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The Effect of Eight Weeks of Aerobic Exercise on Interleukin- 6, Insulin Resistance and Blood Glucose of Overweight Female

Masumeh Esmaili Alamdari [1], Mehrdad Fathi [*1], Nahid Bije [1], Elham Pouryamehr [2]
1. Department of Sport Physiology, Ferdowsi University of Mashhad, Mashhad, Iran
2. Department of Sport Physiology, Bojnourd Branch, Islamic Azad University, Bojnourd, Iran

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***Corresponding author:**
Mehrdad Fathi. Department of Exercise Physiology, Ferdowsi University of Mashhad, Mashhad, Iran

Phone: +989152570058

Fax: +985138829580

Email: mfathei@um.ac.ir

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Abstract

Introduction: The important factors in the development of chronic diseases are obesity and overweight. The purpose of this study was to investigate the effect of eight weeks aerobic training on interleukin- 6, insulin resistance and glucose in overweight young girls.

Methods: Twenty-one girls with an age range of 20-30 years were selected voluntarily and randomly divided into experimental (n = 11) and control (n = 10) groups. The aerobic exercise program lasted for 8 weeks, with a frequency of 3 sessions per week, with training sessions starting from 30 minutes in the first session and 50 minutes in the final session, and the intensity of 60-70% of the heart rate reserve. The blood sample was taken before beginning the main study program and after 8 weeks of aerobic exercises. The independent sample t-test, paired sample t- test and the Kolmogorov–Smirnov test were used to compare the pre-test and post-test information between the groups.

Results: Eight weeks of aerobic exercise had no significant effect on body mass index (p=0.43), fat percentage (p=0.72), waist to hip rate (p=0.85), interleukin-6 (p=0.86), insulin resistance (p=0.59) and glucose (p=0.78), nevertheless significantly reduced the weight (p=0.004).

Conclusion: It appears that eight-week aerobic exercise protocol could be beneficial for weight loss, but it did not affect glucose concentration, insulin resistance, interleukin-6 serum, fat percentage, waist to hip ratio and BMI.

Key Words: Interleukin-6, Insulin Resistance, Glucose, Overweight, Training

Introduction

One of the most common metabolic disorders in industrialized and developing countries is obesity and overweight. Cardiovascular disease is one of the pathological consequences of obesity and overweight (1). Obesity is often associated with insulin resistance, type 2 diabetes, fatty liver and metabolic syndrome, and is one of the main causes of chronic illness and death (2). Some of these factors can directly induce intolerance of glucose and insulin resistance by interfering with the process of insulin metabolism in peripheral tissues, especially the liver and skeletal muscle (2). Meanwhile, Interleukin- 6 (IL- 6) has attracted a lot of attention because, on the one hand, it is released in the post-exercise period, that is, when insulin is boosted, and on the other hand, it is related to obesity and lower insulin function (3). Interleukin- 6 is released from immune cells and a cytokine which is characterized by monocytes, macrophages, endothelial cells, fibroblasts and other cells in response to inflammatory stimuli (4, 5). This cytokine has several effects on the tissues of the body (including stimulating the acute phase protein synthesis, activating the hypothalamic-pituitary axis and producing heat) (6,). The level of IL- 6 in blood may increase in exercise without modification or after prolonged intense exercise and may be released during exercise, but this increase does

