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The Effect of Endurance Training on Pre-inflammatory Cytokines and Cardiovascular Diseases Risk Factors in Healthy Men

Khalid Mohammadzadeh Salamat[*1], Azizbeigi Boukani Kamal[1], Azarbayejani Mohamad Ali[2] and Yektayar Mozafar[1]

[1]Department of Physical Education and Sport Sciences, Sanandaj Branch, Islamic Azad University, Sanandaj, Iran
[2]Department of Physical Education and Sport Sciences, Central Tehran Branch, Islamic Azad University, Tehran, Iran

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ABSTRACT

Although a number of studies have been previously undertaken on the effect of training on cardiovascular diseases risk factors, there has been a recent focus on its effect on new cardiovascular diseases risk factors including pre-inflammatory cytokines and C reactive proteins. The present study attempted to investigate the effect of endurance training on pre-inflammatory cytokines and cardiovascular diseases risk factors in healthy men. Accordingly, as part of a semi-experimental research, 24 healthy non-athletic students (21-27 yr) were volunteered to participate and randomly divided into two groups: Endurance training group (n=12) and non-exercising control group (n=12). The training group performed a progressive 8-week training (3 days a week) at about 50 to 80 % of HRR which included running around the track. Also, prior to and after the training, a blood sample was collected from the subjects in order to measure pre-inflammatory cytokines, C reactive proteins, lipoproteins and blood cholesterol. Following an 8-week training, a significant difference was found in IL-6, hs-CRP, LDL, HDL and the subjects' Systolic blood pressure ($p<0.05$) compared to baseline. However, this was not the case with the other variables despite reported increases after training. Furthermore, between groups comparisons showed significant difference in IL-6, TNF-α, LDL, HDL and Systolic blood pressure ($p<0.05$). Generally, it can be concluded that endurance training has a positive effect on pre-inflammatory cytokines and some cardiovascular diseases risk factors. It is suggested that young individuals take aerobic exercises in order to prevent the gradual trend of inflammatory disorders.

Keywords: Pre-inflammatory Cytokines, Cardiovascular Diseases Risk Factors, Endurance Training

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INTRODUCTION

Inactive lifestyle, hypertension, hyperlipidemia, smoking and obesity are 5 main cardiovascular diseases risk factors. Scientific evidence suggests that decreasing this risk factors will reduce the possibility of suffering from a stroke and other cardiovascular diseases [1,2]. On the other hand, regular physical exercise has positive effects on many risk factors of cardiovascular diseases. It is obvious that regular physical exercise leads to reduced weight and blood pressure. In addition, there will be a reduction in low-density lipoprotein (LDL) and cholesterol and an increment in high-density lipoprotein (HDL) after endurance training [3]. Accordingly, it's claimed that reducing HDL is a metabolic adaptation of reduced risk of suffering from cardiovascular diseases and lower plasma HDL is the commonest lipoprotein profile disorder of individuals suffering from cardiovascular diseases [1]. Also in a study an 8-week combined (endurance and resistance) and endurance training lead to a significant reduction in Triglyceride (TG) and total cholesterol (TC) and an increase in HDL. However, in above mentioned study resistance training protocol only leads to a significant decrease in TG and TC and has no significant effect on HDL level in trained men [4]. Furthermore, in a controlled trial showed that resistance training results in a significant decrease in body fat, while aerobic and resistance training had no effects on plasma glucose, Insulin, TC, LDL-C and TG, whereas aerobic exercise increase HDL-C. The above results are indicative of the effect of types of exercise on risk factors of cardiovascular diseases [5].

It is believed that there is an inverse relationship between physical fitness and risk factors of cardiovascular diseases including, glucose tolerance, blood pressure, resting heart rate, obesity and indicators of systemic inflammation such as CRP and pre-inflammatory cytokines [2]. It has been shown that exercise training causes lipoprotein oxidation reduction, endothelial function improvement, decreased production of Atherosclerotic plaques from blood mononuclear cells and a decrease in collagen accumulation in the arterial wall [2,5].

