

Effect of Concurrent Training on Leptin, C - reactive protein and HOMA-IR in Overweight MenBahram Abedi¹, Mohsen Akbarpour Beni², Mohsen Assar Zadeh Noosh Abadi³, Davood Khorshidi⁴¹ Departments of Physical Education and Sports Sciences, Islamic azad University, Mahallat Branch, Mahallat, IRAN² Department of Physical Education and Sports Sciences, University of Qom, Qom, IRAN, +989131839198³ Departments of Physical Education and Sports Sciences, Islamic Azad University, Mobarakeh Branch, Mobarakeh, IRAN.⁴ Departments of Physical Education and Sports Sciences, Islamic azad University, Saveh Branch, Saveh, IRAN. akbarpour.mohsen@gmail.com

Abstract: Purpose: The main purpose of this study was to examine the effect of concurrent endurance and resistance training on serum leptin, C-reactive protein (CPR) and insulin-resistance index (HOMA-IR) among overweight men. **Methods and Materials:** The present research method was a semi-experimental study. 30 overweight men (age of 20.9 ± 1.9 years old and BMI of 26.47 ± 0.75 kg/m²) were randomly assigned to experimental (20 people) and control (10 people) groups. The experimental group performed concurrent training (aerobic activity: 60 to 70% of maximal oxygen consumption for 20 min and resistance activity: 2 sets with one repetition or 70% of 1 repetition maximum for 12 weeks) while the control group did not do any physical activity. At the end of concurrent training, blood samples were taken from the experimental group. Leptin, C-reactive protein (CPR) and insulin-resistance indicator were measured before and after 12 weeks of training. **Results:** At the end of the twelfth week, a significant decrease was observed in serum CPR (1.45 ± 0.27 versus 1.39 ± 0.3 mg/l, $P < 0.05$), leptin (7.27 ± 0.68 versus 7.24 ± 0.65 ng/ml, $P < 0.05$) and insulin-resistance indicator (1.6 ± 0.14 versus 1.5 ± 0.23 , $P < 0.05$). **Conclusion:** Concurrent endurance-resistance training program can have a positive effect on the concentration of insulin-resistance, C-reactive protein and leptin of serum. Therefore, it is recommended that doing concurrent training can be a suitable method for developing glucose transport into muscle cells; also, regulating the secretion of leptin and C-reactive protein can be most probably a preventive method for postponing cardiovascular diseases and type-2 diabetes in overweight men.

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Key words: Concurrent Training, Leptin, CPR, Insulin-resistance index

Introduction

Obesity, insulin-resistance and endothelial disorder depend on a number of factors. Obesity, especially visceral obesity, which leads to insulin-resistance and endothelial inefficiency, is mainly derived via metabolic productions of lipid, hormones and adipokines. Independent from body mass index (BMI), obesity develops several heart metabolic risk factors by changing the secretion of adipokines and increasing insulin-resistance (Despres & Lemieux, 2006). Some of the fat-cell derivations such as leptin, tumor necrosis tumor alpha (TNF- α), free fat acid (FFA) and interleukin-6 (IL-6) can affect vascular function and insulin-resistance, which are strong stimuli for producing C-reactive protein (Yudkin, Stehouwer, Emeis, & Coppack, 1999). C-reactive protein is the live blood indicator for low-grade inflammation and it is imagined to be mechanically responsible for some obesity-related diseases. Obesity and C-reactive protein are considered as important indicators of insulin-resistance and endothelial

disorder due to low-grade inflammation (Yudkin, et al., 1999). The level of blood C-reactive protein has been related to cardiovascular diseases and other diseases, which strongly predict the risk of coronary diseases (Davood Khorshidi & Bahram Abedi, 2012; Ross, 1999). Insulin-resistance and obesity have been also associated with low-grade inflammation and visceral obesity is a symbol of insulin-resistance and type-2 diabetes (Lemieux et al., 2001; Ramson, Jurimae, Jurimae, & Maestu, 2012). On the other hand, obese gene product, leptin, is a secreted hormone which is transferred to the brain. Leptin secretion depends on the fat tissue level. It has been reported that insulin secretion via pharmaceutical stimulation has no obesity-independent effect on the leptin synthesis of hyperlipidemia people who are insulin-resistant while the relationship between hyperlipidemia and insulin-resistance independent from body mass index (BMI) has been shown for Dutch women and men (Ruijter et al., 1999). These studies have demonstrated that leptin and insulin are

involved in a complicated regulatory cycle and leptin plays an important role in glucose homeostasis. Also, they have suggested that, when leptin levels are normal and low, it can act as an insulin sensitizer and may be related to insulin-resistance at the time of leptin increase (Ruige, et al., 1999).

