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THE EFFECT OF VIGOROUS PHYSICAL ACTIVITY ON INFLAMMATORY BIOMARKERS

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Contribution
All the authors contributed significantly to the research that resulted in the submitted manuscript.

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ABSTRACT

Objective: To compare the effect of vigorous physical activity on inflammatory biomarkers levels on football players and untrained people.

Mathodology: In this case control study, 44 men were enrolled .The case group included 22 football players of Rafsanjan team that regularly exercised for 3 hours per day. The control group(20 participants) were carefully selected healthy men who were not engaged in any regular structured exercise activity and did not have physically demanding jobs (e.g. manual labor). All participants underwent a physician supervised maximal treadmill test. ESR, Fibrinogen, Ferritin, D-Dimer and CRP were measured 15 minutes before exercise test.

Results: A total of 44 participants with mean age 22.00±0.6 were evaluated. Serum levels of fibrinogen and D-dimer level were significantly lower in untrained (p=0.003) and (p = 0.002) respectively. Moreover in football players group, hs-CRP levels were significantly lower than the untrained (p = 0.000). However, serum ferritin levels were lower in the athletes group than the untrained but the difference was not significant (p = 0.3). ESR was slightly higher in the trained group but the difference was not significant (p = 0.4).

Conclusion: Exercise decreased the levels of inflammatory biomarkers as hs-CRP, but increased the levels of fibrinogen and D-dimer.

Key Words: Exercise, hs-CRP, Fibrinogen, D-dimer

INTRODUCTION

It is well documented that routine physical activity decreases the risk of atherosclerosis and CVD for both older and younger adults and even moderate levels of activity can be cardioprotective.[1,2] Routine physical activity improves endothelial control, lowers blood pressure, lowers body fat and obesity,[2-4] improves insulin sensitivity,[3-5] and total cholesterol to HDL cholesterol ratios, raises HDL cholesterol levels, reduces smoking frequency[4] and decreases systemic inflammation.[6] Despite the overwhelming evidence of the benefits of physical activity, more than 60% of adults in the United States are not regularly physically active and 25% are not active at all.[1] Physical activity recommendations have included from 20 minutes of vigorous activity three days per week to at least 30 minutes of moderate activity most days of the week.[1]

Since atherosclerosis is an inflammatory process, a marker of inflammation is a logical choice to monitor progression.[7] Almost every phase of the atherosclerotic disease process involves acute phase reactants that are characteristic of the inflammatory process.[8,9] Serum markers of inflammation have the potential to directly or indirectly monitor atherosclerosis and perhaps to identify asymptomatic individuals as appropriate candidates for aggressive primary prevention.[10,11] Several acute phase reactants have been studied as potential markers of low grade inflammation including erythrocyte sedimentation rate (ESR), white blood cell count (WBC), fibrinogen and CRP.[12-15] Santos-Silva *et al* in a study revealed that the training status affects not only the antioxidant capacity but also the oxidative molecular damage degree.[7] Moreover, Radak *et al* in 2008 reported physical inactivity was associated with physiological dysfunctions and reduced whole-body resistance to oxidative stress.[8] We, therefore, steered this comparative study to evaluate the effect of vigorous physical activity on inflammatory markers levels on Rafsanjan football team and untrained people.

METHODOLOGY

In this case-control study, 44 men (22 subjects and 22 controls) were enrolled. The study protocol was approved by ethical committee of the University of Medical Sciences. The study was explained to all participants and written informed consent was obtained.

The case group included 22 players of Rafsanjan football team (men) who regularly exercised for 3 hours a day. The control group (20 participants) were carefully selected healthy men who were not engaged in any regular structured exercise activity and did not have physically demanding jobs (e.g. manual labor).

Inclusion criteria comprised absence of any acute or chronic inflammatory disease, metabolic disease (e.g. diabetes mellitus), hypertension, cardiovascular or peripheral artery disease, thyroid dysfunction, no concomitant medication intake, no alcohol, nicotine, or drug abuse, and normal routine laboratory tests (HDL, LDL, TG, Cholesterol, Creatinine, BUN, CBC, Platelet count), ECG and echocardiogram. Participants were excluded if they had used vitamin or mineral supplements four weeks prior to the study. Furthermore, any participation in intense physical efforts was forbidden during the four weeks prior to the laboratory tests. Also, people who were severely overweight or obesity were excluded. Both the groups were matched regarding age and BMI and were fully examined by a cardiologist. All the subjects were not allowed to take anti-inflammatory drugs, calcium channel blockers, beta blockers, nitrates and smoking within two days before the study.

