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Full Length Research Paper

The effect of regular moderate exercise on muscle damage and inflammation at individuals of different cardiovascular risk groups

Serkan Hazar

Nigde University School of Physical Education and Sports, Nigde, (51000) Bor Yolu / Niğde, Turkey. E-mail: shazar@nigde.edu.tr. Tel: 0 90 (388) 3130013/112, 05052296731. Fax: 0 90 (388) 3130014.

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The aim of the study was two-fold; to determine the effect of a single step-aerobic exercise and an eight-week exercise program on muscle damage and to determine the effect of a single step-aerobic exercise and an eight-week exercise program on inflammation on sedentary females in low, moderate and high cardiovascular risk groups according to basal CRP classification. This study was performed at Niğde University, school of physical education and sports in Turkey. The subject group was composed of 18 middle-aged sedentary females who performed a step-aerobic exercise program 3 times per/week for eight-weeks. Cardiovascular risk classification was constructed according to basal CRP levels. Each subject underwent a 50-min step-aerobic exercise at the beginning and at the end of the program. CK and CRP were analyzed in blood sample. High risk group had higher body weight and body mass index (BMI). Subjects' CRP levels were significantly associated with their age, height, weight and BMI. Besides resulting in higher muscle damage in high risk group subjects, single exercise also caused significant differences in their CK and CRP responses. Additionally, applied eight-week exercise program resulted in a significant decrease in CRP in high risk group. Basal CRP levels were associated with physical characteristics and single exercise caused greater muscle damage in high cardiovascular risk group. CRP levels in high risk group decreased significantly after the exercise program.

Key words: Exercise, cardiovascular risk, muscle damage.

INTRODUCTION

A sedentary lifestyle is one of the major risk factors for cardiovascular disease (Myers, 2003; Slavícek et al., 2008) (CVD). In addition to numerous benefits of exercise, it has been reported by many researchers for such a long time that exercise is extremely useful in prevention of cardiovascular diseases, reducing rate of deaths associated with these diseases and rehabilitation (Alhassan and Robinson, 2008; Hamer and Stamatakis, 2009). Exercise is commonly recommended in treatment of cardiovascular diseases and prevention of such diseases in recent years. Physically, active and fitter individuals tend to develop less coronary heart disease (CHD) (Myers, 2003). Therefore, the individuals who are predisposed to cardiovascular disease risk are orientated to aerobic exercises (Geler, 2008). However, apart from its benefits, exercise, which individuals are not accustomed, has some adverse effects. One of these effects is exercise induced muscle damage and inflammation.

So many researches have reported that unaccustomed exercise causes skeleton muscle cell damage at micro level and this damage induces to inflammation in addition to several stresses on organism (Byrne at al., 2004; Howatson and Someron, 2008; Brancaccio et al., 2007). Magnitude of this damage depends on duration, intensity, type of exercise and age, sex, and physical fitness level of the participants (Willoughby et al., 2003; Tiidus, 2001; Stomme et al., 2004). Muscle damage is usually determined in two ways. The first is imaging techniques and the second is monitoring rates of the muscle of specific enzyme activity within the plasma (Smith and Miles, 2000). When exercise-induced muscle was damage, activity of Creatine Kinase (CK), the intra-cellular enzyme within plasma and serum, increases (Ebbeling and Clarkson, 1989). CK is a strong indicator in determining the muscle damage. Inflammation is a common finding together with the exercise-induced muscle damage (Nosaka and Clakson, 1995). Magnitude of inflammation is correlated with size of the damage that takes place (MacIntyre et al., 2001). Apart from acute inflammation caused by the exercise, chronic inflammation is mentioned in the patients with high cardiovascular disease risk (Ridker, 2001).