Physical activity and physical fitness are inversely related to cardiovascular risk factors (CVD), C-reactive protein (Esposito et al., 2003; Ryan et al., 2003) and leptin (Eriksson et al., 2008; Sari, Balci, Balci, & Karayalcin, 2007) and some investigations have stated inverse results in this regard (Marcel TJ, 2005; Sari, et al., 2007). As far as physical (aerobic) activities and insulin-resistance are concerned, it should be referred that aerobic training may improve insulin sensitivity in youngsters, the old and those who are insulin-resistant (Bell et al., 2007; Yassine et al., 2009). However, in contrast to endurance training, the few studies which have tested the effect of resistance training have found contradictory results. Considering that some have reported the improvement of glucose regulatory response after resistance training (Fenicchia et al., 2004), no other studies have been able to observe changes in insulin sensitivity (Chapman, Garvin, Ward, & Cartee, 2002).

Thus, due to the contradictory results of sports activities and lack of information with regard to concurrent endurance and strength training, the present study was designed and implemented to

determine the effect of 12 weeks of concurrent (endurance-resistance) training on leptin, C-reactive protein and insulin-resistance indicators among overweight men.

Methods and Materials

Subjects

This semi-experimental two-group study was approved by the Ethical and Research Committee of Tiran Islamic Azad University and performed in accordance with the principles outlined in the Declaration of Helsinki. In this study, one control (10 people) and one experimental (20 people) groups were randomly selected to participate in a training program. The inclusion criteria were the age range of 18 to 25 years old, body mass index of 25 to 30 kg/m², no background of regular sports activities, no body weight change of more than 2 kg and no specific diseases and smoking at least for 6 recent months. Exclusion criteria included the body mass index of less than 25 kg/m² and acute diseases which interfere with exercising along with any kind of drug intake during recent months and violation of any of inclusion criteria during the research. The participants got informed of the purpose, advantages and probable risks of the research design and filled out testimonials before starting the research. The characteristics of the participants are given in Table 1.

Table 1. Descriptive characteristics of concurrent and control groups.

	Concurrent group			Control group		
	Before exercise	After exercise	P	Before exercise	After exercise	P
Age(y)	20.75±1.64	-	-	21.4±2.37	-	-
Height(cm)	170±5.95	-	-	172.1±8.54	-	-
Weight(kg)	76.43±5.28	76.41±5.30	0.82	78.6±7.6	78.69±7.7	0.36
BMI(kg/m ²)	26.46±0.87	26.28±0.65	0.12	26.5±0.45	26.45±0.59	0.48
Vo _{2max} (ml.kg-1.min-1)	37.25±1.92	37.96±1.14	0.004	38.78±2.29	38.8±1.78	0.92
Body Fat %	20.25±0.79	19.97±0.73	0.029	20.38±15.14	20.4±0.99	0.9

Physiological Measurements

In the morning from 8 to 10, the participants referred to the laboratory in order to conduct blood factor measurements, body composition, 1 repetition maximum (1RM) and maximal oxygen consumption (VO_{2max}). First, blood factors were measured; body weight was measured using a digital scale (digital glass scale, type GES-07, America, accuracy of ± 0.1 kg) with no clothes on. Height was measured using a wall height gauge (model 44440 made by Kaveh Company, Iran, accuracy of ±0.1 cm) while they were standing by the wall without shoes and the shoulders were in normal conditions. Waist circumference was

measured in the narrowest part of waist when the participant was at the end of normal exhalation. To measure hip circumference, its most prominent part was determined. Measurement of hip circumference and waist circumference was done using a tape meter with no elasticity and with imposing no pressure on the persons' body. Body mass index was calculated by dividing weight (kg) by the square of height (m). Body mass index was calculated using caliber (model Harpenden) (the technique of pinching at three areas of chest, stomach and thigh on the right part of the body in three sessions was used with 20 sec of time interval between each session for returning to the

