



THE EFFECTS OF THE RESISTANCE TRAINING ON SERUM CORTISOL, IL-6, IL-8, AND TNF- α

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ABSTRACT:

Objective: The purpose of this study is to investigate effects of resistance training on IL-6, IL-8, TNF- α , blood hematocrit and cortisol levels.

Materials and Methods: Thirteen players from Manisa Celal Bayar University soccer team and 14 sedentary male students were used as the study subjects. The subjects, whose average age was 18-24 years old, were healthy and free of any cardiovascular diseases. Anthropometrics measurements and blood samples were obtained from all the subjects. Blood samples were obtained basal sample (before the exercise), immediately after the training program (post-exercise), and 2 hours after the training program (2h post-exercise). All subjects participated in the training program in which intensity prescribed individually in 10 different exercises; seated leg press, knee extension, knee flexion, chest press, chest flys, lat pull down, shoulder press, triceps extension, biceps curl and sit-ups. The exercise protocol was 8-10-12 repetitions of each exercise at 70 to 80 % of one-repetition maximum in accordance with the pyramid training system and three sets for each station. The volume of resistance training was 50-60 minutes.

Results: Post exercise IL-6 ($p= 0.05$) and IL-8 ($p= 0.04$) concentration of athletes were statistically lower compared to that of sedentary group. Two hours after the exercise, the TNF- α values of the sedentary individuals were also statistically higher than those of the trained individuals. Furthermore, serum cortisol concentrations were found to be decreased in both study groups in post exercise and 2h post exercise samples compared to basal values ($p<0.05$). Post exercise IL-8 ($p=0.04$) and TNF- α ($p=0.04$) values of sedentary group increased significantly compared to values at 2h post exercise. There was no statistically significant change in IL 6 values of the trained and sedentary subjects immediately after the exercise.

Conclusion: IL-6, IL-8, and TNF- α responses to resistance training vary depending on the recruitment of different muscle fiber types by the trained individuals during the resistance training and the recovery of glycogen storage, which is found to be different from that of sedentary individuals. The decrease in the serum IL-6 and IL-8 concentrations at post exercise and 2h post-exercise samples in the training group when compared to the sedentary group revealed us that, training lowers the proinflammatory marker IL-6 and IL-8 which reflects a positive effect of the training on the overall body inflammation status.

KEY WORDS Resistance Exercise; IL-6; IL-8; TNF- α ; Cortisol

INTRODUCTION

It is well-known that inflammation is increased by clinical conditions such as atherogenesis, thrombogenesis, cardiovascular diseases, insulin resistance, obesity and type-2 diabetes mellitus [1]. In these cases, inflammation is accelerated by the elevated

secretion of pro-inflammatory cytokines released by macrophages in the visceral adipose tissue. It has been observed that physical activity has a similar inflammatory pathogenesis. In addition, this inflammatory response has been reported to vary not only due to the type, intensity and scope of the exercise but also the



physical fitness level of the person undertaking the physical workload [2].

In the clinical inquiry, inflammatory markers such as interleukins, cytokines and hormones are used as independent variables [1]. Cytokines are released in response to inflammatory reactions such as infection and tissue damage [3]. Exercise induces increased circulating levels of a number of cytokines [4]. Recent studies on exercise and cytokine response have shown that, certain cytokines are visible in the blood during and after exercise [5, 6, 7, 8, 9].