Systemic inflammation gives rise to an increase in the inflammation markers. C-reactive protein (CRP) is an acute phase reactant that reflects low-grade systemic inflammation. It is a commonly used inflammation marker owing to its advantages such as cost-effectiveness, ease in application, rate of being affected by the environmental factors, ease of storage, not being affected by diet and long half life (Rifai and Ridker, 2001). Following the exercise, increasing CRP, gives information of exercise induced inflammation. On the other hand, increased basal CRP is a strong indicator of future cardiovascular risk in healthy populations (Blake and Ridker, 2002; Pearson et al., 2003). The association between CRP levels and future cardiovascular disease risk has been found to be independent of age, smoking, cholesterol levels, diabetes, and other major cardiac risk factors (Shishehbor et al., 2003). Briefly, CRP is a strong predictor of future coronary events in healthy individuals (Pearson et al., 2003; Rifai and Ridker, 2001). CRP level of less than 1.0 mg/L is considered low risk, 1.0 - 3.0 mg/L are moderate risk and the one greater than 3.0 mg/L are high risk (Shishehbor et al., 2003).

Although, so many researches have been conducted about the effect of exercise on muscle damage and inflammation, it is important to investigate acute effect of the aerobic exercise on cardiovascular risk groups and chronic response to such exercise. The purpose of this study was to determine the acute and chronic effect of exercise on muscle damage and inflammation after eight week aerobic exercise protocol at middle aged sedentary individuals in low, moderate and high cardiovascular risk groups according to CRP grouping.

METHODOLOGY

Subjects

This study was performed at Niğde University, school of physical education and sports in Turkey in 2008. 18 of 25 sedentary females were recruited to participate in the study. Seven subjects were rejected from the study due to some private health conditions (such as smoking, drug use, etc). The subjects had a mean age of 39.5 ± 4.8 years, height of 158.9 ± 5.1 cm, and weight of 69.6 ± 10.5 kg (Table 1). All subjects enrolled in the study signed a consent giving the permission to the researcher for using their medical info in this research paper.

Categories of basal CRP levels for cardiovascular risk grouping were constructed, based on the classification proposed by American Heart Association (Pearson et al., 2003): low cardiovascular risk group CRP < 1 mg/L, moderate cardiovascular risk group CRP 1 - 3 mg/L, and high cardiovascular risk group CRP > 3 mg/L.

Exercise protocol

The study group performed a step-aerobic exercise at 3 days in a week, for 8 weeks with a time range of 45 - 55 min at 50 - 60% heart rate. Exercise began with a 5 min walking, followed by 5 min warm-up, and a 5 min of stretching at the end of exercise period. Intensity of exercise was based on the heart beat counts of 15 seconds between sets. All measurements and tests conducted on the study group were made twice; the first one was two days before the training period, and the second one was two days after the training period.

Measurements

In this study, 50 min step-aerobic exercise was performed before starting the 8-week exercise period and two days after the exercise period. Blood samples were taken from each subject before performing the single exercise, immediately after, 24 and 48 h later single exercise. Blood samples were drawn from the antecubital vein. Serums were frozen -80°until analysis. CK and CRP values were analyzed by Olympus AU 600 auto analyzer by using Olympus branded test kits. In order to calculate body fat percentage, skin curve thickness was measured on supra-iliac and femur area using Crymych U.K. branded skinfold caliper according to the formula of Pollock et al. (Pollock et al., 1978).

$MaxVO_2$ was determined by Astrand-Rhyming cycle Ergometer test (Astrand and Rhyming, 1954). Subjects pedaled on a cycle ergometer (Monark) at a chosen constant workload for 6 min. Heart rate is measured every minute with telemeter. The steady state heart rate was determined and was looked up on nomogram to determine an estimation of $MaxVO_2$.

Statistical analyses

To compare the same measurement time of the single exercise before and after training period of the groups Wilcoxon Signed Ranks Test was conducted. To compare the same measurement times of the different groups, Kuruscal Wallis test was conducted. After Kruscal Wallis test Mann-Whitney U test was used for multiple comparison. In order to determine acceptability level of significance in this test, Bonferroni correction method was used (Field, 2005). Differences were considered significant at the $p < 0.16$ level. In intra-groups comparison of the measurement times, Friedman two way variance analyses were conducted. Multiple comparisons test were conducted with Wilcoxon signed rank test. In order to determine acceptability level of significance in this test, Bonferroni correction method was used. Level of significance was accepted as $p < 0.012$. Correlation tests were conducted with Pearson correlation.