not appear due to the abnormal synthesis of this cytokine during exercise. Increased IL-6 production after exercise led to an increase in the number of circulating monocytes, resulting in more IL-6 production. Waleberg *et al.* (2010) Several studies have shown that obesity is associated with high levels of IL- 6و IL-18, CRP, insulin, and insulin resistance index (8-10). Numerous researchers have shown IL- 6 as an indicator of the incidence of insulin resistance and the factors involved in its occurrence (11, 12). Various factors such as inheritance, environmental effects, obesity and other conditions are associated with inflammation and infection with the development of insulin resistance in people with glucose intolerance and type 2 diabetes (13). Studies show that energy storage of muscle cells (including ATP and glycogen) is reduced and evacuated (13, 14) in long-term exercises with intensity of 60% to 80% of $vo_{2\ max}$, especially if they are repeated for one or more weeks; while liver glycogen is broken down to release glucose into the bloodstream for access to other tissues (15). Regarding that, Yoshida *et al.* (2010) showed in their studies that insulin activity decreases during aerobic exercise. Factors such as the intensity of exercise, gender and diet affect insulin metabolism (16). By 2005, there were at least 400 million (8.8%) of obese adults worldwide (17). Regular exercise increases IL-6 and decreases stress by increasing immune system capacity (18, 19). Regular exercise can increase IL- 6, which can reduce vascular metabolic effects (18). The release of general immune system factors (cytokines) during and after exercise may be a protective mechanism for coping with general suppression of post-exercise immune responses. The release of inflammatory cytokine, IL- 6, induces and secretes many of the acute phase proteins, especially the C-reactive protein, which are released from the liver in response to tissue damage and inflammation of the exercise dimension (19). The prevalence of laziness and overweight in our healthy and young women led our society to examine the effect of aerobic exercise on the levels of IL-6 and glucose and serum insulin levels in female students. Given the importance of the obesity role and its effect on the general health system and the possible role of exercise in reducing the complications of obesity, including increasing the immune status, the purpose of this study was to determine the effect of regular exercise on the level of IL-6, glucose and insulin on overweight girls.

Methods

This research method was quasi-experimental, in which the subjects were divided into two groups of pre-test and post-test .The statistical population included 21 girls with an age range 20-30 years and body mass index of 25-30 kg / m2. After introducing the goals, function, and stages of the research, 21 of them volunteered to participate in the study. Finally, the subjects were randomly assigned into experimental and control groups (11 in the experimental group and 10 in the control group). To individuals completed the questionnaire of personal and medical records, treatment status and supplementation, and assessment of physical activity. The inclusion criteria for the these subjects, comprised having no specific disease history, not changing their diet plan, being non athletic and not having regular exercise, and not taking any medication or supplement and not suffering from any cardiovascular disease. Kaiser physical activity survey (20) was used to assess the physical activity level. In this questionnaire, the habits and patterns of physical activity were evaluated, especially in women, which included four sections: house and family care chores, occupational activity, active lifestyle and exercise participation, this by Ainsworth *et al.,* in 2000, it was approved for women aged 20-60 years. The internal validity of it (0.84 Cronbach alpha) was obtained. According to this questionnaire, women who had normal physical activity in

their daily lives had less physical activity and were not athletic, that is, they had not had regular exercise in three or five years and did not exercise more than one session a week in the last two months. Both groups were asked to record the food they ate three days before blood sampling in both the pre-test and the post-test. Also they were asked to have the same food the night sleep before blood sampling, 24 hours after the last exercise session blood sample was taken stadiometer made in Germany was used to measure the height. The exact height was measured as this; a person without shoes, flat and stretched on a device so that the body weight is evenly divided on both legs and the eyes are parallel to the horizon, then at the extreme end of the exhalation, the horizontal ruler of the device is put on the head is tangential to the head and to create a vertical angle with the ruler. In this way, the subject height was measured in cm. The Inbody 720 made in Korea was used to measure body weight, body composition, waist-hip ratio and fat percentage. The aerobic exercise protocol started with an intensity of 65% of the maximum heart rate, and after each two weeks, 5 percent was added to the intensity of the exercise and the entire course was performed for 8 weeks and 3 sessions (in general 24 sessions) (21). The time of exercise of the subjects was 60 minutes at each session and the exercises consisted of three sections: warm up (10 minutes), aerobic exercise (40 minutes) and cool down (10 minutes). The intensity of the exercise was controlled through a Polar TB machine (T-31) during exercise. Exercise conditions were the same for all subjects. Exercise intensity was determined based on Karvonen 's heart rate method (22). Several simple calculations were performed using this method. In a way that: the maximum heart rate = 220- age. To measure aerobic power, the Bruce test was used at the beginning and the end of the study to determine the maximum oxygen consumption (VO_{2max}). Bruce test is conducted on a treadmill and has seven steps. Usually, at the beginning, the person walks on the treadmill and, with increasing speed and slope, from the third and fourth stages start walking fast, and runs on if it is to continue the task. Each stage of the Bruce test takes 3 minutes and the slope and the speed of the machine increases in each step. In the maximal Bruce test, an individual can rarely continue until the 6th and 7th stages, and only long-distance runners have this ability. The activity is stopped whenever someone becomes overwhelmed and unable to continue. Time of activity and heart rate are recorded at the end. The maximum oxygen consumption is the milliliter per kilogram of body weight per minute.

