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Eight weeks resistance training reduces interlukin-17 in women with multiple sclerosis

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Abstract

Introduction: Multiple sclerosis (MS) is an immune mediated demyelinating disease of the central nervous system. The aim of present study was to investigate the effect of eight weeks resistance training on interlukin-17 (IL-17) in women with MS.

Material & Methods: Twenty seven women with MS disease in a range of 18-48 year of old and EDSS lower than 4.5 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 resistance training program, 3 days a week for 8 weeks, whereas control group continued their usual routine activities. Serum level of IL-17 was measured by ELISA kits before and after training.

Results: The disability score and IL-17 were significantly decreased from 1.8 to 1.3 and from 716.3 to 601.3 pg/ml respectively in test MS subjects after 8 weeks resistance training.

Conclusions: In summary, the results suggest that resistance training has useful anti-inflammatory effects by decrease in serum IL-17 production in women with MS.

Keywords: Multiple sclerosis, Resistance training, Inflammation, Cytokines

1. Introduction

Multiple sclerosis (MS) is an inflammatory disorder of the central nervous system (CNS) characterized by recurring episodes of inflammatory demyelinating lesions with prominent astrogliosis (1). MS is the most common neurological disorder in young adults, which has many implications for patients and society with over two million sufferers worldwide (2). It leads to substantial disability through deficits of sensation and of motor, autonomic, and neurocognitive function (1,3). The cause of MS involves both genetic and environmental factors (4). Damage to the axonal myelin, by inflammatory cells, leads to defects in electrical signal transfer (5). This axonal damage is the essential cause of clinical disability and progress of the disease although the exact pathogenesis of MS is largely unknown (6,7). MS is primarily an inflammatory disorder and this inflammatory process proposed to be mediated mainly by pro-inflammatory cytokines, chemokines and other mediators (8). Understanding the mechanisms of cytokine-mediated CNS damage is necessary to develop new therapies that promote reversal of the MS pathology (9). Clinical and animal studies have showed that MS is an autoimmune disorder caused by myelin-specific CD4+T cells of the Th1 (10) and Th17 type (11-13). Furthermore, anti-inflammatory cytokines of the Th2 type (e.g. IL-10, IL-4) have been associated with remissions and recovery from disease (14). In contrast, Th1 and Th17 type cytokines (e.g. IL-6 and IL-17) are pro-inflammatory and play a key role in the pathogenesis of MS (15). Increasing IL-17 mRNA expression is shown in blood (16-18) and cerebrospinal fluid of MS patients and joint fluid in patients with arthritis (19).

Several studies have indicated that exercise training can revert the chronic inflammation and its related pathologies. The anti-inflammatory effect of exercise training in chronic illnesses is mediated by decreased pro-inflammatory cytokine IL-6, IL-8, TNF-α, and IFN-γ (20,21) and an increase in anti-inflammatory IL-10 concentration (20-22). The critical roles of pro- inflammatory cytokines in the pathogenesis of MS make them a pivotal target for the therapeutic approach. Since studies on exercise and immunology highlight the potential of regular exercise as an anti-inflammatory therapy for patients with chronic inflammatory disease (23,24), exercise training may have therapeutic potential for the treatment of neuroinflammatory and neurodegenerative disease. Previously Golzari et al. (2010) reported that plasma IL-17 and IFN-γ level was significantly decreased after 8 weeks combined training in women with MS (25). Although the changes in IL-17 levels might be an important clue for understanding the beneficial effects of exercise on MS, a little data on exercise-induced changes of IL-17 have been reported. Therefore, in this study we examined the effect of eight weeks resistance training on IL-17 in women with MS.

2. Material & 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).

► *Biochemical analyses*

Fasted, resting morning blood samples (5 ml) were taken at the same time after familiarization. For menstrual status, all the participants were menstruating regularly and defined as eumenorrheic (28- to 32-day menstrual cycles during the previous year); all testing was performed during the follicular phase of the menstrual cycle. All the subjects fasted at least for 12 hours and a fasting blood sample was obtained by venipuncture. Plasma obtained was frozen at –80 °C for subsequent analysis. The plasma IL-17 was measured in duplicate using an enzyme-linked immunosorbent assay (ELISA) kits (Boster Biological Technology Co., Ltd, Hubei, China). The sensitivity of kit was <1 pg/ml.