initial state and the mean of three sessions was recorded), Jackson and Pollock formula and Siri equation (Jackson & Pollock, 1978; Siri, 1993). After that, the participants referred to the gym to get familiarized with the techniques. Correct weight techniques were trained for them and they started their work in the following way in order to get familiarized and determine 1RM: first, they performed 4 to 5 times of the desirable activity using a light weight (40 to 60% of maximum pressure) as a warm-up. After one min resting along with stretching activities, they repeated 3 to 5 repetitions with 60 to 80% of maximum pressure. To determine maximum pressure, a small amount was added to the weighs. If the movement was successfully done, they would receive 3 to 5 min resting. The aim was to find one maximum repetition in 3 to 5 maximum efforts. This trend continued in order to obtain the maximum effort. The highest amount of weigh which was raised was considered one repetition maximum (Lippincott Williams & Wilkins, 2006). To estimate VO_{2max} of the participants, the Bruce maximum test was used. This test is composed of a multi-stage protocol which is done on a treadmill. In this protocol, pressure increases with changing speed and slope percentage. In the first stage of test (1 to 3 min), normal people start to walk on the treadmill with the speed of 1.7 mile per hour and 10% slope. In the beginning of the second stage (4 to 6 min), slope and speed increase by 2% and 2.5 mile per hour (67 m per min), respectively. In the following stage of the test, slope and speed increase by 2% and 0.8 or 0.9 mile per hour (21.44 or 24.12 m per min) until the time when the participant fails, respectively. The participants' heart rate was calculated every minute by the treadmill. After these stages, the specific predictive equation which estimated VO_{2max} for inactive men was used:

$$VO_{2max} = 14.76 - 1.379 (time) + 0.451 (time)^2 - 0.12(time)^3$$

Also, to determine intensity as a percentage of VO_{2max} , the maximum heart rate at the time of failure and Karvonen formula were used.

$$(Target\ heart\ rate) = (maximum\ heart\ rate) - (resting\ heart\ rate) \times (exercise\ intensity) + (resting\ heart\ rate)$$

It should be stated that the required guidance was given to the participants on their maximum efforts before the test and they competitively participated in the test for their maximum effort (Lippincott Williams & Wilkins, 2006). The tests were done in the same temperature and time conditions by an experienced person.

Concurrent Training Program

Concurrent training program included general warm-up (10 min), specific warm-up (3 to 5 min), resistance and aerobic training and cool-down and stretching activities (5 min). This program included the aerobic training of running on the treadmill for 20 min at 60 to 70% of maximal oxygen consumption and resistance training with the intensity of 70% of 1 repetition maximum with 10 repetitions in each activity for 2 sets while the resting time of 30 sec and 2 min was considered between the stations and cycles, respectively. Resistance training included 10 station activities which were circularly done. The stations were composed of Leg flexion, Leg extension, Leg press, Squat, Cable standing lat row, Chest press, Dumbbell side delt abduction, Barbell biceps flex, Cable triceps extension and Sit-up, respectively.

Blood Sampling

After 8 to 10 hours of fasting and in two stages of before and after performing the activity, 10 ml venous blood was taken from each participant while they were sitting and resting. Immediately after that, the serums were separated using a 3000 rpm centrifuge and were maintained in the fridge at -70 degrees Centigrade until the day of the test. To take blood, the participants were asked to avoid doing any kinds of physical activities since two days before the experiment.

Biochemical Measurements

The level of fasting glucose was measured using the glucose oxidase enzymatic method (the kit from Pars Azmoon Company, Tehran, Iran) and 902 Hitachi auto-analyzer systems (Germany). The level of insulin in the fasting serum was measured using the competitive sandwich ELISA method (the kit of DRG Company, Germany, with 0.5 μ UI/ml sensitivity and the internal and external change coefficients of 6.45 and 6.45%, respectively). Insulin-resistance indicator (Homeostasis Model Assessment Insulin Resistance) was calculated based on the multiplication of the concentration of fasting blood sugar (mg/dl) by the concentration of fasting insulin (micro unit/ml), divided by 405 as the constant (Matthews DR, 1985). The level of leptin serum was measured using the leptin kit (DRG-Diagnostica, GmbH, Germany) with the sensitivity of 1 ng.ml⁻¹ and internal and external change coefficients of 4.5 and 6.6%, respectively, using competitive sandwich ELISA. Serum level of C-reactive protein was calculated using nephelometry method by CRP method (MININEPH TM human CRP kit; The Binding site Ltd., Birmingham, UK) with the sensitivity of 0.04 ng.ml⁻¹ and internal and external change coefficients of 4.7 and 5%, respectively.