Table 1. Slope and speed in maximum Bruce test

Level	Slope (percent)	Speed		
		Miles per hour	Km / h	M per minute
First	10	1.7	2.7	45
Second	12	2.5	4	67
Third	14	3.4	5.5	92
Fourth	16	4.2	6.8	113
Fifth	18	5	8	133
Sixth	20	5.5	8.8	147
Seventh	22	6	9.6	160

The duration of each step is 3 minutes

Table 2. Estimation of Maximum Oxygen Consumption in the Bruce Test

VO_{2max} ml.kg-1 .min-1	Time (minutes)	VO2max ml.kg-1 .min-1	Time (minutes)	VO2max ml.kg-1 .min-1	Time (minutes)
18	2	33.3	9	57.2	16
19.1	3	36.5	10	60.4	17
20.6	4	39.9	11	63.4	18
22.5	5	43.4	12	66.3	19
24.7	6	46.9	13	68.7	20
27.3	7	50.4	14	70.9	21
30.3	8	43.8	15		

48 hours before and after the last exercise session, and while subjects were fasting for 8 hours, 5 cc from the blood sample vein was taken in a sitting mode. The subjects were asked to be present for sampling at 8 A.M in the morning and at each sampling step in the same sampling time before and after, the sampling time was at 8 A.M and continued until 9 A.M. Samples were collected in special laboratory tubes and after centrifugation, the serum samples were isolated and stored in separate tubes at -20 ° C for further testing. The method used to measure IL-6 values was ELISA, and again after 8 weeks, blood sampling was taken. Glucose levels were measured and recorded by enzyme-calorimetric photometric method and insulin by the electrochemical luminescence method. The HOMA-IR formula was used to determine the insulin resistance as below.

HOMA-IR = Fasting glucose (Mg / dl) × Fasting Insulin (Mu/ ML) / 450

SPSS software version 15 was used to analyze the data. Descriptive statistics were used to calculate the mean, standard deviation, variance, and frequency tables. After assuring that the distribution of data was normal with the Kolmogorov–Smirnov test, to test the hypotheses the difference between the pre-test and post-test in each of the experimental and control groups was obtained, ,Insulin= 0.432, Inter6=0.076, and finally, for comparison of the pre-test information the post-test between groups, independent sample t- test and U Man Whitney test was used for data analysis For comparing pre-test and post-test information, the dependent sample t- test and Wilcoxon test were used ($p < 0.05$).

Results

The results of independent sample t- test showed that there were no significant different between changes of body mass index (p=0.43), fat percent (p=0.72), waist to hip rate (p=0.85), interleukin- 6 (p=0.86), insulin resistance (p=0.59) and glucose (p=0.78) in experimental and control groups; nevertheless, weight significantly reduced in experimental group rather than control group (p=0.004). The results of paired sample t- test showed that there were no significant different in body mass index, fat percentage, waist to hip rate, interleukin- 6, insulin resistance, and glucose in pre- test and post- test of experimental group ($p \geq 0.05$) nevertheless weight significantly reduced in post- test rather than pre- test ($p \leq 0.05$). the results of paired sample t- test showed that there were no significant different in body mass index, fat percent, waist to hip rate, interleukin- 6, insulin resistance, and glucose in pre- test and post- test of control group ($p \geq 0.05$) nevertheless weight significantly reduced in post- test rather than pre- test ($p \leq 0.05$).

Table 3. Demographic characteristics and descriptive statistics of study subjects (Mean ± SD)

Variables	Experimental		Control	
	pre-test	Post-test	pre-test	Post-test
Body Mass Index (Kg/m2)	25.17±2.65	24.76±2.64	27.51±3.23	27.40±3.37
Fat percentage (kg)	25.25±5.55	24.49±0.04	0.91±0.06	0.90±0.06
Waist to hip ratio (m)	0.86±0.04	0.85±0.04	0.91±0.06	0.90±0.06
Maximum Oxygen (Consumption LT / M)	22.46±3.83	34.55±3.72	25.40±9.64	32.80±7.90