All participants underwent a physician supervised maximal treadmill test (ESAOTEBIOMEDOCAL model), according to the modified Bruce protocol. Briefly, the test included seven stages (3 min each) with increasing speeds (2.74-8.05 km/h) and grades (0-18 %) of the treadmill. All participants were allowed to continue the running at the level of vigorous exercise that was defined as metabolic equivalent more than 6 (METs $>$ 6) and equal to 21ml of O_2 uptake/kg/min. The test was interrupted if dizziness and chest pain occurred. A blood sample (10cc) was drawn from the cubital fossa 15 minutes prior to the exercise test. In order to measure ESR and fibrinogen (Teco), 3 cc of blood sample was mixed with sodium citrate and 7 cc was saved to measure ferritin (Diaplo), D-Dimer levels, CRP (Nycocard), and routine lab tests (CBC, Platelet count).

During exercise test, heart rate and blood pressure were monitored. Further blood samples were obtained and inflammatory markers measured similarly 30 minutes and 24 hours after the exercise test.

The data was analyzed using SPSS version 20 .Values were given as means ± S.D. Two-way ANOVA for repeated measure (RM)-based analyses was performed in order to reveal the effects derived from life style (untrained vs. trained), exercise testing (pre *vs.* post) and interactions between the two factors. Student's t-test for independent samples was used to compare measurements between the two groups. A p-value of <0.05 was taken statistically significant.

RESULTS

We evaluated 20 football players with mean age of 22.00 ± 0.8, and 20 untrained participants with mean age 22.00 ± 0.5 years, with a non-significant age difference($p=0.1$) as shown in Table 1.

Both groups had normal ejection fraction and it was slightly higher in athletes group, but the difference was not significant ($p=0.05$). Septum and left ventricular free wall

Table 1: Baseline characteristics

Variables	Trained	Untrained	p-value
Age	22.2±0.8	22.1±05	0.10
Height	169.4±2.75	170.3±3.5	042
Weight	65.3±7.17	64.45±3.55	0.13
BMI	23.8±5.09	22.1±2.17	0.12

Table 2: Echocardiographic differences between the two groups

Variables	Trained	Untrained	p-value
Lean body mass	7.4±1.9	7.5±2.1	0.67
LVEDS(mm)	45.4	47.2	0.1
LVESS(mm)	31.9	32.1	0.4
Septum thickness(D)(mm)	11.1	9.9	0.03
Septum thickness(S) (mm)	13	13.3	0.002
LVFM(D)(mm)	11.5	10.6	0.06
LVFM(s)(mm)	14.4	13.3	0.2
Ejection Fraction (%)	60.1	60.3	0.5
Fractional shortening (%)	29.2	31.6	0.05

Table 3: The inflammatory biomarkers, D-dimer, BP and HR in the two groups

Variables		Trained			Untrained			p-value
		Before exercise	30mins after exercise	24 hours after exercise	Before exercise	30 mins after exercise	24 hours after exercise	
Fibrinogen (mg/d)		250.5± 40.1	227.8± 28.9	270.6± 36.5	282.2± 42.24	280.7± 40.1	284.2± 43.0	0.003
Hs-CRP		1.98± 0.46	2.1± 0.36	2.67± 0.5	2.18± 0.87	2.4± 0.23	2.03± 0.81	0.001
D-dimer (ng/dl)		520± 34.1	630.2± 43.5	567.6± 53.2	381.3± 53.0	452.6± 35.1	433.1± 43.5	0.002
Ferrritin (µg/dl)		99.5± 79.4	85.6± 34.5	87.3± 22.1	113.6± 85.3	105.4± 33.1	111.4± 26.1	0.32
ESR		10.8± 7.43	12.5± 3.41	11.7± 2.21	9.62± 3.38	10.04± 4.51	11.2± 1.25	0.4
Heart rate		70.5± 3.1	100.8± 5.2	80.2± 6.3	82.3± 4.4	117.4± 23.1	86.4± 4.6	0.002
VO_2max (mg/kg/min)		61.9± 2.5	111.5± 6.4	64.3± 5.1	53.3± 2.1	78.2± 3.1	65.1± 4.8	0.001
BP(mm Hg)	Sys	118.4± 10.1	125.2± 4.5	112.2± 18.4	125.7± 12.2	136.5± 5.3	112.4± 12.5	0.001
	Dias	78.2± 3.3	85.4± 3.41	83.6± 4.98	86.6± 6.3	89.5± 3.3	84.5± 2.5	0.003

