The Effect of Resistance Training on Serum Levels of C-Reactive Protein (CRP) and Fibrinogen in Male Drug Addicts

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Abstract

Objective: Addiction to narcotic drugs is associated with cardiovascular diseases; and increased levels of biomarkers such as C-reactive protein and fibrinogen are independently correlated with the risk of cardiovascular diseases. Therefore, this study aimed to investigate the effects of 8 weeks of resistance training on C-reactive protein and fibrinogen levels in drug addicted men. **Method:** In this pretest-posttest quasi-experimental study, a number of 30 male addicts were randomly divided into two groups of resistance training group (n = 15) and non-sports control group (n = 15). Then, the resistance training program was conducted within two months, four days a week, and 50 to 60 minutes a day. The serum levels of C-reactive protein, fibrinogen, body composition, and metabolic parameters were evaluated before and after the training period. **Results:** After the passage of 8 weeks of resistance training, skeletal muscle strength significantly increased ($P < .05$). At the same time, levels of C-reactive protein and fibrinogen decreased significantly in response to resistance training ($P < .05$). **Conclusion:** Short-term resistance training program improves muscle mass and strength in drug addicted men after abstinence and this improvement is associated with the reduced levels of C-reactive protein and fibrinogen.

Keywords: Drug Addiction, Cardiovascular Diseases, C-Reactive Protein, Resistance Training, Fibrinogen

Introduction

Addiction is a physical, psychological, and social disease, which many individual, environmental, and social factors are involved in its existence. Unfortunately, in many cases, the onset of drug addiction is in the late adolescence or early adulthood and drug addiction is more common among men than women (Amour &Smith, 1941). The increasing amount of drug abuse in today's world is such that one of the famous toxicologists called Ludwing states: if we exclude food, there is no substance on earth that can enter to the life of nations in such a simple way as drugs (Moal, 2007). Due to its location in the main transit routes of narcotic drugs and also because of some other historical and social reasons, Iran is considered as one of the innocent victims of drug addiction (Hoffan, Shepanski, & Buckwalter, 2004). Drug abuse affects mainly the functions of the Central Nervous System (SNS), the Autonomic Nervous System (ANS), and intestines. However, drug abuse also affects other systems of the body including the respiratory and the cardiovascular (the circulatory system) systems (Haghighi, Ravasi, & Ghaeini, 2006; Hoffan, Shepanski, & Buckwalter, 2004). On the other hand, the evidence, including American Heart Association, suggests that the inflammatory markers such as C-reactive protein (CRP) and plasma fibrinogen levels are among the strong diagnostic indicators of cardiovascular diseases and even they have more predictive value than low-density lipoprotein cholesterol (LDL-C) level. CRP and fibrinogen are reliable indicators of inflammatory condition, which are secreted from the liver in response to inflammatory cytokines such as Interleukin-1 (IL-1) and Interleukin-6 (IL-6). Increased levels of CRP and fibrinogen have been reported in the patients suffering from myocardial infarction and ischemic stroke. Furthermore, it has been observed that the levels of CRP and fibrinogen are higher than normal levels in drug addicted people. In total, the results of previous studies indicate that drug addiction can be considered as a serious risk factor for cardiovascular diseases and the inflammatory processes such as increased levels of CRP and fibrinogen are among its main mechanisms (Masoumi, Nasri, & Farajpour, 2001; Vries, Bruin, & Comans, 2000; Timmons, 2008; Banitalebi, Faramarzi, & Nuri, 2010).

Physical activity improves cardiovascular health and reduces inflammatory markers such as CRP and fibrinogen in non-addicted individuals. Doing Physical exercises helps to improve the heart health after addiction treatment by improving aerobic fitness and reducing blood cholesterol. Therefore, until now, the response of these inflammatory markers (CRP and fibrinogen) and cardiovascular health to resistance training is not clear in drug addicts. Drug addicts have less motivation to do aerobic exercises such as running; thus, based on the previous studies, they tend to do static and less dynamic activities. Consequently, this issue prompted the researchers of the present study to investigate the effects of resistance trainings on the health aspects of these

individuals. Therefore, the aim of the present study was to examine the effects of resistance training on serum CRP and fibrinogen levels in male drug addicts.

