was done to examine the effects of 8 weeks aerobic training on DHEA-S and cortisol in female patients with MS disease.

2. Material & methods

Subjects

The participants in this study were 27 female between 20 and 47 years of age. All participants were volunteers from the MS Center of Shiraz, Iran. The inclusion criteria for the subjects with MS were diagnosis with relapsing-remitting MS by modified McDonald criteria, presenting any type of orthopedic, any cardiovascular or pulmonary disease, pregnancy, cancer, bone fracture of less than 6 months, use of prostheses, any serious nervous system disorder, any health problems to prevent effort on the physical test and taking part in regular physical activities before this study and age between 20 and 50 years. Their mean Expanded Disability Status Scale (EDSS) score was 2.3, with a range of 1 to 5.5 and participants were randomly divided into an exercise group (n=13) and control group (n=14).

Anthropometric and body composition measurements

Height and weight were measured, and body mass index (BMI) was calculated by dividing weight (kg) by height (m^2). Waist circumference was determined by obtaining the minimum circumference (narrowest part of the torso, above the umbilicus) and the maximum hip circumference while standing with their heels together. The waist to hip ratio (WHR) was calculated by dividing waist by hip circumference (cm). Body fat percentage was assessed by bioelectrical impedance analysis using a Body Composition Analyzer (BoCA x1, Johannesburg, South Africa).

Training protocol

The 8 weeks exercise training program included 3 running sessions per week. The intensity of exercise was customized for each subject based on the relationship between heart rate and oxygen uptake measured at baseline. During the 8 weeks intervention, the subjects were trained for 30 min per session at a heart rate corresponding to 50-60% of the maximal oxygen uptake measured at baseline. Each participant wore a heart rate monitor (Beurer, PM70, Germany) to ensure accuracy of the exercise level. Fasted, resting morning blood samples (7 ml) were taken at the same time before and after 8 weeks intervention. All the subjects fasted at least for 12 hours and a fasting blood sample was obtained by venipuncture. Serum obtained was frozen at -22 ^{oC} for subsequent analysis. The plasma DHEA-S and cortisol levels were measured in duplicate using an enzyme-linked immunosorbent assay (ELISA) kits (AccuBind™ Monobind Inc, USA). The sensitivity of kits for DHEA-S and cortisol was <4.2 µg/dl and < 3.6 ng/ml respectively.

Statistical analyses

Results were expressed as the mean $\pm$ SD and distributions of all variables were assessed for normality. Paired t-test was used to compute mean ($\pm$ SD) changes in the variables in control and exercise group pre and after the intervention. Differences among groups were assessed by using analysis of independent sample t-test. The level of significance in all statistical analyses was set at $P \leq 0.05$. Data analyses were performed using SPSS software for windows (version 17, SPSS, Inc., Chicago, IL).

3. Results

Anthropometric and body composition characteristics of the subjects at baseline and after the intervention are presented in Table 1. Before the intervention, there were no significant differences in body mass, BMI, body fat percentage and WHR among the two groups. The results demonstrated that BMI and body fat percentage were decreased (P<0.05) after 8 weeks concurrent training compared to the control group. For body mass and WHR no significant changes were observed after the intervention. The results also showed that DHEA-S and cortisol did not change in the exercise training compared with the control group (Table 1).

Table 1. Anthropometric, body composition and biochemical characteristics (mean ± SD) of the subjects before and after training