Studies investigating the immune response to exercise are divided into two categories according to the type of the exercise. Resistance exercise may cause myofibrillar disruption and inflammatory response. In fact, cytokines are increased in the circulation in response to intense concentric and eccentric muscle contractions [10] The first and the most common study area is the effect of aerobic activities on the immune system markers. In response to the exercise, IL-6 is released into the blood, which is synthesized in the skeletal muscles [4,11]. In a study conducted with marathon runners, the concentration of IL-6 cytokine just after the marathon was found to have increased 50 times compared with the baseline values [11]. This was believed to be subsequent to the glycogen depletion in the muscles [12]. In the same study, it was also observed that long-term aerobic exercise involving both concentric and eccentric contractions either increased or did not change the plasma concentration of IL-8. Likewise, in another study, it was reported that the remarkable increase in the plasma concentration of IL-8 was only as a response to aerobic concentric exercise [12], and the elevated levels of IL-6 and TNF- α in circulation were associated with the development of sarcopenia. Despite the significant increase in IL-6 and TNF- α concentrations in blood circulation following aerobic exercise, the result was not the same for muscles. While some studies reported an increase in the TNF- α levels after exercise, others found that the levels were reduced [13,14]. In addition to aerobic exercise, studies on the second exercise type, the resistance exercise, have been carried out since 2000 [9, 15]. One of the most important difference

between resistance and aerobic exercise is that after the resistance exercise muscle glycogen is not fully consumed. Another important discrepancy results from the structural and functional properties of muscle fiber types used during resistance exercise of different intensities, and from the muscle varied content of the muscle glycogen of the recruited fibers [16]. In addition, IL-6 release in acute exercise varies according to the duration and intensity of the exercise, the muscle mass involved in exercise [17]. Furthermore, training background of the participants could also affect the aforementioned variables and the causes of different results on immune markers right after resistance training. while a single bout of resistance training increases plasma cytokines, chronic long-term resistance training increases antioxidant capacity and the long term effects due to adaptation to training results in low plasma cytokines [18].

There have been a limited number of studies conducted with trained and untrained individuals to demonstrate the effect of a single resistance training session and the acute changes in circulating cytokines [7, 8, 9, 10, 19, 20, 21]. Therefore, the aim of this study is to investigate the effect of resistance exercise on the levels of serum cortisol hormone, IL-6, IL-8 and TNF- α in trained and sedentary individuals.

METHODS

The participants of this study were 27 men attending the School of Physical Education and Sports in Manisa Celal Bayar University (MCBU). Thirteen players from the school's football team constituted the trained study group, and the sedentary control group was formed from 14 male students with similar anthropometric measurements. The football players were randomly selected from the 25 students competing in the school team. The control group participants were randomly selected from healthy male students of MCBU between the ages of 18 and 24 with no cardiovascular diseases and with a normal skeletal-muscle function. To form the

sedentary group, face-to-face and phone call interviews were conducted and fourteen voluntary individuals who had not undertaken regular physical exercise for 6 months were selected. The research was approved by the Ethics Committee of the MCBU Faculty of Medicine.

Study Design

Prior to the study, all the participants underwent a physical examination and an electrocardiography (ECG). Before the experiments, the anthropometric measurements were obtained. The body weight and body fat index analyses were performed using the Tanita Bioelectrical Impedance system (Tanita 300 MA, Tanita C.O., Tokyo-Japan). In order to determine the initial exercise loads, 8, 10 and 12 repetition maximums (RM) were obtained from each participant and each exercise station at least 72 hours before the experiment [22, 23]. Before the resistance exercise or other experiments, the participants engaged in a slow-pace warm up exercise run was performed on the Nordictrack (USA) 9600 model and SportsArt 6310 model treadmills. Jimsa brand (Bursa-Turkey) resistance machines were used for seated leg press, knee extension, knee flexion, chest press, butterfly press, lat pulldown, triceps extension, shoulder press and sit-up stations [24, 25]. Exercises involving free weights such as the biceps curl were performed using Jimsa barbell and weights.