thickness in systole and diastole in trained group was more than the untrained but difference was not significant ($p>0.05$). End diastolic and systolic thickness of the septum was higher in trained group and difference between two groups was significant ($P = 0.03$){Table 2}.

Serum levels of fibrinogen and D-dimer level were significantly lower in untrained ($p=0.003$) and ($p = 0.002$) respectively. Moreover in football players group, hs-CRP levels were significantly lower than untrained ($P = 0.000$). Serum ferritin levels were lower in athletes group than untrained but the difference was not significant ($P = 0.3$) ESR level was slightly higher in trained group but difference was not significant ($P = 0.4$).

Vo2 max in both groups increased in response to physical activity and it was reported statistically significant between the two groups ($P = 0.001$). The difference between the two groups regarding blood pressure and heart rate response was significant ($p=0.002$) {Table 3}.

DISCUSSION

Previous studies have revealed conflicting evidences about the effect of physical exercise on inflammatory biomarkers and coronary artery disease (CAD). Moreover, general population-based research has not yet fully understood how exercise practice can affect redox homeostasis and alter systemic resistance against oxidative challenges. In this field, some studies suggest that regular and moderate physical exercise reduces the incidence of oxidative stress-based diseases.[16] Sesso *et al* in a study in Harvard University indicated that only vigorous activities are associated with a reduced risk of CAD, while moderate or light activities have no direct association with the risk of CAD.[17] In our study, we compared professional football players with untrained healthy population to evaluate the immediate effect of exercise on inflammatory biomarkers.

Both the groups were properly matched in terms of age and BMI. Inflammatory biomarkers such as hs-CRP and fibrinogen in football players were significantly lower than control. These findings are in agreement to several studies that revealed the inverse association between serum CRP levels and self-reported physical activity; these studies signified that regular physical activity reduces CRP level by an inflammatory action.[18-20] Moreover, Geffken *et al* in a study evaluated the association between physical activity and five inflammatory biomarkers and showed that physical activity reduces the most inflammatory biomarkers as CRP, fibrinogen and WBC.[21] Our findings are coherent with other reports in this field[22-24] that indicated the association between fibrinogen levels and physical activity. In the present study, the systolic and diastolic blood pressures in football players were significantly lower than control. Coherently earlier clinical studies have verified that exercise reduces the risks related to CAD as blood pressure, glucose intolerance, and insulin sensitivity.[25] Although, the inverse correlation between physical activity and risks of CAD is well defined, there is much disagreement about the extent and duration of physical activity required to decrease the risk of CAD. This is because of the nature of physical activity that is very difficult to take accurate information on habitual daily activity without disrupting free living. Therefore, the specifics of the correlation between CVD risk and physical activity remain uncertain.

On the other hand, how exercise training decreases inflammation and suppresses CRP levels is not well known. However, several studies confirmed physical activity is related to some confounders that are independently associated with lower CRP levels. For example, age, BMI, waist-to-hip ratio, smoking, hypertension, total and non-high-density lipoprotein cholesterol, triglycerides, and apolipoprotein B concentrations are inversely related to physical activity, whereas these factors are directly related to CRP levels.[26] Furthermore, physical activity is directly related to the proportion of white population, education level, alcohol consumption, fruit and vegetable intake and insulin sensitivity, all of these factors being inversely associated with CRP.[27]

LIMITATIONS

The main limitation of our study was the relatively small sample size, further investigations are recommended with larger series to indicate the correlation between inflammatory biomarkers and exercise.

CONCLUSION

Exercise decreased the levels of inflammatory biomarkers as hs-CRP, but increased the levels of fibrinogen and D-dimer.

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