	Baseline (mean ± SD)	After intervention (mean ± SD)	Paired t-test (Sig)	Independent t-test (Sig)
Body mass (kg)				
Exercise (n=13)	66.1 ± 12.3	65.2 ± 12.3	0.08	0.1
Control (n=14)	58.4 ± 10.02	59.2 ± 9.0	0.2	
BMI (Kg/m²)				
Exercise (n=13)	25.6 ± 5.7	25.2 ± 5.5	0.04*	0.009*
Control (n=14)	22.7 ± 3.9	23.2 ± 3.6	0.02*	
Body fat (%)				
Exercise (n=13)	35.5 ± 6.4	33.0 ± 6.5	0.001*	0.004*
Control (n=14)	30.6 ± 7.0	31.4 ± 5.9	0.2	
WHR				
Exercise (n=13)	0.83 ± 0.05	0.81 ± 0.6	0.1	0.2
Control (n=14)	0.79 ± 0.06	0.8 ± 0.06	0.4	
Cortisol (ng/ml)				
Exercise (n=13)	159.2 ± 34.2	152.3 ± 26.8	0.5	0.3
Control (n=14)	130.8 ± 28.0	138.0 ± 32.6	0.5	
DHEA-S (pg/ml)				
Exercise (n=13)	258.5 ± 75.3	248.8 ± 81.7	0.6	0.07
Control (n=14)	205.0 ± 76.2	217.0 ± 90.0	0.5	

Data are the mean ± SE of baseline and final values of the anthropometric, body composition and biochemical changes on each variable in each group. Comparison different significance between groups after 8 weeks exercise was determined by using the independent sample t-test. *P<0.05.

4. Discussion

MS is a chronic inflammatory disease of the CNS, which causes multifocal demyelination along with astrocytic gliosis and variable axon loss in the brain and spine. MS is one of the most common causes of non-traumatic disability in young adults and approximately 1-2.5 million people around the world are estimated to be affected, depending on the publication (21,22). Hormonal disorders are one of the most important compliant of MS patients and exercise may be effective to improve hormonal dysfunction in MS patients however it is not well known. Thus this study was done to examine the effects of 8 weeks aerobic training on DHEA-S and cortisol in female patients with MS disease.

Although previous studies indicated that moderate endurance training resulted in improved muscle strength of both lower and upper extremities and some functional measures like walking speed, fatigue, and quality of life in MS patients (23,24), but a little data on exercise-induced changes of DHEA-S and cortisol in these patients have been reported. DHEA-S exerts multiple immunomodulatory effects and its circulating level change in a contrasting manner in the course of some immune-inflammatory diseases (25). Our results showed that DHEA-S did not change after 8 weeks aerobic exercise. Previously Rashidfar et al. (2014) reported that DHEA-S increased after 8 weeks resistance training in female patients with MS (17). These discrepant results may be attributed to differences in subject populations and variation in the exercise protocols.

Our results demonstrated that cortisol level had not significant changes after 8 weeks aerobic training in female patients with MS. Previously Hejazi et al. (2013) and Schulz et al. (2004) also, were found no significant changes in cortisol level after the exercise in patients with MS (19,20). Contradictory to these results, Najafi and Moghadasi (2017) showed that cortisol level was decreased after 8 weeks yoga training in female patients with MS (18). According to Melief et al. (2013) patients with low cortisol levels had greater numbers of active lesions and tended towards having less remyelinated plaques than patients with high cortisol levels (26). HPA axis hyperactivity significantly increased with disease progression significantly (27). Hyperactivity of the HPA axis, over responsiveness to stressful events and high basal cortisol secretion, may be central to the development of a number of serious health consequences therefore adjusting HPA axis is essential to good health. Also improvements in HPA function may correlate with treatment with pharmacotherapy, psychotherapy and overall symptom improvement. It seems that our protocol had not sufficient stimulus to induced changes on HPA axis in female patients with MS.

There are several limitations of this work, which have to be considered. First of all, this study comprised a relatively small sample thus limiting statistical power to detect differential effects. Second, as it is well known the half-life of cortisol is 60-90 min (28) so one can conclude that a test result taken 48 h after last session in semi-long-term result of aerobic training. Owing to financial and human resource limitations, we were unable to provide a follow up study to determine the consistency of results. But a follow-up timeframe of less than two years is useful in order to determine consistency of the results.

5. Conclusions

Our results suggest aerobic training with specific intensity and duration utilized in this study had not effects on cortisol and DHEA-S levels in female patients with MS.

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