RESULTS

Table 2 shows the data in regard to CRP values prior to and after the exercise program, body weight is higher in the high risk group than in the low risk group. BMI is higher in the high risk group than the two other groups. Furthermore Table 3 shows the data positive correlation between CRP and age, weight, BMI; and a negative correlation between height and CRP.

Table 1. Physical characteristics of the participants.

	Minimum	Maximum	Mean ± SD
Age (years)	33.00	48.00	39.5 ± 4.8
Height (cm)	153.00	172.00	158.9 ± 5.1
Weight (kg)	53.50	84.00	69.6 ± 10.5
BMI (kg/m^2)	19.27	33.23	27.6 ± 4.4
Body fat (%)	15.10	33.00	27.4 ± 4.8

Table 2. Physical characteristics of the groups.

		Low risk group (mean ± SD) N = 6	Moderate risk group (mean ± SD) N = 7	High risk group (mean ± SD) N = 5
Age (years)		35.600 ± 3.949	40.857 ± 4.913	40.800 ± 5.019
Height (cm)		161.600 ± 6.767	159.285 ± 4.535	155.800 ± 2.949
Weight (kg)	Pre	58.600 ± 3.130 (m)	70.642 ± 9.664	79.400 ± 4.435 (m)
	Post	57.800 ± 3.213 (n)	69.214 ± 8.435	80.600 ± 3.714 (n)
BMI (kg/m^2)	Pre	22.525 ± 2.100 (p.g)	27.731 ± 2.592 (p.h)	32.683 ± 0.659 (g,h)
	Post	22.197 ± 1.799 (ı,j)	27.202 ± 2.291(ı,k)	33.190 ± 0.692 (j,k)
Body fat (%)	Pre	22.980 ± 5.089 (a)	29.642 ± 3.502 (b)	28.920 ± 3.458 (c)
	Post	21.840 ± 6.090 (a)	27.228 ± 2.664 (b)	26.940 ± 4.839 (c)
MaxVo$_2$	Pre	2.2000 ± 0.339(d)	2.100 ± 0.355 (e)	2.340 ± 0.391 (f)
	Post	2.9000 ± 0.330 (d)	2.728 ± 0.442 (e)	2.680 ± 0.277 (f)

a, b, c, d, e, f: Represents the difference between the groups before and after the exercise protocol of the groups ($p < 0.05$).
g, h, ı, j, k, m, n, p: Represents the differences between the groups in the same measurement times ($p < 0.016$).

Table 3. Relation between basaline CK and CRP values of participants and physical characteristics.

		Age	Height	Weight	BMI (kg/m^2)	Body Fat (%)	CRP	MaxVO$_2$
CK (U/L)	r	0.104	0.130	0.302	0.253	-0.028	0.331	0.119
CRP (mg/L)	r	0.571(*)	-0.532(*)	0.652(**)	0.828(**)	0.316	-	0.218

*:p<0.05 **:p<0.01
There was a positive correlation between CRP and age, weight, BMI; and a negative correlation between height and CRP.

Table 4 presents the data of the effect of eight-week training program on muscle damage and acute inflammation at different cardiovascular risk groups after the single exercise. Result showed that the degree of the damage caused by the exercise was higher in the high risk group than in the low risk group. After the single exercise following the training period these differences significantly disappeared.

Acute inflammation emerged after the single exercise prior to the training period was the highest in the high risk group, and higher in the moderate risk group than in the low risk group. This difference decreased remarkable after the training period.

Table 5 shows that eight-week training program significantly decreases the muscle damage and acute inflammation emerged after the single exercise especially in the high risk group.