Method

Statistical Population, Sample, and Sampling Method

The present study is a pretest-posttest quasi-experimental study in terms of its design and it is practical with regard to the obtained results. The statistical population of the study included all male drug addicts in Narcotics Anonymous Camp in Chaharmahal and Bakhtiari Province (Farsan City) who had passed at least one month of their drug withdrawal. The number of 30 individuals was selected from the Camp based on the availability factor and then they were randomly assigned to two groups of experimental (n= 15) and control (n= 15) groups. Before the intervention and in order for homogenization, the participants of the two groups were compared with each other in terms of their age, height, weight, duration of drug use, withdrawal period, Body Mass Index (BMI), waist circumference, and physical fitness and no significant differences were found between these two groups. All of the participants received written information regarding the study and after studying and checking it, they were asked to sign the written consent form. The required ethical approvals for implementation of the present study and collaboration with drug addiction treatment centers were received from Drug Coordinating Council of Chaharmahal and Bakhtiari Province. Moreover, this study was conducted under the supervision of a specialist and some exercise physiologists and the subjects who did not have the exclusion criteria were entered into the study with the physician's approval. The exclusion criteria included: having any history of cardiovascular diseases, high blood pressure, diabetes, kidney and liver diseases affecting the fibrinogen level and immune system, and using any drugs affecting the results.

Instruments

1. Body Composition Measurements: The individuals' weights were measured using Seca scales with the accuracy of 0.5 kg, their height was determined using the height-gauge coils mounted on the wall with the minimum of 0.1 cm, and their waist circumference was measured with a tape measure from the narrowest point between the hip bone and the rips.

2. Biochemical Analysis of Blood: one day before the training session and 48 hours after the last training session and after 10-12 hours of fasting, 10 ml of blood sample was extracted from the participants' brachial vein in a sitting position. Meanwhile, extracting of blood samples was carried out between the hours of 7-9 am in order to meet a same circadian rhythm in the two phases of blood extraction. Two mls of extracted blood was used in a tube with sodium citrate to prevent blood clots in order for measuring the fibrinogen level and the

remaining amount was used to measure CRP and blood lipids (total cholesterol, triglycerides, HDL- cholesterol, and LDL- cholesterol). The ELISA method (Randox, England) was applied for quantitative detection of CRP and fibrinogen, the concentrations of total cholesterol (TC) and triglycerides (TGs) were also measured by enzymatic colorimetric methods with commercial kits (Pars Azmoon Inc., Tehran, Iran). LDL- cholesterol was determined with the direct enzymatic colorimetric method (Bali gene, Germany), and serum LDL-C was calculated according to the Friedewald equation.

Procedure

The participants were informed about the blood sample collection procedure and about the manner of doing exercise with weights in one session and then, one repetition maximum (1RM) (the maximum amount of weight that can be lifted just once) movements were measured using trial and error method. In order to reduce some intervening and confounding factors affecting the results of the study, and to reduce the effects of certain foods on immune and inflammatory markers, the participants were asked to avoid eating prepared foods and caffeine containing drinks for at least 24 hours before the exercise program and blood extraction. Blood samples were collected in two stages; before the training (stage 1) and immediately after the training (stage 2). In each stage, a 10 ml blood sample was taken. Sports activity was conducted only in the experimental group and the control group did not receive any exercise intervention. Considering the physical condition of the participants and that they had passed one month of their drug withdrawal, the researchers of the present study chose the exercise of weight training. The training program lasted for 8 weeks, with four workouts each week, and all of the training sessions were being started with a 15-minute warm-up (jogging, stretching, and exercising). The weight training exercises included leg press, quadriceps (front of thighs), hamstrings (back of thighs), bench press, biceps (front of arms), and double-sided down stretching that involve large muscles of the upper and lower body. The resistance movements were performed based on the recommendations of the American College of Sports Medicine (ACSM, 2000). During the first week, the participants were performing 2 sets of 15-20 reps using 30-40% 1RM. The second week's program included 3 sets of 15-20 reps using 40-50% 1RM. Between the 3-6 weeks, the number of reps reduced to 12-15, while the intensity increased by 50-60% 1RM. Between the weeks 7 and 8, the number of reps reduced to 8-12, while exercise intensity increased by 60-70% 1RM. In the case of being absent from the training sessions for any reason, the participants were forced to compensate the workouts in the next day. All of the training sessions were performed between 5 to 8 pm under the supervision of a sport psychologist. Furthermore, 1RM weight for the bench press and leg press were considered as indicators of the upper and lower body muscular strength, respectively.