► *Resistance 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 resistance training 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. Resistance training 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 pre-test were measured again as post-test.

Statistical analysis

Results were expressed as the mean ± SD and distributions of all variables were assessed for normality. Paired t-test and Wilcoxon test were 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) and Mann-Whitney U 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 training are presented in Table 1. Before the intervention, there were no significant differences in any of variables among the two groups. Body weight, BMI, body fat mass and body fat percentage decreased ($P<0.05$) after 8 weeks resistance training compared to the control group, while no significant changes in the WHR and lean body mass were found after the training (Table 1). The results demonstrated that mean values of EDSS decreased ($P<0.05$, 27.7%) in the resistance training group, while no significant change in the control group was found (Table 1).

Table 1. Body composition characteristics and disability status of the subjects

	Baseline (mean ± SD)	After intervention (mean ± SD)	Paired t-test (Sig)	ANCOVA
Body weight (kg)				
Exercise (n=14)	66.1 ± 16.2	64.1 ± 16.1*	0.001	0.006
Control (n=13)	65.03 ± 12.5	65.4 ± 13.7	0.5	
BMI (Kg/m^2)				
Exercise (n=14)	25.8 ± 6.5	24.9 ± 6.2*	0.001	0.003
Control (n=13)	25.03 ± 4.9	25.9 ± 4.2	0.4	
Body fat (%)				
Exercise (n=14)	33.8 ± 8.7	32.5 ± 9.09*	0.04	0.04
Control (n=13)	33.8 ± 7.1	34.06 ± 7.2	0.6	
Body fat mass (kg)				
Exercise (n=14)	23.5 ± 10.2	22.3 ± 10.0*	0.01	0.03
Control (n=13)	22.7 ± 8.5	23.2 ± 8.5	0.3	
Lean body mass (kg)				
Exercise (n=14)	39.9 ± 6.4	40.6 ± 6.2	0.07	0.08
Control (n=13)	39.6 ± 4.7	39.1 ± 4.8	0.4	
WHR				
Exercise (n=14)	0.8 ± 0.05	0.77 ± 0.06	0.02	0.3
Control (n=13)	0.81 ± 0.01	0.8 ± 0.04	0.5	
EDSS				
Exercise (n=14)	1.8 ± 1.2	1.3 ± 1.5	0.01	0.04
Control (n=13)	2.1 ± 1.4	2.1 ± 1.5	0.7	

Data are the mean ± SE of baseline and final values and of the body composition parameters and disability status in each group. Wilcoxon test was used to compute mean (± SD) changes in the variables in control and training group pre and after the intervention. Comparison different significance between groups after 8 weeks resistance training was determined by using the ANCOVA test. * $P<0.05$

Mean concentration of the IL-17 for both test and control MS subjects are reported in the Figure 1. IL-17 concentrations were changed significantly ($P<0.05$) after 8 weeks resistance training in MS patients. In these cases, IL-17 was decreased from 716.3 ± 709.2 pg/ml to 601.3 ± 675.7 pg/ml. There was no significant difference in IL-17 concentration of control MS subjects who had no exercise training between weeks 0 and 8 of the experiment.

