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### Changes of dehydroepiandrosterone and prolactin in response to aerobic exercise in female patients with multiple sclerosis

Sama Parvazi<sup>1</sup> and Mehrzad Moghadasi<sup>2\*</sup>

<sup>1</sup>Department of Exercise physiology, Islamic Azad University, Yasuj Science & Research branch, Iran

<sup>2</sup>Department of Exercise Physiology, Shiraz branch, Islamic Azad University, Shiraz, Iran  
Corresponding author

#### KEYWORDS

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#### A B S T R A C T

Multiple Sclerosis (MS) is an autoimmune genetic disease with symptoms such as hormonal dysfunction. Exercise may be effective to improve hormonal dysfunction in MS patients however it is not well known. Thus, the aim of this study was to examine the effects of 8 weeks endurance training on dehydroepiandrosterone sulfate (DHEA-S) and prolactin (PRL) in female patients with multiple sclerosis disease. 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 endurance 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 PRL were measured by ELISA kits before and after training. The results showed that PRL and DHEA-S concentrations did not change significantly after the intervention. In conclusion, the results suggest endurance training with specific intensity and duration utilized in this study had not effects on PRL and DHEA-S levels in female patients with MS.

#### Introduction

Multiple sclerosis (MS) is thought to be an autoimmune disorder that leads to the destruction of myelin, oligodendrocytes and axons [1]. Hormonal disorders are one of the most important compliant of MS patients. Previous studies demonstrated that the persons with MS have low levels of Dehydroepiandrosterone sulfate (DHEA-S) [2] and hyperprolactinemia also more common in MS patients [3].

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. It is possible that DHEA-S plays an important role in physical development during puberty [4]. Fatigue

unrelated to physical activity is a common symptom in MS and approximately 65% of individuals with MS report fatigue limitations [5]. Fatigue in progressive MS could be related to low serum levels of DHEA and DHEA-S [2]. On the other hand, the hyperprolactinemic patients exhibit greater disability. Half of the relapsing MS patients show a rise in PRL levels specifically during the acute stage of relapse, and a decrease during the recovery/remission stage [3].

Although previous studies demonstrated that exercise training increases the levels of DHEA-S and PRL in healthy subjects [6], athletics [7] and in bipolar patients [8], but a little data on exercise-induced changes of DHEA-S and PRL in patients with MS have been reported. Recently Rashidfar et al. (2013) noted that DHEA-S increased after 8 weeks resistance training in female patients with MS [9]. Alipour et al. (2013) studied the effect of 8 weeks resistance training on PRL level after in 8 weeks resistance training in female patients with MS [10]. They noted that PRL increased significantly after the intervention [10]. As the effect of aerobic exercise on DHEA-S and PRL is still unclear, this study was done to examine the effects of 8 weeks endurance training on DHEA-S and PRL in female patients with MS disease.

## **Methods**

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). Height and weight were measured, and body mass index (BMI) was calculated by dividing weight (kg) by height (m<sup>2</sup>).

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). 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 -80 °C for subsequent analysis. The plasma DHEA-S and PRL levels were measured in duplicate using an

enzyme-linked immunosorbent assay (ELISA) kits (Enzo Life Sciences GmbH, Germany and Pishtaz Teb, Tehran, Iran respectively). 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 covariate (ANCOVA) test. The relationship between DHEA-S and PRL after the intervention was determined using Pearson correlation 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).

## **Results and Discussion**

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 PRL did not change in the exercise training compared with the control group (Table 1). Pearson correlation test demonstrated that there was a positive relationship between DHEA-S and PRL after the intervention ( $r = 0.4$ ,  $P = 0.03$ )

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 [11,12]. Hormonal disorders are one of the most important complaints 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 endurance training on DHEA-S and PRL 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 [13,14], but a little data on exercise-induced changes of DHEA-S and PRL in these patients have been reported. PRL and DHEA-S exert multiple immunomodulatory effects and their circulating levels change in a contrasting manner in the course of some immune-inflammatory diseases [15]. Our results showed that DHEA-S and PRL did not change after 8 weeks aerobic exercise. Previously Rashidfar (2013) and Alipour (2013) reported that DHEA-S and PRL increased after 8 weeks resistance training in female patients with MS [9,10]. These discrepant results may be attributed to differences in subject populations and variation in the exercise protocols.

There is a positive relationship between DHEA-S and PRL and Vermeulen et al. (1977) noted that plasma DHEA and DHEA-S levels were significantly higher in women with elevated PRL levels [16]. Numerous investigators have shown hyperactivity of the hypothalamo-pituitary-adrenal (HPA) axis in MS patients [17] and in one study, 30% of MS patients had mild to moderate high PRL levels which were

suspected to be associated with hypothalamic lesions [18]. This hormone is produced by activated lymphocytes, as an immunoregulatory co-factor participating in the immunopathogenic mechanism of MS [19]. Results of the present study showed that there is a positive relationship between

DHEA-S and PRL after the intervention, thus it seems that the lack of effect of exercise training on DHEA-S might be due to the absence effect of exercise on PRL level however, additional research is needed to examine these mechanisms.

**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)	ANCOVA
<b>Body mass (kg)</b>				
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	
<b>BMI (Kg/m<sup>2</sup>)</b>				
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*	
<b>Body fat (%)</b>				
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	
<b>WHR</b>				
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	
<b>PRL (mIU/L)</b>				
Exercise (n=13)	533.0 ± 739.9	333.2 ± 127.2	0.2	0.3
Control (n=14)	596.9 ± 754.2	416.7 ± 260.8	0.3	
<b>DHEA-S (pg/ml)</b>				
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 ANCOVA test. \*P<0.05.

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