EXCELLENT PUBLISHERS

International Journal of Current Research and Academic Review

ISSN: 2347-3215 Volume 2 Number 9 (September-2014) pp. 92-98

www.ijcrar.com

Effect of resistance training on dehydroepiandrestrone sulfate levels and fatigue in women with multiple sclerosis disease

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KEYWORDS

Multiple sclerosis, Resistance training, Fatigue, DHEA-S

A B S T R A C T

Multiple Sclerosis (MS) is an autoimmune genetic disease that associated with chronic inflammation of the central nervous system, demyelization, axonal loss, and brain atrophy. Fatigue is a one of the most common problems in MS. Exercise may be effective to decrease fatigue in MS patients however it is not well known. The aim of this study was to examine the effects of 8 weeks resistance training (RT) on dehydroepiandrestrone sulfate (DHEA-S) levels and fatigue in women with multiple sclerosis disease. Twenty seven women with MS disease in a range of 20-40 year of old and EDSS lower than 5 participated in this study as the subject. Subjects were divided into control group (n=13) or training group (n=14) randomly. The training group performed progressive RT program, 3 days a week for 8 weeks. The control group was in absolute rest at the same time. Fatigue level was assessed by FSS questionnaire before and after training, and also, serum level of DHEA-S was measured by ELISA kits before and after training. The results showed that serum levels of DHEA-S increased and fatigue decreased after 8 weeks RT compare to the control group ($P<0.05$). In conclusion, the results suggest that RT with specific intensity and duration utilized in this study increases serum levels of DHEA-S and decreases fatigue in female patients with MS.

Introduction

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 [1,2]. Women are more likely to develop the disease than men (female: male ratio approximately 2-3:1). MS usually manifests between the age of 20 to 40 years, rarely much earlier during childhood, or in old age [3].

Fatigue unrelated to physical activity is a common symptom in MS that has been observed since the initial descriptions of this disease. Approximately 65% of individuals with MS report fatigue limitations [4] and as many as 40% describe it as the single most disabling symptom – a higher percent age than weakness, spasticity, balance or bowel/ bladder problems [5]. So this life style which reduces mobility can lead to secondary sequels such as obesity, osteoporosis, and/or cardiovascular damage [6]. 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 [7]. Previous studies demonstrated that reduced levels of DHEA-S linked with fatigue in MS [8,9]. Regular physical activity may alleviate fatigue while enhancing functional reserve capacity [10].

It is not clearly established whether exercise training can positively influence fatigue in MS patients. The findings show inconsistency because some studies show an effect [11,12], whereas others do not [13]. On the other hand, 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 in patients with MS have been reported. We hypothesized that exercise training would increase the DHEA-S and decrease the fatigue in MS patients. Thus the aim of this study was to examine the effects of 8 weeks RT on DHEA-S levels and fatigue in female patients with MS.

Methods

Subjects

The participants in this study were 27 female between 18 and 48 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 18 and 50 years. Their mean Expanded Disability Status Scale (EDSS) score was 2, with a range of 1 to 4.5.

Study design

This was a cross-sectional study, and each subject was tested during a single session lasting approximately 60 min. The study protocol was approved by the Fars Science, Research branch; Islamic Azad University, Fars, Iran and all study participants provided written informed consent before testing. Before the examinations a neurologist assessed EDSS and participants were randomly divided into an exercise group (n=14) and control group (n=13).

Measurements

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 mass, body fat percentage and lean body mass were assessed by bioelectrical impedance analysis using a Body Composition Analyzer (BoCA x1, Johannesburg, South Africa).

Fatigue Assessment

Fatigue measured by Fatigue Severity Scale (FSS). The FSS is a method that evaluates fatigue in individuals diagnosed with MS and others that also have conditions such as chronic fatigue immune dysfunction syndrome and systemic lupus erythemaytosus. FSS is widely used in MS studies and shows high reliability, validity and internal consistency. This scale is specifically designed to differentiate fatigue from clinical depression, since both may share common symptoms. A score of 4.5 is on average seen in people with depression alone, but people with fatigue-related MS, score an average of 6.5. The FSS is a 9-item questionnaire, each item rating from 1-7, and requires the subject to rate his or her own level of fatigue. Each participant was asked to answer the questions depending on how appropriate they felt the statement applied to them over the preceding week. A low value indicates low agreement with the statement whereas a high values indicates high agreement. The score is calculated by adding all 9-items and dividing it by 9 [17].

Biochemical analysis

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 ^{oC} for subsequent analysis. The plasma DHEA-S levels were measured in duplicate using an enzyme-linked immunosorbent assay (ELISA) kits (Demeditec Diagnostics GmbH, Germany).