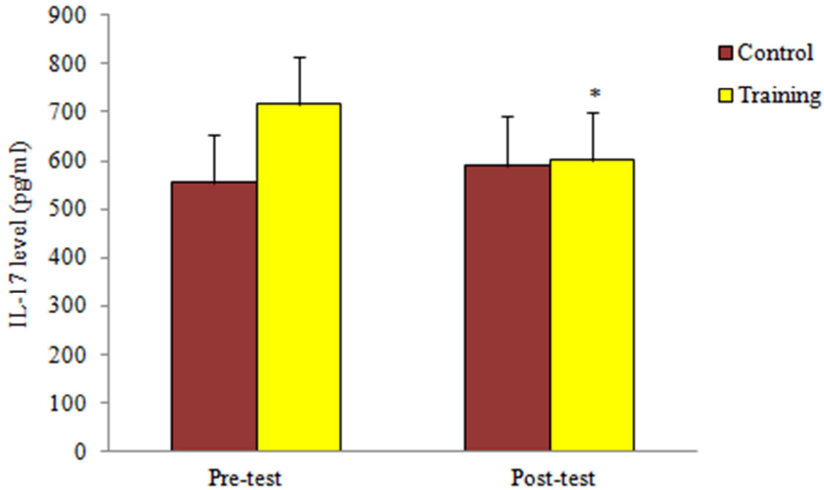

Figure 1. Changes of IL-17 after 8 weeks resistance training

Data are the mean ± SE of baseline and final values of the IL-17 level in each group. Paired t-test was used to compute mean (± SD) changes in the variables in control and training group pre and after the intervention. Comparison different significance between groups after 8 weeks RT was determined by using the Mann-Whitney U test. * $P<0.05$

4. Discussion

Clinical studies investigating the impact of exercise training on IL-17 levels in individuals with MS are limited. The aim of present study was to investigate the effect of eight weeks resistance training on IL-17 in women with MS. The results indicated that body weight, BMI, body fat mass and body fat percentage decreased ($P<0.05$) after 8 weeks resistance training compared to the control group. Several studies have shown that caloric restriction can improve body composition by reducing body weight, BMI, body fat mass and body fat percentage. Also, physical activity has been shown to have a modest effect on body weight (26). Formica et al. (1997) have reported that fat-free mass decreases in sedentary MS patients, which can be induced by skeletal muscle atrophy (27). Dietary restriction only is accompanied by decreased fat-free mass that leads to reduction in basal metabolic rate. This can maintain fat reserves and slow weight loss (26). Therefore, maintaining lean body mass by exercise is an appropriate way to maintain long-term weight loss and fat-free mass, particularly in patients with MS. Decreases of body weight, body fat mass and body fat percentage and no significant changes in the lean body mass after 8 weeks resistance training suggesting resistance training can maintain muscle mass during weight loss in MS patients.

Disability status tended to decrease in all subjects following the exercise program suggesting an improvement in their disability after 8 weeks of resistance training (from EDSS 1.8 to 1.3; $P = 0.02$). Several studies have shown that regular exercise improves disability status in MS (28-30). The benefits of regular exercise in MS include enhanced fitness, reduced fatigue, improved mood and the ability to perform tasks of daily living with increased energy. In fact, improved muscle strength as a potential predictor of ambulatory function (31) explains current regimen success in improving mobility.

MS is an inflammatory demyelinating disease of the CNS that created by the imbalance between pro-inflammatory and anti-inflammatory cytokines (32). There is some evidence suggesting the role of IL-17 in MS patients. Babaloo et al. (2010) reported that IL-17A and IL-17F mRNA expression increases in peripheral blood mononuclear cells of patients with MS (16). In 2013, Babloo et al. again confirmed the critical role of IL-17 in MS disease (2). Kebir et al. (2007) have showed that the endothelial cells express high levels of IL-17 receptors and are more permeable in response to IL-17, and promote CNS inflammation in MS patients (33). The results of present study indicated that IL-17 level was decreased in the training group compare to the control group ($P<0.05$). Golzari et al. (2010) also reported that plasma IL-17 level was significantly decreased after 8 weeks combined training in women with MS (25). Golzari et al. (2010) did not give any clear explanation about the details of exercise training. The positive effect of moderate exercise on the immune system has been confirmed by many researchers. In an another study Heidarianpour et al. (2016) indicated that serum levels of IL-17 were decreased after 8 weeks of moderate exercise in morphine-dependent rats (34). Lowder et al. (2010) also found that moderate exercise reduces the production of Th2 and Th17 cytokines in both healthy and asthmatic rats (35). Heidarianpour et al. (2016) noted that one reason for the decrease in the IL-17 level after moderate exercise can be the positive impact of this kind of exercise on increasing the serum

IFN-γ level and the inhibitory effect of cytokines on the development of Th17. Regarding the identification of IL-17-producing cells in adipose tissues such as Tγδ cells, the reduction of the tissues after moderate exercise can decrease the production of this inflammatory cytokine (34).

5. Conclusion

IL-17 decreases after 8 weeks resistance training in the present study, suggesting resistance training is a useful anti-inflammatory intervention for MS.

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