DISCUSSION

Sedentary life style is among the major risk factors of cardiovascular disease (CVD), such as high blood pressure, rate of blood lipids, smoking and obesity (Myers, 2003). Regular exercise reduces the blood pressure by reducing body weight and increasing

Table 4. Multiple Comparisons between Groups in the Same Measurement Times

Time		Risk groups		CK (U/L) Z	CK (U/L) Sig.	CRP (mg/L) Z	CRP (mg/L) Sig.
Before training period	Pre-exercise	LRG	MRG	-0.244	0.808	-2.847*	0.004
			HRG	-1.256	0.206	-2.635*	0.008
		MRG	HRG	-2.048	0.041	-2.852*	0.004
	Immediately after	LRG	MRG	-1.555	0.121	-2.847*	0.003
			HRG	-2.635*	0.008	-2.627*	0.009
		MRG	HRG	-2.572*	0.010	-2.689*	0.007
	24 h after	LRG	MRG	-34.771*	0.016	-2.044	0.041
			HRG	-2.471*	0.013	-2.627*	0.008
		MRG	HRG	-1.159	0.246	-2.872*	0.004
	48 h after	LRG	MRG	-1.227	0.220	-2.517*	0.012
			HRG	-2.207	0.032	-2.627*	0.008
		MRG	HRG	-2.857*	0.003	-2.852*	0.004
After training period	Pre-exercise	LRG	MRG	-0.325	0.755	-2.198	0.028
			HRG	-1.167	0.243	-2.627*	0.009
		MRG	HRG	-1.222	0.222	-1.874	0.061
	Immediately after	LRG	MRG	-1.874	0.061	-2.842*	0.004
			HRG	-2.207	0.027	-2.627*	0.009
		MRG	HRG	-0.083	0.934	-0.407	0.684
	24 h after	LRG	MRG	-0.976	0.329	-2.355	0.019
			HRG	-1.768	0.074	2.417*	0.016
		MRG	HRG	-1.059	0.289	-2.200	0.028
	48 h after	LRG	MRG	-0.163	0.871	-2.355	0.019
			HRG	-2.627*	0.009	2.620	0.009
		MRG	HRG	-2.526*	0.012	-0.244	0.807

*: A difference was detected between the groups. (p < 0.016).

elasticity of the blood vessels (Halbert et al., 1997; Korkmaz and Öter, 1998). In line with the reduction in the body weight, it gives rise to a decrease in the blood lipids which are named as bad cholesterol (Halbert et al., 1999). It is also known that exercise increase oxygen carriage and usage capacity, muscle strength and elasticity, bone and joint health (Myers, 2003). Moreover, regular exercise prevents people from having habits causing cardiovascular risk such as smoking and alcohol consumption, malnutrition, stress, anxiety etc. and experiencing healthier lifestyle. Regular exercise is a quite effective tool in prevention of cardiovascular diseases. Besides, exercise is effective in rehabilitation of the patients with CVD. The studies report that, physical activity increases blood pumping capacity of heart, capability of coronary vessels to feed the cardiac tissue, regulates the blood pressure, and reduces mortality rate in patients with CVD (Hamer and Stamatakis, 2009). Due to foregoing benefits, patients with CVD and the individuals under the risk of CVD should be orientated to exercise. However, there are some adverse effects of the unaccustomed exercise. One of such effects is muscle tissue damage and inflammation caused by exercise.

When participants of this study were grouped according to their CRP values, differences were noted under their physical characteristics. It was found out that high risk group was fatter when compared to the low risk group, BMI values were higher in the high risk group when

Table 5. Comparison of pre-single exercise serum CK and CRP activities before starting and after completing exercise program.