Controlling Diet

The information related to the participants' diet was recorded by the 24-hour recall questionnaire in three days (two days at the beginning and one day at the end of the week) and also in three sessions (first week, sixth week and twelfth week) during physical activity by the participant in a diet sheet (Bouassida, Chamari, et al., 2010; Ramson, et al., 2012). The participants were asked to mention all the foods and beverages consumed during the 24 hour before that. To analyze the data, first, the consumed food was converted to gram, then information related to diet was analyzed using Dorosty Food Processor Software (NIII, FP2) and the level of macronutrients was determined. During the training program, the participants were guided to use the replaced diet in order to have the same diet. Basal metabolic energy requirements were calculated based on age, gender and weight according to the Harris & Benedict formula and total daily energy requirement was computed after matching the activity factor (Harris, 1919). However, in order to more control their diet, the participants were asked to copy and maintain the 3-day recall questionnaire (before blood sampling) in order to have the same initial diet three days before the blood sampling phase.

Statistical Method

First, all the data were tested in order to determine their normality of distribution using Shapiro-Wilk test. To specify the effect of 12 weeks of combined activity on blood factors, a paired t-test was used. In all the cases, the significance level of less than 0.05 was considered. All the data were analyzed using SPSS18 software.

Results

The results of diet analysis showed lack of a significant difference in diet absorption in three measurement sessions before and during the activity. Concurrent training significantly decreased CRP concentration (1.45 ± 0.05 versus 1.39 ± 0.04 mg/l, $P=0.033$, $t=2.298$) (Fig.1A), leptin (7.27 ± 0.03 versus 7.24 ± 0.02 ng/ml, $p=0.03$, $t=2.35$) (Fig.1B) and insulin-resistance index (1.6 ± 0.02 versus 1.5 ± 0.04 , $p=0.012$, $t=2.77$) (Fig.1C) before and 12 weeks after the activity. Additionally, maximum oxygen consumption (37.25 ± 1.92 versus 37.96 ± 1.14 ml/kg min, $p=0.004$, $t=3.27$) and body fat percent of the participants (20.25 ± 0.798 versus $19.97 \pm 0.73\%$, $p=0.03$, $t=2.36$) improved after 12 weeks. However, body weight (76.43 ± 5.28 versus 76.41 ± 5.3 kg, $p=0.82$, $t=0.233$) and body mass index (26.46 ± 0.87 versus 26.28 ± 0.65 kg/m², $p=0.12$, $t=1.63$) did not make any changes during the training.