To determine the basal levels of the biochemical parameters before the exercise program, forearm venous blood samples

were collected from all participants between 08.00 and 09.00 after a minimum of 12-hour fasting. Before the exercise, the participants also jogged for 5 minutes followed by a 5-minute stretch for muscle groups. The experimental exercise routine lasted 50-60 minutes on the following 10 stations; seated leg press, knee extension, knee flexion, chest press, butterfly press, lat pulldown, shoulder press, triceps extension, biceps curl and sit-up. The exercise protocol was 8-10-12 repetitions of each exercise at 70 to 80 % of one-repetition maximum (1RM) in accordance with the pyramid training system and three sets for each station [26, 27]. Resting intervals were 2 minutes between each station and 1-1.5 minute between each set. In-between the sets and stations, the participants stretched their working muscles [28]. Blood samples were collected from the participants twice; one being immediately after exercise (post exercise) and the other two hours later (2h post exercise) [7, 29].

Blood Collection and Biochemical Analysis

Cortisol, hematocrit (hct), IL-6, IL-8 and TNF- α concentrations were analyzed in the serum samples. Serums TNF- α , IL-6 and IL-8 concentrations were assessed by commercial reagents (Human TNF- α , IL-6, IL-8 Bender MedSystems GmbH, Europe-Vienna, Austria) by using enzyme immunoassay (ELISA) method. The serum cortisol levels were analyzed with the electrochemiluminescence method on analyzer (DXI-800, Beckman Coulter Inc. Fullerton, CA, USA). Complete blood count analysis and hct levels were performed on analyzer (LH700, Beckman Coulter Systems, Fullerton, CA, USA).

Statistical Analysis

The SPSS (Statistical Package for the Social Sciences) 16 software package for Windows

XP was used for the statistical analysis. *Mann Whitney U* test was employed to determine whether there was a statistical difference between the study and sedentary

groups in terms of descriptive and anthropometric measurements and independent variables (Hct, cortisol hormone, IL-6, IL-8 and TNF- α values before, immediately after and two hours after

resistance exercise). The within-group analysis was performed using the *Wilcoxon Signed Rank Test*. The significance level was taken as 0.05.

STATISTICAL RESULTS

Table 1 presents the descriptive statistics of the trained and sedentary groups that participated in this study. Contrary to expectations, there was no significant

difference between the two groups in terms of the descriptive statistics and the anthropometric measurements.

Table 1. The descriptive statistics of the sedentary and trained young male participants

Group	Trained (n=13)	Sedentary (n=14)	P
Age	20.92 \pm 2.29 (18-24)	20.86 \pm 2.66 (18-24)	0.19
Height (cm)	182.23 \pm 6.03 (170-189)	178.64 \pm 7.21 (168-194)	0.49
Weight (kg)	74.81 \pm 8.19 (59.3-84.3)	71.99 \pm 7.80 (59.6-90.1)	0.74
Fat (%)	13.09 \pm 4.60 (4.4-19.9)	12.15 \pm 3.27 (6.8-17.4)	0.26
BMI (kg/cm ²)	22.56 \pm 2.64 (17.1-26.2)	22.59 \pm 2.21 (19.5-26.9)	0.58
Fat-Mass	9.90 \pm 3.96 (2.6-15.2)	8.90 \pm 3.10 (4.3-15.7)	0.20
FFM (kg)	64.90 \pm 4.88 (56.7-70.8)	63.08 \pm 5.58 (54.8-74.4)	0.75
TBW (kg)	47.51 \pm 3.57 (41.5-51.8)	46.18 \pm 4.09 (40.1-54.5)	0.75

BMI: Body mass index, FFM: Fat-free mass, TBW: Total body water

*p < 0.05 Values are presented as mean \pm standard deviation and the minimum and maximum values are given in parenthesis under the mean values. The analysis between the groups was performed using the *Mann Whitney U test*.

According to results of the *Mann Whitney U* analysis, there is given the trained and sedentary individuals in terms of their cortisol, Hct, IL-6, IL-8 and TNF- α values

before, immediately after and two hours after the exercise (Table 2).