		Time		Mean ± SD	Z	Sig
CK (U/L)	Low risk group	Pre-exercise	Pre	65.60±16.37		
			Post	71.40±11.23	-0.730	0.465
		Immediately after	Pre	91.60±23.45		
			Post	88.60±11.86	-0.271	0.786
		24 h after	Pre	135.80±26.79		
			Post	99.20±11.75	-1.753	0.080
		48 h after	Pre	129.40±16.67		
			Post	87.80±9.85	-2.023*	0.043
	Moderate risk group	Pre-exercise	Pre	68.14±13.65		
			Post	73.42±12.39	-1.185	0.236
		Immediately after	Pre	111.14±16.23		
			Post	107.28±15.62	-0.762	0.446
		24 h after	Pre	170.57±15.33		
			Post	113.28±23.39	-2.366*	0.018
		48 h after	Pre	114.28±22.76		
			Post	86.28±17.23	-1.690	0.091
	High risk group	Pre-exercise	Pre	80.80±8.07		
			Post	82.00±10.77	-0.680	0.496
		Immediately after	Pre	141.40±11.06		
			Post	103.80±7.22	-2.041*	0.041
		24 h after	Pre	182.00±10.94		
			Post	116.00±8.21	-2.041*	0.041
		48 h after	Pre	159.20±8.87		
			Post	117.00±12.30	-2.041*	0.041
CRP (mg/L)	Low risk group	Pre-exercise	Pre	0.37±0.15		
			Post	0.41±0.20	-0.674	0.500
		Immediately after	Pre	0.37±0.12		
			Post	0.58±0.12	-2.023*	0.043
		24 h after	Pre	0.64±0.33		
			Post	0.94±0.45	-1.753	0.080
		48 h after	Pre	0.41±0.31		
			Post	0.94±0.44	1.753	0.080

Table 5. Contd.

Moderate risk group	Pre-exercise	Pre	1.60±0.44		
		Post	0.97±0.57	-1.690	0.091
	Immediately after	Pre	2.19±1.06		
		Post	1.82±0.73	-1.014	0.310
	24 h after	Pre	2.07±1.14		
		Post	1.72±0.58	-0.845	0.398
	48 h after	Pre	1.63±0.84		
		Post	1.70±0.52	-0.169	0.866
High Risk Group	Pre-exercise	Pre	4.08±0.89		
		Post	1.60±0.62	-2.045*	0.042
	Immediately after	Pre	4.38±0.62		
		Post	1.60±0.62	2.041*	0.041
	24 h after	Pre	5.72±0.73		
		Post	2.44±0.71	-2.054*	0.039
	48 h after	Pre	4.16±0.91		
		Post	1.76±0.52	-2.043*	0.041

compared with the low and moderate risk group, and BMI were higher in the moderate risk group than in the low risk group. Although, body fat percentage was higher in the high risk group, it was found out to be statistically insignificant (Table 2). Also, looking into relationship between CRP and physical characteristics, a positive correlation between CRP and age, weight, and BMI, a negative relation between CRP and height was found. No significant correlation was found between CK and these variables. At the end of the exercise period, body fat percentage decreased and $MaxVo_2$ values increased significantly all participants Table 3.

Several studies report that CRP concentration is associated with the BMI (Keskin et al., 2005), body weight and physical fitness level. A study conducted by Visser et al. reports that high BMI is associated with high CRP concentration (Visser et al., 1999). Also, a study conducted by Church et al. suggests that CRP level in fat individuals and the obese with moderate fitness level is lower than the fat individuals and the obese with lower fitness level (Church et al., 2002). It is a common opinion that basal CRP concentration is related to physical fitness level, as the physical fitness level increases, basal CRP concentration decreases (Church et al., 2002; Nakajima et al., 2008; Aronson et al., 2004). Looking into results of the study, CK and CRP responses to the single exercises performed before and after training period varies among the risk groups (Figures 1 and 2). Looking into the variance analysis results related to difference between different measurement times of a group at single exercise before training period and after training period of the groups, it is observed that CK values had significant differences. When multiple comparison tests were conducted, difference between measurement times was not significant according to Bonferroni correction. On the other hand, comparing the same times of the groups (Table 5), it was observed that there was a significant difference between the measurements of the low cardiovascular risk and high cardiovascular risk group immediately after the exercise performed before training period, and a higher CK response was created in the high risk group. All of the three groups reached the highest level in CK 24 h after the exercise (Figure 1). However, the peak point of the moderate and high cardiovascular risk groups was significantly higher than the lower risk group. When looking into values obtained in 48 h after the exercise, it was observed that, difference between values of mode-rate risk group and high risk group was significant. To sum up, the degree of damage observed in the individuals in high risk group was higher in the different cardiovascular risk groups.