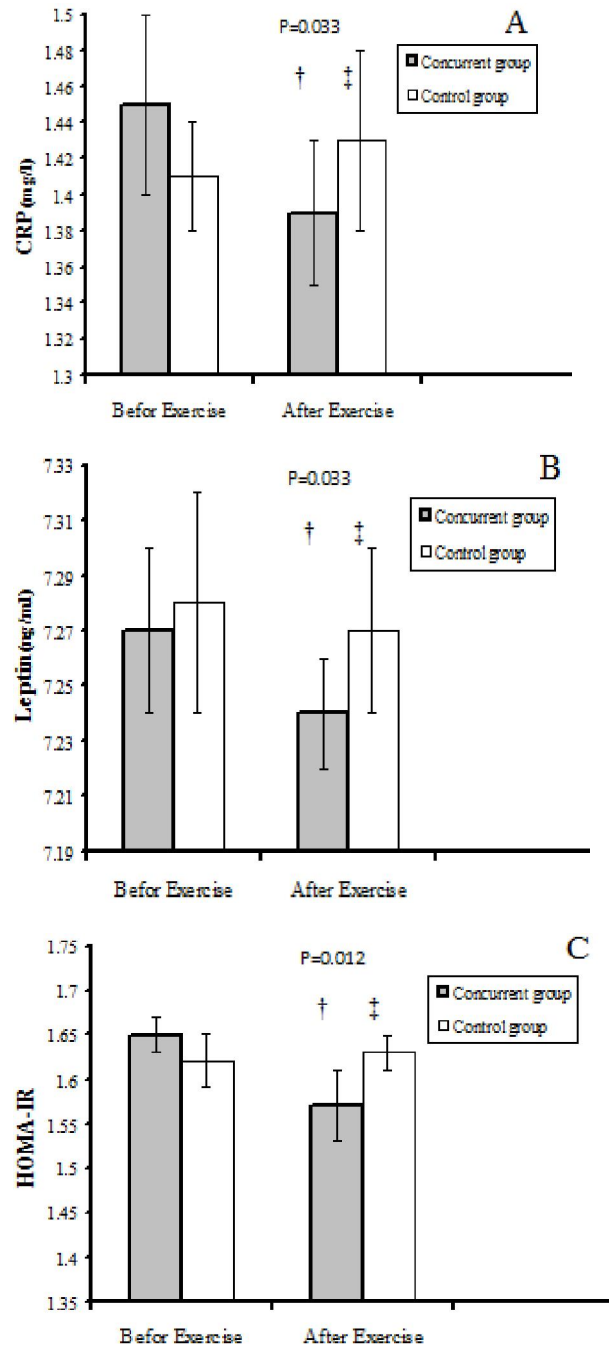


Fig1: Concentrations of Serum CRP (mg/l) (A), Leptin (ng/ml) (B), HOMA-IR (C) at during 12 weeks between study groups.

† Denote Significant difference to the before exercise
‡ Denote Significant difference to the concurrent group

Discussion

This study showed the decrease of insulin-resistance after 12 weeks of concurrent training. These results were in line with some studies which reported

improvement in insulin-resistance after endurance training in obese healthy people (Marcel TJ, 2005). An interesting result of this study was that insulin-resistance decreased with no change in weight and BMI, which was in line with the findings of the previous study (Duncan et al., 2003). Therefore, it is recommended that another mechanism may be effective in the changes of body composition for decreasing insulin-resistance.

It has been evidently determined that endurance training (acute and long-term) improves insulin-resistance due to temporary contraction of muscle and increase in glucose absorption and skeletal muscle mass (Henriksen, 2002). Some studies have suggested that, similar to endurance training, resistance training may cause the improvement of insulin-resistance. Moreover, it has been suggested that resistance training may be a useful intervention for directly increasing insulin sensitivity in normal people and the young who have insulin-resistance in their lean tissue mass (Poehlman ET, 2000). Some data in animals (Knowler et al., 2002) and humans (Holten et al., 2004) have prepared pieces of evidence that resistance training may create qualitative changes in the skeletal muscle. Recently, Krisan et al. (2004) determined that 12 weeks of resistance training can effectively improve insulin-resistance via increasing glucose absorption stimulated by insulin in rodents. Improvement of glucose metabolism as a result of the increase in the Glut-4 protein concentration has been well related to several other key proteins involved in insulin-signaling cascade (Krisan et al., 2004). These results were expanded in humans by Holten et al. (2004) who investigated the effect of 6 weeks of resistance training in adults with type-2 diabetes (Holten, et al., 2004). As a result, the mentioned researchers confirmed the results of the present study that training can improve the activity of insulin in sedentary people in the absence of weight change and BMI. Although improvement in insulin-resistance is independent from weight and BMI changes, decrease in body fat mass and waist to hip circumference ratio (W/H) in this study justified the possibility of decrease in insulin-resistance to some extent. However, whether changes in the mentioned cases are potential mechanisms for the observed decrease in insulin-resistance is controversial. Therefore, it is imagined that improvement in insulin-resistance via training may be mainly mediated by other mechanisms such as leptin and C-reactive protein.