Table 2. Parametric values of the trained and sedentary groups before (basal), immediately after (post exercise) and two hours after the exercise (2h post exercise).

	n	Basal	p	Post Exercise	p	2h Post Exercise	p
Cortisol (pg/ml)	Trained 14	14.29 \pm 4.20	0.31	7.32 \pm 1.95	0.30	7.19 \pm 2.58	0.29
	Sedentary 14	13.51 \pm 4.45		8.23 \pm 2.98		7.65 \pm 3.21	
Hematocrit	Trained 14	45.13 \pm 3.53	0.36	44.66 \pm 3.36	0.18	43.64 \pm 3.52	0.35

(%)								
IL-6 (pg/ml)	Sedentary	14	45.85±3.36	0.08	46.03±4.40	0.05*	44.20±3.60	0.28
	Trained	14	3.77±1.67		3.68±0.47		3.70±0.6	
IL-8 (pg/ml)	Sedentary	14	3.85±0.85	0.01*	4.07±1.82	0.04*	4.73±1.82	0.08
	Trained	14	19.07±15.21		16.26±14.39		27.26±20.06	
TNF-α (pg/ml)	Sedentary	14	40.62±28.13	0.09	29.45±20.13	0.13	41.04±25.91	0.00*
	Trained	14	3.43±5.46		3.18±6.59		2.51±2.99	
	Sedentary	14	4.00±3.03		2.80±2.57		5.76±4.99	

Values are presented as mean±standard deviation.

*p < 0.05 The analysis between the groups was performed using the *Mann Whitney U test*.

According to the results of the analysis, the basal IL-8 values of the sedentary individuals were found significantly higher than those of the footballers (p=0.01), and this difference was apparent in the results obtained after the exercise (p=0.04). Also, the IL-6 values of the trained group immediately after the exercise were found to be statistically lower than those of the sedentary

group (p=0.05). Furthermore, two hours after the exercise, the TNF-α values of the sedentary individuals were also statistically higher than those of the trained individuals.

Table 3 presents the values of the two groups in terms of the change values obtained before, immediately after and two hours after the exercise.

Table 3. Change values (Δ) within the trained and sedentary groups in terms of the results obtained before, immediately after (post exercise) and two hours after the exercise (2h post exercise)

Values are presented as mean±standard deviation. The intra-group analysis was performed using the *Wilcoxon signed*

	Trained Group			Sedentary Group		
	Basal- Post exercise % Δ	Post exercise.- 2h post exercise % Δ	Basal- 2h post exercise % Δ	Basal-post exercise % Δ	Post exercise.- 2h post exercise % Δ	Basal- 2h post exercise % Δ
Cortisol(pg/ml)	-95.2 ^a	1.8	-98.7 ^b	-64.1 ^d	-7.5	-76.6 ^e
Hematocrit(%)	-1.0	-2.3	-3.4 ^c	0.9	-4.1 ^f	-3.7 ^g
IL-6 (pg/ml)	-2.4	0.5	-1.8	5.4	13.9	18.6
IL-8 (pg/ml)	-17.2	40.3	30.0	-37.9	28.2 ^h	1.0
TNF-α (pg/ml)	-7.8	-26.6	-36.6	-42.8	51.3 ⁱ	30.5

rank test method p < 0.05

^ap=0.001 ^bp=0.002 ^cp=0.009 ^dp=0.002 ^ep=0.004 ^fp=0.003 ^gp=0.001 ^hp=0.041 ⁱp=0.041

According to the results of the Wilcoxon Test, there was a significant decrease in the cortisol change values of football players before and immediately after the exercise (p=0.001), and this decline was similar for the cortisol (p=0.002) and hematocrit (p=0.009) values before and two hours after the exercise.

Statistical analysis indicated a significant decrease in the cortisol (p=0,002) change values of sedentary participants before and immediately after the exercise. Statistical

analysis shown a significant reduce in the cortisol (p=0,004) and hematocrit (p=0,001) change values of sedentary participants between baseline and 2 hours after the exercise. Also statistical analysis indicated a significant decrease in the cortisol cortisol change values of sedentary participants immediately after the exercise

Also a similar trend was observed in terms of hematocrit (p=0,003) change values between after the exercise and 2 hours after the exercise. In addition, a significant increase

was observed in the IL-8 and TNF- α change values ($p=0.041$) immediately after and two hours after the exercise.