Table 4. Comparison of intra-group and intergroup variance of research variables

Variables	Groups	Pre-test (Mean±SD)	Post-test (Mean±SD)	Changes	
				Intra-group P-Value	Inter-groups P-Value
Weight (Kilograms)	Experimental	68.63±7.50	67.08±6.75	0.048	0.004*
	Control	69.03±8.58	70.12±9.18	0.007	
Body mass index (kg / m 2)	Experimental	25.17±2.65	24.67±2.64	0.098	0.437
	Control	27.51±3.23	27.40±3.37	0.799	
fat percentage (kg)	Experimental	25.25±5.55	24.49±4.95	0.347	0.721
	Control	28.98±5.74	28.57±6.060	0.488	
Blood glucose (Mg / dl)	Experimental	80.82±9.16	79.55±5.24	0.657	0.78
	Control	83.40±12.50	83.50±8.00	0.981	
Insulin resistance	Experimental	89.76±60.09	84.27±54.97	0.158	0.597
	Control	1.61±0.25	1.71±0.29	0.352	
Maximum Oxygen Consumption (LT / M)	Experimental	7.88±6.05	7.47±5.26	0.000	0.239
	Control	25.40±9.64	32.80±7.90	0.066	
Waist to hip ratio (M)	Experimental	0.91±0.06	0.90±0.06	0.346	0.858
	Control	0.91±0.06	0.90±0.06	0.322	
Interleukin- 6 (Ng/L)	Experimental	308.20±161.31	347.72±198.81	0.635	0.868
	Control	512±235.45	481.77±254.80	0.185	

* Significant level of P≤0.05

Table 5. Results of Leven test to examine the variance equality of research variables in two groups

Research variables	Test Statistic	P	Result
Body mass index (kg / m2)	0.841	0.371	Equality of variances
Blood glucose (Mg / dl)	0.390	0.539	Equality of variances
Fat percentage (Kilograms)	0.324	0.576	Equality of variances
Insulin resistance	0.646	0.432	Equality of variances
Interleukin- 6 (Ng / L)	3.470	0.078	Equality of variances
Maximum Oxygen Consumption (LT / M)	8.297	0.010	Inequalities of variances
Height (centimeter)	4.900	0.039	Inequalities of variances
Waist to hip ratio (centimeter)	0.728	0.404	Equality of variances

Discussion

The results of present study showed that eight weeks of aerobic exercise did not affect IL- 6 serum. The results of this study were consistent with the results of Smith (2007). However, it was not consistent with the results of Peque *et al.* (2005). Smith *et al.* (2007) examined the effect of a regular aerobic exercise on serum IL-6 levels in healthy male subjects. The subjects started running on a treadmill with a downward slope of 13.5 degrees for 60 minutes in two separate drill sessions, while the interval between the first and second sessions was 14 days. Blood samples were measured at 12 and 24 hours after each exercise session. The results showed that after 12 hours of the second session, the concentration of IL-6 decreased (23). Peek *et al.* (2005) conducted a study on the level of IL-6 and its relationship with the intensity of exercise in professional runners. It was concluded that IL-6 levels did not change significantly (24). During exercise, the contractile skeletal muscle releases IL-6 levels into the bloodstream. The IL-6 response reflects a critical reduction in muscle glycogen reserves and more skeletal muscle damage to blood glucose as a source of energy. In this study, it was found that IL-6 levels increased significantly. The effect of exercise and physical activity on the production of IL-6 is strongly dependent on the duration of exercise and muscle mass. The concentration of intracellular glycogen in the muscles is an important stimulant for the production of IL-6. IL-6 produced by the muscle contraction often occurs in extreme and short-term exercises. This increase is due to the effects of exercise and lipid metabolism and lipolysis and lipid oxidation on glycogen Hemostasis in the liver and its anti-inflammatory effect. The increase in IL-6 depends on the duration, intensity, amount of muscle mass involved in endurance, and endurance capacity. Since contractile skeletal muscle is an important source of IL-6, a workout with a limited muscle mass, such as upper limb muscles, may not be sufficient to increase serum levels of IL-6 above pre-exercise levels. By contrast, running which involves many muscle groups, there is a significant increase in serum IL-6. (25, 26). The eight-week aerobic exercise program did not affect blood glucose. The results of this study were consistent with the results of many studies, such as McLean *et al.* (2008). However, the results were not consistent with the results of the research by Sula *et al.* (2002). Macline *et al.* (2008) showed that aerobic exercise led to a significant decrease in fasting glucose, but had no effect on insulin levels of blood and peptide (27). Most muscle tissue does not rely on glucose for energy, and most of its energy comes from the use of fatty acids. The main reason is that the natural membrane of the resting muscle has a slight permeability to glucose, except when it is stimulated by insulin. However, the amount of insulin that secretes at mealtime is so low that it cannot enter as much glucose into the cell, but the muscles consume a lot of glucose in the two states, one of which is a moderate to severe physical activity time. In this situation, muscle cells consume a lot of glucose with a small amount of insulin. Because muscle fibres are active in the absence of insulin through the contraction process, they become permeable to glucose (1, 2). Considering what has been mentioned, it can be said that muscle contraction has an insulin-like effect that sends a large amount of glucose into the cell to spend on energy production. It also allows muscle fibres during activity to have a low glycogen concentration for a relatively long period. On the other hand, with the completion of exercise, muscle cells also rebuild their glycogen stores. Consequently, after exercise, blood glucose concentration is low for a few hours (3, 4). The eight-week aerobic exercise program did not affect insulin resistance in the blood serum. The results of this study were consistent with Yoshida et al. (2010). But it was not consistent with the results of the research by Kadglow (2007). Yoshida (2010) in his studies showed that insulin activity