This study demonstrated decrease in the concentration of serum C-reactive protein via concurrent (resistance-endurance) training in overweight people. The study by Lakka et al. (2005) on 652 sedentary participants which conducted a 20 week training program including 30 to 50 min cycling

for three sessions per week indicated the decrease in the levels of serum C-reactive proteins (more than 3 mg.l⁻¹) (Lakka et al., 2005). In this study, the mean of C-reactive protein levels was 1.45±0.27 mg.l⁻¹ in the basal state. However, the training program decreased the level of serum C-reactive protein from 1.45±0.27 mg.l⁻¹ to 1.39±0.3 mg.l⁻¹. Thus, the number of participants, levels of initial C-reactive protein, duration and intensity of activities were the main variables for decreasing the levels of serum C-reactive protein. In the study by Klein et al. (2004), no changes were observed in the concentration of serum C-reactive protein after the liposuction surgery (Klein et al., 2004). Moreover, You et al. (2004) investigated the effect of 6 weeks of dieting along with physical activity in obese postmenopausal women and observed a significant decrease in the serum C-reactive protein (You T, 2004). Additionally, White et al. (2006) examined the effect of resistance training among people with the risk of cardiovascular diseases and reported a significant decrease in the level of serum C-reactive protein (White, Castellano, & Mc Coy, 2006). The reason of some of these differences may be due to training design, weight loss program, participant type and diet. In the study by Kopp et al. (2003), weight loss was accompanied by lower energy absorption and there was a decrease in the concentration of serum C-reactive protein (Kopp et al., 2003). Andersson et al. (2010) reported that the level of serum C-reactive protein in the resting state after the activity was lower than its initial level considering the severe endurance training (12 to 30 km skiing per day for 14 days) (Andersson J, 2010). In the present study, some of these differing factors were controlled (using the 24-hour recall questionnaire, a 12-week period of concurrent resistance-endurance training and overweight participants).

Considering the mechanism aspects, it should be referred to that trained athletes have more erythrocyte and muscle antioxidative enzyme activities. Animal studies have also demonstrated the improvement in the antioxidant defense mechanism after sports activities. Increase in the antioxidative support may decrease the production of interleukin-6 and other active muscle cytokines (Mattusch, Dufaux, Heine, Mertens, & Rost, 2000). Church et al. (2002) suggested that tumor necrosis factor alpha and interleukin-6 were involved in the production of C-reactive protein and this may lead to the decrease of C-reactive protein (Church et al., 2002).

The present study demonstrated that 12 weeks of concurrent training decreased the level of serum leptin in overweight people. Longitudinal studies with regard to the response of long-term physical activities on leptin presented contradictory results. Among obese women, 12 weeks of aerobic training (3 to 4

weeks of one-hour competition with moderate intensity) did not result in the concentration decrease in the plasma leptin compared with the control group (Sari, et al., 2007). Perusse et al. (1997) observed the decrease in leptin concentration after a 20-week aerobic program (3 sessions per week, 30 to 50 min per session and 55 to 75% $\text{VO}_{2\text{max}}$). Nevertheless, this decrease was attributed to the decrease in fat mass and lack of improvement in the insulin sensitivity (Perusse et al., 1997). Thong et al. (2000) analyzed the effects of sports and weight loss on the leptin concentration. The observed changes were associated with the changes of total subcutaneous fat. The authors observed that, despite the change in the energy balance and weight loss, sports caused the development in the decrease of leptin concentration (Thong, Hudson, Ross, Janssen, & Graham, 2000). Okazaki et al. (1999) examined the effect of moderate aerobic training (50% of $\text{VO}_{2\text{max}}$) for 12 weeks on the decrease of fat and leptin among sedentary, obese, middle-aged women. The ratio of leptin concentration to fat mass and BMI decreased after training. The authors suggested that decrease in leptin concentration may be due to the weight loss (Okazaki, Himeno, Nanri, Ogata, & Ikeda, 1999); however, the way leptin acts against sports activities is not definitely known and there are contradictory results in this regard. Probably, difference in the studied population (male or female; trained or untrained), applied training programs (type, intensity, duration and volume) and energy balance state of the participants may justify these contradictory results with regard to leptin and sports activities (Bouassida, Chamari, et al., 2010; Bouassida, Lakhdar, et al., 2010).

Conclusion

The results of this study demonstrated that concurrent endurance-resistance training program can have a positive effect on the concentration of insulin-resistance, C-reactive protein and leptin of serum. Thus, it is recommended that doing concurrent activities may be an appropriate method for developing glucose transport into muscle cells; also, it can most probably be a preventive method for postponing cardiovascular diseases and type-2 diabetes in overweight men by regulating the secretion of leptin and C reactive protein.

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