DISCUSSION

In this study, the effect of resistance exercise of individual-based intensity on the inflammatory symptoms and serum cortisol levels in trained and sedentary individuals, the IL-8 cytokine level was found to be reduced by 2.4 % in the trained group after the exercise while it increased by 5.4 % in the sedentary group. A similar result was obtained regarding the TNF- α values, which is interference helping to regulate inflammation. Compared to the initial basal values, in the trained group, the TNF- α levels decreased by 36.6% immediately after the exercise and by 26.6% two hours after the exercise; while in the sedentary group, it increased by 51.3% and 30.5%, respectively. The most remarkable result in terms of the immune responses of the participants was related to the IL-8 values. The decrease in the IL-8 values immediately after the exercise was 17.2 % in the trained group whereas there was a 37.9 % increase in the sedentary group. The results of our study indicate that in addition to age, body mass index and basal TNF- α and CRP values [2], the sports history and physical fitness level of participants and the intensity of exercise have a great impact on the inflammatory responses to resistance exercise. In the evaluation of immune system responses to exercise, the physical fitness level of participants should be taken into consideration. In the studies conducted with healthy non-athletic male participants [7, 30], the IL-6 values were found to increase after low and high intensity resistance exercise, which is also in agreement with the results we obtained from the sedentary group. Similarly, Edwards et al. [31] observed an increase in the IL-6 values after maximal exercise and found no significant difference after submaximal exercise. However, there was a

significant increase in the IL-6 values at 30 and 60 minutes after exercise. Hirose et al. [30] found that after resistance exercise there was a significant decrease in the TNF- α and IL-8 levels of the sedentary individuals and/or those engaged in recreational sports, which is also in agreement with the results of our study regarding the sedentary group. In another study, 17 healthy untrained men were divided into three different exercise groups; control, bicycle and knee extension. The resistance exercise group undertaking the knee extension performed two-legged knee extensions at loads of 60% of each participant's maximum capacity. The IL-8 results of the knee extension group were similar to those obtained in our study in the sedentary group and the highest level was reached 1.5 hours after the exercise [32]. When the results of our study regarding the responses of trained participants to resistance exercise are compared with those in the literature [33], there was no statistically significant difference in the IL-6 and TNF- α values after resistance exercise, which supports the results of our study. Nienam et al. [25] found an increase in all the cytokine values (IL-6, IL-8 and TNF- α) of the strength-trained subjects after resistance exercise. Yet, it is not meaningful to compare their results with our study since they investigated mRNA using the muscle biopsy technique.

The abundance of studies conducted with sedentary and recreation sports groups allows for the comparison of some of the results we obtained, whereas, the lack of studies with trained individuals signify the contribution of our study to the literature. The difference between the sedentary and trained individuals in terms of their inflammatory symptom responses to resistance exercise can be explained by the type of muscle fibers they recruit for exercise. While the muscle fiber type used by trained individuals at loads corresponding to the 70 to 80 % of maximum load is more frequently limited to type IIa and type I, for the sedentary individuals it also

includes type IIb fibers which contain more glycogen [34, 35]. In addition, glycogen is maintained in the type IIb fibers of trained individuals. However, in the untrained individuals, the fast consumption of glycogen due to the selected muscle group and low anaerobic endurance changes the cytokine responses. This hypothesis proposed by the results of our study is also supported by Hirose et al. [30]. In addition, the effect of different exercise types on glycogen oxidation and cytokine responses has been investigated and sports branches requiring long-term endurance have been compared. The results from marathon runners showed that IL-concentration increased 50 times after the run, which was attributed to the decrease in the muscle glycogen content [11]. This also supports the hypothesis we have proposed.