A number of studies have shown that reduced inflammatory factors, such as TNF-α [6], CRP [7,8], IL-6 and cellular adhesion molecules [9] results in a decrease in risk factors of cardiovascular diseases. Therefore, such indices can be considered as new predictors of cardiovascular diseases. It has also been reported that an increase in CRP, even at previously considered normal level, strongly predicts the incidence of coronary attacks [10]. Although CRP has long been used for diagnosis of tissue damage or inflammation, there have recently been attempts to apply it to the diagnosis of cardiovascular diseases [11]. In addition, countless experiments have confirmed the relationship between high CRP level and risk of infarction and sudden cardiac death [12,13]. Special focus has been given to the reactions of CRP to types of exercise due to its wide function ranges, including phagocytosis stimulation and release of complement components in reaction to tissue and inflammatory damage [14,15]. Despite previous studies, there is still inadequate information on the effect of exercise on serum cytokines and their role in cardiovascular diseases. The present study attempts to investigate the effect of an 8-week endurance training on inflammatory indices (IL-6, IL-1ß, TNF-α) and other risk factors of cardiovascular diseases (systolic and diastolic blood pressure, CRP and plasma lipoprotein profile) in young healthy men.

MATERIALS AND METHODS

Participants

Twenty four healthy males (23.21±2.36 yr) were volunteered to participate in present study. They became fully aware from the study objectives, procedures and possible risks. Participants had not any regular training in one year before study commence. They were randomly and equally assigned to an endurance training group (n=12) and a non-exercising control group (n=12). Then, the Participants were homogeneous according to body mass index (BMI), maximum oxygen consumption and age (Table 1).

Table1. Participants' Characteristics in Terms of Age, Height, Weight, Body Fat& BMI

	endurance training	Control	t	p
Age (year)	23± 1.91	23.42± 2.82	1.04	0.86
Height (cm)	174.49± 3.41	175.01± 4.35	2.14	0.37
Weight (kg)	72.34± 7.84	73.53± 6.12	0.89	0.41
Body Fat (%)	18.10± 6.18	18.61± 5.87	3.53	0.79
BMI (kg/m^2)	23.76± 3.23	24.01± 2.91	1.16	0.29
VO2max (ml.kg-1.min-1)	39.11± 3.21	40.35± 2.87	3.16	0.68

The data has been reported as mean± SD.

Physiological measurements

Firstly, Participants' characteristics measured in a week prior to training program commence. In the following day, their maximum oxygen consumption was measured using treadmill (TechnoGym, Italy) modified Bruce protocol. Body fat percent was indirectly measured using caliper (Laffayette, 01127 mod, USA) and Jackson-Pollock 3-point (abdomen, super iliac and triceps) method. It should be noted that all the measurement was performed at 9 to 12 am. Systolic and diastolic blood pressure was measured (beurer, Germany) in baseline and after training program.

Training Program

The experimental group accomplished an 8-week training 3 sessions a week at 5 pm. Control group only participated in daily activities. The experimental group had a 5-minute jogging as warm-up and finished daily training with range of motion (ROM) as cooling down. The training program was including aerobic running started with 45-50 % of each subjects' heart rate reserve (HRR) or 130-140 beats per minute for 20 min at the first week. In the last week, running time reached to 33 min at the intensity of 172-182 b/min or 75-80 % HRR. Training intensity and time was increased 5% each week for observance overload principle, except fifth week in which training was done in the same as fourth week. Polar instrument was used to heart rate monitoring. In order to control training program intensity polar monitors issued heart rate by producing signal during running.

Biochemical Measurements

Two days prior to the training program, the subjects attended hematology lab in Kurdistan University of medical sciences for a blood sampling. After blood sampling and severance, serum and plasma were kept at -70° for further analysis. The same procedure was followed after eight week training program. Besides, ELISA kits (Bender MedSystems, Norway) were used to measure Interleukin-6 (IL-6), interleukin-1 beta (IL-1β), alpha tumor necrosis factor (TNF-α) and ELISA kits (Monobined, USA) were used to measure high sensitive C-reactive protein (hs-CRP), LDL, HDL and TC. It should also be noted that ELISA reader (Awaneness, Technology co, USA) was used to read ELISA kits.

Data Analysis

Descriptive statistics was used to calculate mean and standard deviation of descriptive variables. Kolmogorov-smirnov and Levene's tests were applied to measure the normality and homogeneous variances of variables, respectively. In addition, to inter and intra comparison of data dependent and independent t student tests were used respectively. SPSS16 for windows was used in all data analysis.