Results

individual and clinical characteristics of the sample before the exercise interventions have been presented in the following table based on the participants' age, height, weight, duration of drug use, withdrawal period, Body Mass Index (BMI), and muscle strength (bench press and leg press strength) in the two different groups and tests.

Table 1: Individual and Clinical Characteristics of the Sample Group

Variables	*Experimental Group*		*Control Group*	
	Pre-test	***Post-test***	***Pre-test***	***Post-test***
Age (year)	27.13±1.08	-	27.33±1.29	-
Duration of Drug Use (year)	6.13±0.66	-	6.73±0.82	-
Withdrawal Time (month)	1.13±0.008	-	1.11±0.01	-
Height (cm)	176.58±1.79	-	176.21±1.85	-
Weight (kg)	64.00±7.81	68.20±7.83	64.00±7.81	64.62±7.99
BMI (kg/m^2)	20.47±1.38	21.82±1.28	20.69±1.52	21.22±1.50
Waist Circumference (cm)	77.50±7.86	80.23±7.46	77.68±5.81	78.66±5.93
Bench Press (kg)	32.13±4.79	45.20±8.88	31.46±4.77	34.13±5.15
Leg Press (kg)	88.26±8.76	114.53±8.84	85.53±6.70	93.93±6.63

The results of data analysis showed that after resistance training, the body weight ($t = 5.66$, $P<0.001$), the bench press strength ($t = 6.54$, $P<0.001$), and the leg press strength ($t = 7.87$, $P<0.001$) have been increased significantly.

The descriptive statistics of the studied biochemical variables have been presented for the two groups of study with regard to types of test in Table below.

Table 2: The Descriptive Statistics of the Studied Biochemical Variables in the Two Groups of Study

Variables	*Groups*	*Number*	*Pre-test*		*Post-test*	
			Mean	***SD***	***Mean***	***SD***
CRP (mg/l)	E	15	170.8	31.50	45.20	15.36
	C	15	170.3	30.35	117.6	29.47
Fibrinogen (mg/dl)	E	15	434.4	54.73	247.2	38.59
	C	15	430.6	69.30	318.7	60.96
TC (mg/dl)	E	15	173.3	14.43	206.2	30.39
	C	15	164.1	15.24	175.5	24.18
TG (mg/dl)	E	15	135.4	30.14	134.4	25.54
	C	15	118.8	21.10	120.8	17.38
HDL- cholesterol (mg/dl)	E	15	50.46	10.51	32.40	5.08
	C	15	51.53	6.51	34.13	4.88
LDL- cholesterol (mg/dl)	E	15	95.32	11.71	146.9	30.56
	C	15	88.82	15.60	117.2	21.92

E (Experimental Group), C (Control Group)

Multivariate analysis of covariance (MANCOVA) was used in order to evaluate the effectiveness of resistance training in improving the studied metabolic parameters. Before performing the MANCOVA test, the assumption of error variances homogeneity was examined. The results of Levene's test indicated that this assumption has been met for the given sample. The Box's M test was used in order to test the assumption of equality of covariance matrices and the results showed that this assumption has also been observed (F= 1.74, P>0.05). The results of multivariate analysis indicated that the difference between the two groups is significant on a linear combination of variables (Wilk's Lambda =0.44, F=3.74, P<0.01). To examine patterns of variation, univariate analysis of variance was used as follows.