Another reason for the different cytokine responses of trained and untrained individuals has been reported as trained individuals having a higher number of capillaries per muscle fibers and increased GLUT4 proteins inducing the glucose uptake into the skeletal muscles [35, 36], which increases the amount of glycogen consumed by trained individuals particularly during high intensity exercise. Furthermore, higher number of capillaries per muscle fibers and increased GLUT4 proteins inducing the glucose uptake into the skeletal muscles by trained individuals particularly during high intensity exercise [35, 36], lead to higher level of glycogen consumption and different cytokine responses. In terms of the blood Hct values, there was a statistically significant decrease in both trained and sedentary groups two hours after the exercise. In the literature, the Hct values were found to increase after long-term aerobic exercise, which is attributed to a small amount of decrease in the blood serum due to fluid loss during exercise [37]. The increase in the Hct levels after exercise has been explained by the fluid loss during endurance or long duration training. We believe that the resistance exercise used in the current study was not

sufficiently long or intensive to create a difference in the blood serum levels. However, since the participants were not restricted in terms of their liquid intake before and after the exercise, the decrease in the Hct levels could be related to liquid intake. Similarly, Ramel et al. [38] observed a decrease in the hematocrit values of trained individuals two hours after the exercise. However, contrary to our study, the increase in the sedentary group two hours after exercise was not found to be significant.

In the current study, when compared with the basal values, the decrease in cortisol levels immediately after and two hours after the exercise was significant. There was no difference between the trained and untrained individuals in terms of their cortisol responses to the intensity and type of exercise. However, in the literature, hormonal responses to different exercise types have been investigated. In similar studies, while there was no significant change in the cortisol values after resistance exercise [33, 38, 39], a significant increase was observed in cortisol levels following long-term exercise [40, 41]. It was assumed that the difference in the results obtained from two different types of exercise was attributed to the glycogen content during and after the exercise. When the whole glycogen content is depleted during recovery after aerobic exercise, not all the glycogen content is used after 1-hour exercise, particularly with anaerobic weights. In addition, during the recovery of ATP used in exercises performed with weights, the blood is accumulated and there is an increase in the lactate, pyruvic acid and glycogen content, which accelerates glycogen resynthesis during recovery. All these factors are considered to change the hormonal balance. In addition, in the resistance exercise, type II muscle fibers are extensively used and their recovery rate is much faster than type I muscle fibers used in the aerobic exercise [42].

In our study, the change in the cortisol hormone during the recovery can also be associated with the measurements and exercise taking place early in the morning. This is also supported by other studies in the literature [43]. Similar to our research, another study [41] conducted with participants of similar age and comparable demographic data using exercise of different intensity and types showed that after resistance exercise there was a statistically significant decrease in cortisol levels obtained in the morning.

In conclusion, the lack of statistical difference between the footballers and sedentary participants in terms of their anthropometric parameters can be explained by the intermittent anaerobic nature of football training. In addition, the increased anaerobic threshold of trained individuals due to the type of training and their biochemical responses to the resistance exercise performed with fixed loads have an impact on the type of muscle fiber type recruitment during the exercise and the glycogen metabolism after the exercise and during the recovery. Therefore, when the IL-6, IL-8 and TNF- α responses associated with the muscle glycogen metabolism are compared, in addition to age, body mass index, basal TNF- α and CRP values and the type of exercise [2], it is also important to take the athletic of the and physical fitness level of the participants into consideration.

Additionally, the differences between the cortisol levels measured in the morning in our study and at different times of day in other studies will not only contribute to further studies on immune system and resistance exercise but can also assist in determining the appropriate time of day to undertake resistance exercise programs in team sports.

In the future studies; we recommend that the training background, the frequency and intensity of the training, the levels of muscle glycogen content and the time of day of the

training of the participants should be taken into consideration.

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