RESULTS

Table2. Inter and intra group comparison in terms of Inflammatory Cytokines

variable	group	Pretest	posttest	independent t test
		Mean ±SD	Mean ±SD	P value
IL-6 (pg/ml)	Endurance training	5.29±0.46	4.68±0.39	0.02*
	control	5.03±0.38	5.31±0.43	
IL-1β (pg/ml)	Endurance training	2.23±0.26	2.59±0.42	0.11
	control	2.44±0.42	2.36±0.35	
TNF-α (pg/ml)	Endurance training	4.55±0.74	3.89±0.48	0.04*
	control	4.32±0.69	4.12±0.61	

**Discernible differences at P<0.01.*

Table3. Inter and intra group comparison in terms of Risk Factors of Cardiovascular Diseases

variable	group	Pretest	posttest	P value	
		Mean ±SD	Mean ±SD	dependent	independent
HDL (mg/dl)	Endurance training	32/44±6.23	41.74±5.90	0.001*	0.01*
	control	33.23±5.79	34.36±5.	0.92	
LDL (mg/dl)	Endurance training	95.85±9.13	69.94±8.56	0.002*	0.001*
	control	94.74±8.72	92.29±7.08	0.27	
TC (mg/dl)	Endurance training	167.03±16.81	155.88±17.02	0.07	0.06
	control	169.11±15.01	167.63±15.71	0.78	
SBP (mm Hg)	Endurance training	137.80±18.5	121.60±17.9	0.04*	0.02*
	control	136.3±16.9	133.20±16.4	0.29	
DBP (mm/Hg)	Endurance training	81.1±1.00	80.5±0.7	0.31	0.18
	control	79.9±0.9	80.2±0.8	0.84	
hsCRP (Microg/ml)	Endurance training	1.47±0.31	0.98±0.26	0.04*	0.21
	control	1.50±0.44	1.60±0.35	0.27	