decreases during exercise. Factors such as exercise intensity and gender affect insulin metabolism (28). Kadgloo in 2007, with a study of 60 overweight diabetic patients, showed that 6 months of aerobic exercise for 4 days a week and 45-60 minutes each session, with 50-70% vo2max resulted in improved glucose control and fat and intolerance indices, and decrease insulin resistance (29). In insulin resistance, the ability of the liver and muscle cells decreases to remove glucose from the blood and to store it as glycogen. By performing aerobic exercises, the structure and biochemistry of the muscles result in optimal changes in the maximum oxygen consumption (such as increased oxidative enzymes and increased capillary density) and thus improves the process of transporting glucose and decreases the insulin resistance of the cells. In fact, the compatibility of aerobic training is that, firstly, in response to aerobic exercise in type 2 diabetic patients, increases muscle cell density, as well as the improvement in maximum oxygen consumption and oxidative activity in skeletal muscle. Secondly, aerobic exercise increases the sensitivity of an individual to insulin. As a result, after exercise less insulin is needed to adjust blood glucose levels than before. This improvement in insulin sensitivity is probably related to the capacity of binding of insulin to the receptor site of each muscle cell. There is also an increase in liver insulin sensitivity (7). Therefore, less insulin is needed to absorb excess glucose from blood circulation. Also, the role of aerobic exercise activity in increasing insulin function has been demonstrated through reduction of intracellular TG accumulation, increased oxidation of fatty acids and mitochondrial biogenesis (8). The eight-week aerobic exercise program had a significant effect on weight loss. The results of this study were consistent with the results of many studies, such as Galestl *et al.* (2001), but was not in line with the results of Sulau *et al.* (2002). Galestl *et al.* (2001) studied the effect of an interventional program, including increased physical activity and reduced intake energy on leptin concentration and inflammatory factors in obese children and adolescents. For this purpose, 49 obese children and adolescents experienced a weight loss program for three weeks, including reduced intake energy and regular physical activity at an institution. The results of this study confirmed the positive effect of decreased intake energy along with regular exercise program on weight loss, body composition and adipocyte hormones (30). Regular sports exercises increase the expression of lipolytic enzymes, beta-oxidation, chromosomes and electron transfer chains, increase mitochondrial density, and increase the fat instead of carbohydrates to produce energy (31). Therefore, the amount of fat decreases and it leads to weight loss and body mass index. The findings of these researchers indicate that the physical fitness program (body mass index, waist and fat ratio), and weight loss, the role of physical activity duration is more important than its intensity, and the total time of physical activity in the week is an important factor in improving the health and safety.

Conclusion

With regard to the findings of the present study it seems that eight week of aerobic exercise has not significant effect on glucose concentration, insulin resistance, interleukin- 6 serum, fat percentage and waist to hip ratio in overweight women.

Ethical issues

Not applicable.

Authors' contributions

All authors equally contributed to the writing and revision of this paper.

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