Muscle damage caused by exercise is a common phenomenon in unaccustomed and intensely performed exercises (Byrne et al., 2004). Damage is accompanied

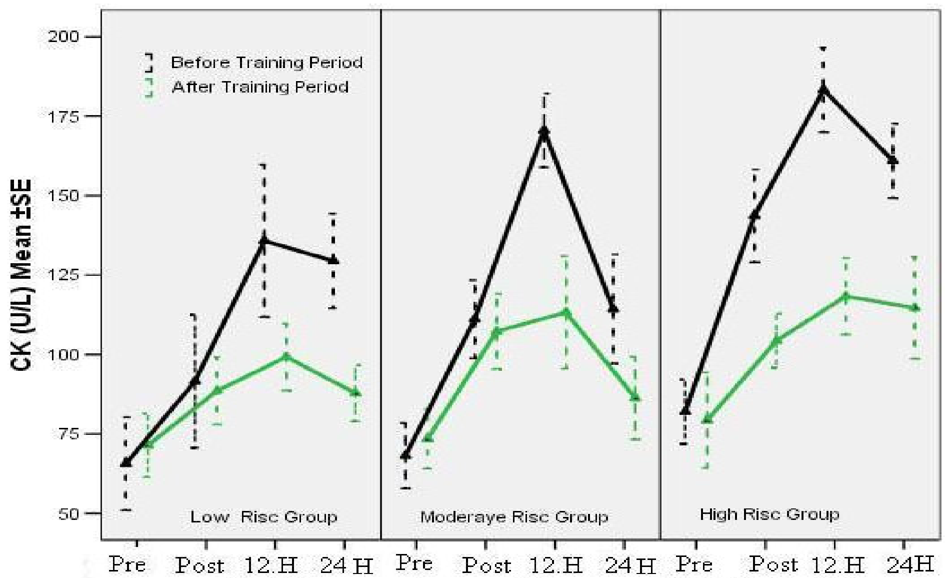

Figure 1. Comparison of serum CK activities.

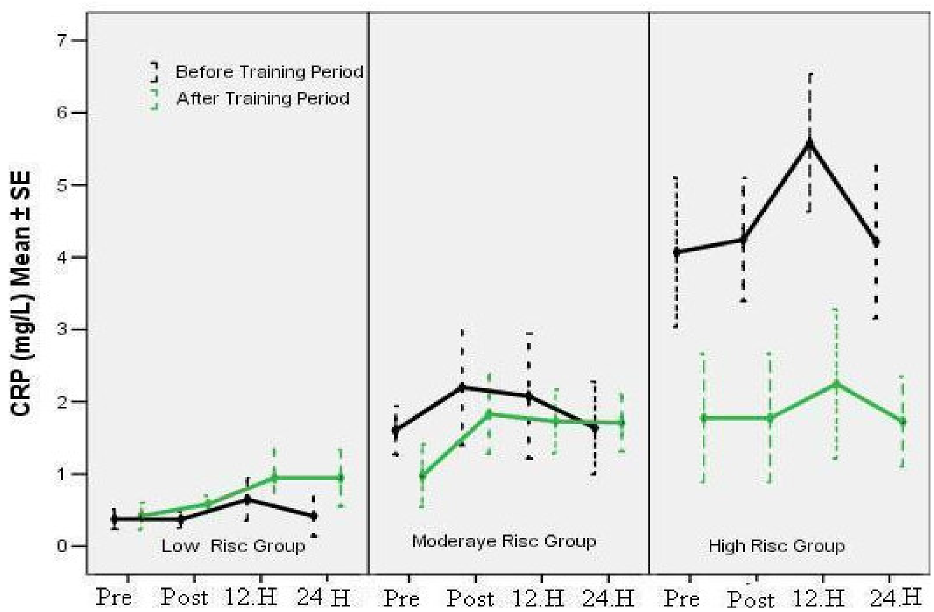

Figure 2. Comparison of serum CRP activities.