Table 3: The Results of Univariate Analysis of Variance for Examining Patterns of Variation

Variables	*Mean Squares*	*F-Statistic*	*Significance Level*	*Effect Size*
CRP	6897.52	456.25	0.0005	0.89
Fibrinogen	9879.56	286.32	0.0005	0.93
TC	5326.69	0.70	0.45	0.05
TG	4524.49	0.75	0.39	0.08
HDL- cholesterol	2458.24	0.84	0.32	0.09
LDL- cholesterol	4128.36	0.92	0.26	0.11

As it can be seen in the above table, resistance training has resulted in a decrease in the fibrinogen and CRP levels.

Discussion and Conclusion

The main findings of the present study indicated that 8 weeks of resistance training leads to increase in physical fitness and muscle strength in addicts after drug withdrawal, and this period of training can also improve inflammatory markers of CRP and fibrinogen in drug addicts after withdrawal. Inflammation as an important mechanism is involved in the development and progression of cardiovascular diseases including atherosclerosis. In this regard, CRP is a sign of vascular inflammation that plays a direct role in causing damage to the arteries and cardiovascular complications. Coronary Artery Disease (CAD) as a major health problem and one of the most common causes of mortality is associated with a set of risk factors including family history, high blood pressure, diabetes, dyslipidemia, obesity, smoking, and drug abuse (Bonaca & Morrow, 2008; Ridker & Libby, 2008). Hence, atherosclerosis (or arteriosclerotic vascular disease) is the result of complex interactions between blood elements, vessel wall abnormality, inflammatory factors and lipoproteins (Ridker & Libby, 2008; Donald & Kiang). The research study indicates that CRP is more than a simple symptom and it is directly involved in the vascular vulnerability and atherosclerosis and its complications is even more than from low-density lipoprotein (LDL) (Cefalu & Cannon, 2007). Therefore, high levels of C-

reactive protein (CRP) is a powerful predictor of clinical and cardiovascular events in healthy people, diabetics, patients with moderate or high blood cholesterol levels, smokers, drug addicts, and patients with Acute Coronary Syndrome (ACS) (Grammer, Marz, & Renner, 2009). In addition, it has been observed that CRP levels is higher than its normal levels in drug addicts (Masoumi et al., 2001). The results of various studies indicate that physical activity as a non-pharmacological approach may be effective in reducing the CRP levels and cardiovascular complications in non-addicts (Soheili, Gaeini, & Souri, 2009; Parsian, Ebrahim, Nikbakht, & Khanali, 2010; Saremi, 2012; Claudia, 2004; Stewart, Flynn, & Campbell, 2007; Kishiko, Kioshi, & Shoji, 2010; Raul, Ana, & Manuel, 2010). Soheili, et al. (2009) found that a resistance training program for 8 weeks with 50 to 60% 1RM causes reduction in CRP levels in non-addicted elderly men. Moreover, Raul et al. (2010) reported that both aerobic exercise and resistance training are associated with a reduction in CRP in men and women. In the present study and at the baseline, it was observed that CRP level is high in individuals after drug withdrawal and this issue supports the idea that addiction is associated with the increase in systematic inflammation. In this study, CRP levels decreased after eight weeks of resistance training. This research finding is in line with the results of You and Niclas (2008) and Nouri, Sheikh Sarraf, and Fath-alahi (2013) which showed that participation in aerobic exercise training is associated with the reduction in inflammation in individuals after drug withdrawal. With regard to the reduction of CRP levels after exercise training, several mechanisms have been proposed, including reduction in inflammatory cytokines such as IL-6, reduction in visceral fat mass, improving insulin sensitivity and antioxidant effects of exercise. In any case, due to limited data in the present study, there is no possibility of recognizing the possible mechanism of CRP level reduction after resistance training. On the other hand, plasma fibrinogen is a high molecular weight protein produced by the liver and its natural average level is 250mg/dl (Nouri et al., 2013; ACSM, 2000). Plasma fibrinogen level increases in inflammatory and liver diseases. Increased level of plasma fibrinogen is the precursor to increase in the formation of blood clots (Donovan, Owen, & Bird, 2005). Although increased level of plasma fibrinogen is seen along with the other risk factors for coronary artery disease such as age, smoking, hypertension (high blood pressure), hyperlipidemia, diabetes, and obesity, but fibrinogen is regarded as an independent risk factor for the development of atherosclerotic cardiovascular disease (atherosclerosis) (Mattusch, Dufaux, & Hein, 2000). In fact, by affecting plasma viscosity and platelet aggregation, fibrinogen set the scene for developing coronary artery disease (Abramson & Vaccarino, 2002).