**Discernible differences at P<0.01.*

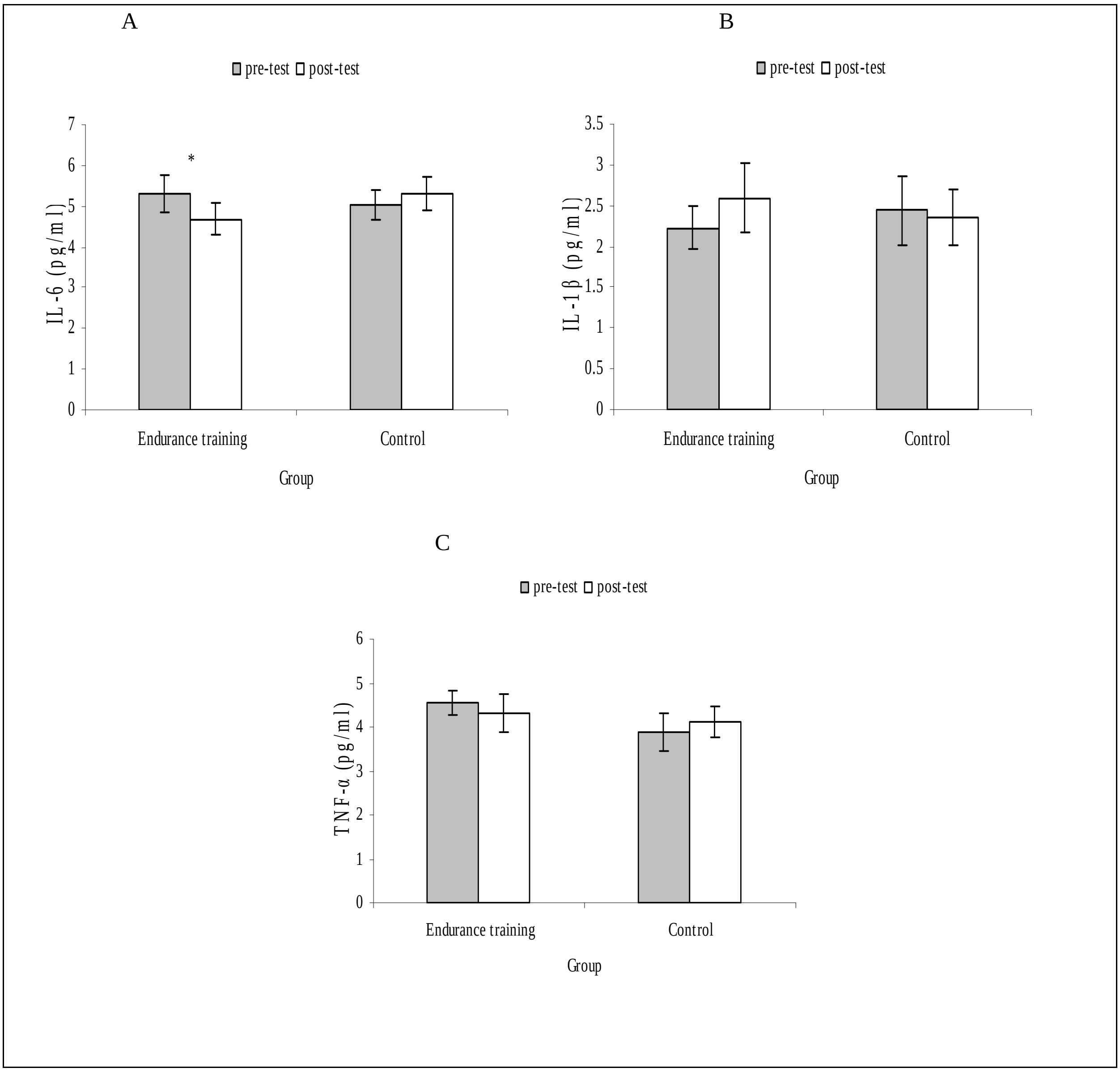

Figure 1. Pre- and posttraining values in comparison of two groups in IL-6(A), IL-1ß(B), TNF-α (C). *Discernible differences at $p < 0.05$.

The results show that eight week endurance training leads to a significant decrease in IL-6, CPR, LDL and systolic blood pressure and a significant increase in HDL ($p<0.05$). Despite an increase after training, no significant difference was found in other variables. However, when compared two groups, a significant decrease was found in IL-6, TNF-α, LDL and systolic blood pressure, and a significant increase was observed in HDL (table 2&3).

DISCUSSION

The present study shows that eight week endurance training results in a significant decrease in IL-6 and CPR. Herein, these variables showed an increase of 11.5% and 33.3%, respectively. It is believed that even a small increase in IL-6 plasma values results in producing anti-inflammatory cytokines of IL-1ra and IL-10 accompanied by CPR. During training, increased IL-6 precedes the production of these two cytokines, which is indicative of IL-6 leading role in cytokines reaction to training [16]. In some studies showed any insignificant difference in TNF-α and IL-1ß after a training program. It may be the result of the variety in intensity and duration of such programs.

However, Bruunsgaard suggests that despite increased gene expression during low systemic inflammation, TNF-α level is not always observable in circulation. Local TNF-α may stimulate producing IL-6 and other intermediates of inflammatory cascade to some extent [17]. It's believes that small systemic increase in IL-6, IL8, CPR, IL-1ra, sTNF-Rs, IL-10 and inflammatory cells may reflect increasing production of TNF-α [17]. Exercise training may have influence on protein expression of TNF-α and IL-1ß in active muscle, but such an expression will not lead to an increase in these two cytokines within monocytes as the main source of such proteins [16].

The present study also indicates that endurance training results in a significant decrease and a significant increase in LDL-c and HDL-c, respectively. Wherein, LDL-C and HDL-C reported an increase of 27% and 28.6%, respectively. Despite a 6.6 % increase, the change in TC was insignificant. It seems that increased HDL-c may be the result of its increased production by the liver and change in different enzymes including increased Lipoprotein lipase (LPL) and Lecithin cholesterol Acyl transferase (LCAT) activities and decreased Hepatic Lipase (LH) activity after physical activity. LH plays a pivotal role in changing HDL2 into HDL3, VLDL into IDL-C and large LDL-C into IDL-C and small LDL-C. It should be noted that LH is low in active individuals, can be increased with more training and keeps HDL-C density at high level [18,19,20]. Accordingly, Tampson et al (2004) investigated the effect of 6-month endurance training with a 60-80 % of maximum heart rate (HRmax) and including running on treadmill and ergometer, skiing and crosscountry running on healthy males. There was an 11% increase in TG after the training program, however no significant change was observed in TC in both groups prior to and after the 6-month period. Furthermore, there was a small but non-significant decrease in LDL-c and a small (2%) increase and HDL-c of the training group. Also, a non-significant decrease was observed in LDL/HDL-c and TC/HDL-c ratios. Besides, after endurance training, aerobic power showed a 10% increase in experimental group. However, none of the changes above were significant in control group [21].

The present study also shows that there is a significant decrease in systolic blood pressure (SBP) by 1.6 (mmHg) in the experimental group. Despite a 1 (mmHg) decrease, diastolic blood pressure (DBP) did not show a significant change. Previous studies indicate that aerobic training leads to a decrease in resting SBP and DBP by almost 4-5 and 3-4 (mm Hg). Also, it is believed that such a decreased blood pressure is accompanied by a 40 and a 15% decrease in the risk of heart stroke and that of suffering from coronary disease, respectively.

CONCLUSION

Generally, as the findings show, eight week endurance training results in an improvement in a number of inflammatory indices and lipoprotein profile in healthy males. Therefore, this training program can recommended as a way of reducing the risk of systemic inflammation and related disorders.

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