by retarding in muscle function, muscle pain, hardening and swelling. The basic reason for such phenomenon is dissemination of intracellular structures of muscles to extra cellular matrix and sarcolemma (Simith and Miles, 2000). It is reported that, basal CK concentration is associated with age, sex, physical fitness level and workout. In the study conducted by Stomme et al. (2004), it was observed that CK values in women were found to be lower than men, the older the individual was, the lower the serum CK activity was, yet a higher activity was seen in persons over 70 and no correlation was found between BMI and CK (Stomme et al., 2004). Considering CRP values for acute inflammation that occurred, following a single exercise, it was found out that there were not significant differences among the values neither before nor after training period, before and after single exercise, and 24 and 48 h after exercise in all of the three groups. The increase in CRP value in the high risk group at 24 h post, the exercise was statistically insignificant. Previous result indicated that there were increases in CRP level depending on intensity and duration of exercise after the single exercise (Abramson and Vaccarino, 2002). It is claimed that, this represents the inflammatory reaction induced by the exercise. However, some researchers suggest that exercises lasting for more than 2 h are required to induce the acute phase proteins (Smith and Miles, 2000). The reason for insignificant increase in CRP levels following the single exercise in the study conducted can be thought to be the duration and intensity of the exercise.

The studies suggest that, chronic inflammation gives more effective and accurate results in determining cardiovascular disease risk (Rifai and Ridker, 2001). Determining chronic inflammation disease, CRP is commonly used (Pearson et al., 2003). Therefore, CRP was used in grouping cardiovascular risk and effect of exercise on cardiovascular risk. Based on the results presented in the study, it was observed that, the eight-week aerobic exercise did not affect the chronic inflammation to a great extent in the low and moderate cardiovascular risk group, yet gave rise to lowered CRP levels in the high risk groups (Figure 2). Normally, this decrease was statistically significant ($p < 0.05$) however, as a result of Bonferroni correction method above mentioned decrease become statistically insignificant ($p > 0.012$). Besides, basal CRP values of high risk group participants decreased from 4.086 ± 0891 mg/L to 1.608 ± 0.621 mg/L level. At the end of the 8 week exercise program, the individuals in the high cardiovascular risk group took place in the “moderate” cardiovascular risk group. Based on the foregoing result, it can be said that exercise program conducted has been more effective on the individuals with high cardiovascular risk.

Regular exercise reduces the basal CRP concentration. Although, this mechanism has not been explained properly, it is attributed to the effect caused by the exercise on TNFα and IL-6 mechanism (Visser et al., 1999). There is a close relation between CRP and cytokine concentration. CRP synthesizing from liver is predomi-nantly regulated by IL-6 (Futterman and Lemberg, 2002). TNFα induces IL-6 (Yudkin et al., 1999). It is a common belief that inflammatory effect taking place in single exercise and CRP increasing in line with rise in cytokine production decreases as a result of the anti-inflammatory effect caused by regular physical exercise (Nakajima et al., 2008; Mackiewicz et al., 1991; Petersen and Pedersen, 2005).

Previous studies suggest that exercise in athletes and sedentary individuals regulate the inflammation process. A study by Mattusche et al. (2000) reported that a 9 month marathon exercise reduces the basal CRP concentration by 31%. Also, Smith et al. report that exercise reduces the CRP concentration by 35% in the individuals with high ischemic cardiac disease (Smith et al., 1999). As a result of study conducted on patients with stable coroner disease; report a 6 week aerobic exercise reduces CRP level by 23.72% (Ranković et al., 2009). These studies suggest that, regular physical activity affects the inflammation process in the sedentary individuals (Ranković et al., 2009) and decreases serum inflammation markers (Panagiotakos et al., 2005), and reduces the chronic inflammation in high cardiovascular risk group more remarkably (Kohut et al., 2006). The studies show that regular exercise causes a long term anti-inflammatory effect with regular physical activity habit (Kasapis and Thopson, 2005). In the study conducted, it has been found out that, the eight-week aerobic exercise reduced CRP concentration. This can be said to be caused by anti-inflammatory effect induced by regular exercise.

As a result, it is suggested that chronic inflammation level is associated with age, height, weight and BMI, the single exercise causes higher muscle damage in the high cardiovascular disease risk group than in the low and moderate risk group, yet response to exercise protocol is more effective in the high risk group. As a matter of fact, CRP values representing chronic inflammation has significantly decreased in the high risk group and, following the exercise program, the individuals in this group took place in the moderate risk group.

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