Evidence suggests that the rate of blood clot formation is greater in patients addicted to opium and its derivatives than non-addicts (Castell, Gomez, & David, 1990). The reports also indicate that physical activity has a notable impact on the reduction of fibrinogen level and inflammation (Soheili et al.,

2009; Sheikh-al-Eslami, Vatani, Ahmadi, & Mojtahedi, 2010; Timmones, 2008; Cerneca, Crocetti, & Gombacci, 1999; Olson, Dengel, & Leon, 2007). Soheili et al. (2009) showed that resistance training reduces plasma fibrinogen in elderly men. Farsi, Rahimi, and Tabatabaeian (2012) also found that 8 weeks of strength training leads to reduction in fibrinogen level in obese students. However, in some other studies, the effect of sport activity on fibrinogen level have been rejected (Simpson, Florida, & Whyte, 2006; Mousavi & Habibian, 2011). At the baseline of the present study, it was observed that the level of plasma fibrinogen is high in individuals after drug withdrawal. This finding supports the idea that addiction is associated with an increase in inflammation, plasma viscosity and platelet aggregation (Gorji, Rashidpour, & Fath-alahi, 2010; Nouri et al., 2013; Yarnell & McCrum, 2004). In the present study, it was observed that fibrinogen level decreases after 8 weeks of resistance training. This finding is consistent with the results obtained by You and Niclas (2008) and Nouri et al. (2013) suggesting that participation in aerobic exercise training is associated with the reduced level of fibrinogen in patients after drug withdrawal. Although the exact mechanism for the impact of resistance training on the reduction of fibrinogen level is not clear, this decline is probably the result of an adaptation to exercise and regular physical activity that directly or indirectly reduces the production of this glycoprotein by controlling the production of fibrinogen in the liver (Parsian et al., 2010). In addition, since fibrinogen is considered as one of the main determinants of plasma viscosity, regular exercise may decrease plasma fibrinogen level by increasing plasma volume and blood rheology and decreasing blood flowing (Mustard, Packham, Kinlough, & Perry, 1978). In conclusion, the results of this study showed that drug addiction is associated with the increase in inflammatory markers affecting cardiovascular diseases (C-reactive protein and fibrinogen); however, physical activities can have a significant effect on reducing CRP (C-reactive protein) and fibrinogen levels. Therefore, an eight-week resistance training program may hinder the cardiovascular risk factors in individuals after drug withdrawal through reducing serum levels of CRP and fibrinogen. In this study, no significant differences were observed between the weight and blood lipid profile measures of the subjects following the resistance training. This lack of change is probably due to lack of controlling the subjects' diet or because of an increase in appetite of addicts after drug withdrawal. Evidence suggests that the loss of body mass and subsequent improvement of blood lipid status occur when the body's energy balance is negative (Donnelly, Smith, Jacobsen, & Kirk, 2004; Michael, Mestek, & Garner, 2006; Cooper, Dundon, Hoffman, & Stoever, 2006; Cowan & Devine, 2008).

The findings of this study indicate that drug addiction is associated with the increased levels of inflammatory markers, and physical activity leads to a decrease in the serum CRP and fibrinogen levels in addicts following the drug withdrawal; in other words, physical activity could prevent cardiovascular

problems and risk of sudden death. Among the limitations of the present study were the small sample size and lack of recording the dietary intake of the subjects. Lifestyle modification (including exercise) can be effective and helpful in the treatment and prevention of some drug addiction complications (inflammation markers).

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