Exercise training

All subjects performed 10 min warm-up at the beginning of each training session consisting of static stretching movements for like extended arm side stretch, biceps stretch, triceps side stretch, quadriceps stretch and hamstring stretch. The duration of each static stretching movement was at least 8 seconds. Subjects executed seven RT selected to stress the major muscle groups in the following order: biceps curls with dumbbell, side arm raisers with resistance band, back arm opener with resistance band, pelvic lift, towel crunches and twists, calf and ankle stretch with resistance band, and squad with dumbbell. RT consisted of 50-60 min of station weight training per day, 3 days a week, for 8 weeks. This training was performed in 7 stations and included 3 sets with 5-12 maximal repetitions at 50-70% of 1-RM in each station. 2 min rest was considered between each position and each training session was followed by cool-down. Subjects completed the protocol under the supervision of an exercise physiologist and a physician. At the end of the study all of the variables that were measured as pretest were measured again as posttest.

Statistical analysis

Results were expressed as the mean ± SD and distributions of all variables were assessed for normality. Paired t-test was used to compute mean (± SD) changes in the variables in control and training group pre and after the intervention. Differences among groups were assessed by using analysis of covariate (ANCOVA) 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

Changes in anthropometric and body composition variables

Anthropometric and body composition characteristics of the subjects at baseline and after training are presented in Table 1. Before the intervention, there were no significant differences in any of variables among the two groups. Body weight, body mass index (BMI), body fat mass and body fat percentage decreased ($P<0.05$) after 8 weeks RT compared to the control group, while no significant changes in the waist hip ratio (WHR) and lean body mass were found after the training (Table 1).

Changes in disability status (EDSS)

The results demonstrated that mean values of EDSS decreased ($P<0.05$, 27.7%) in the RT group, while no significant change in the control group was found (Table 1).

Changes in fatigue score

The results showed that the mean score of fatigue decreased ($P<0.05$, 20.5%) after 8 weeks RT compared to the control group (Figure 1).

Changes in DHEA-S

This results demonstrated that DHEA-S levels increased ($P<0.05$, 8.9%) in the RT group compared to the control group (Figure 2).

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. Hormonal disorders are one of the most important compliant of MS patients and exercise may be effective to improve hormonal dysfunction and fatigue in MS patients however it is not well known. Thus this study was done to examine the effects of 8 weeks RT on DHEA-S and fatigue score in female patients with MS disease. Fatigue occurs in the majority of MS patients and therapeutic possibilities are few. Randomized controlled trials have indicated that exercise training is associated with increased fitness, reduced motor fatigue, improved quality of life, and psychological conditions in MS patients [18,19]. Exercise therapy has the potential to induce a positive effect on MS fatigue, but findings are heterogeneous. Exercise studies have demonstrated benefits in fitness level, quality of life, balance, and walking capacity in people with MS [10] however, no consistent effect on fatigue has been reported.

Some multifaceted rehabilitation studies have shown improvements in fatigue [18,20] but others have shown no effect [21]. Mean score of fatigue decreased ($P<0.05$) after 8 weeks RT compared to the control group in our study. The decrease of fatigue level in our study matches the results of other studies. Previous studies also demonstrated that fatigue levels were decreased after aquatic exercise training, [18,22] RT [23] and endurance training [10]. In healthy subjects RT improves central motor activation and in MS patients RT enhances the efferent motor drive and in MS patients RT seems to reduce MS fatigue [24,25]. The perception of worsened fatigue after overtraining may occur as a consequence of afferent inhibition from strained muscles. Another plausible mechanism behind the effect of exercise on MS fatigue is a training-induced up-regulation of neuroendocrine growth factor production, which increases neuronal plasticity and thereby possibly improves compensatory cortical activation [26]. Also, an exercise-induced up-regulation of anti-inflammatory cytokines may have a beneficial effect on MS fatigue [27].

On the other hand the studies demonstrated that there is an inverse relationship between DHEA-S levels and fatigue in MS [8,9]. The results are in agreement with previous reports showing that DHEA-S increased after 8 weeks RT [28]. Possible mechanisms for exercise induced increases in DHEA-S have been outlined previously, with increased secretion rate by the adrenal cortex as a result of ACTH stimulation [29] and decreased metabolic clearance due to a reduction in hepatic blood flow during exercise [30] being the most commonly cited. Thus it seems that increase of DHEA-S may lead to decrease of fatigue score in female patients with MS.

Acknowledgement

The work was supported by grants from the Fars Science & Research branch, Islamic Azad University. The authors gratefully acknowledge the all subjects whom cooperated in this investigation.

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