DOES EXERCISE HAVE FAVORABLE EFFECTS ON BLOOD LIPIDS, HDL-CHOLESTEROL, OXIDANT-ANTIOXIDANT STATUS AND CORONARY HEART DISEASE RISK FACTORS IN YOUNG TURKISH MEN?

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ABSTRACT

Objective: Our aim was to determine the effects of exercise on blood lipids especially on HDL-cholesterol and the oxidant-antioxidant status and associations between blood lipids, and the oxidant-antioxidant status.

Methods: Blood lipids, antioxidant enzymes like erythrocyte GpX and SOD, plasma TBARS as an indicator of lipid peroxidation, total antioxidant status, antioxidant molecules like albumin, uric acid, and biluribin were measured in healthy young sedentary and exercising men. Our study group was composed of volunteers from the navy ; 34 were sedentary (Group A) while 44 exercised 7-14 hours (Group BI) and 35 exercised 42 hours (Group BII) weekly.

Results: Mean (standard deviation) of HDL-Cholesterol in Groups A, BI, and BII were 35.7(7.3), 36.7(9.6), and 35.3(9.7) mg/dl respectively. Similarly mean (standard deviations) for antioxidant/oxidant status were found as follows: GpX :17.4(7.9), 22.2(7.6), and 29.1(7.6); SOD: 2249.6(1263), 1835(689), and 1594(510) U/ gHb ; for total antioxidant status (TAS): 1.8(0.46), 2.0(0.9), and 1.9(0.4)mmol/L; TBARS: 0.48(0.16), 0.83(0.57), and 0.63(0.08) nmol/L.

Conclusion: No favorable effects of exercise on blood lipids were detected, however the effect of exercise on fibrinogen was beneficial . SOD decreased and GpX increased significantly with exercise. There was no significant difference in TAS among the sedentary and exercising groups.

Key Words: Lipids, Exercise, Coronary risk, SOD, BARS, TAS, GpX, Turkish

INTRODUCTION

Coronary heart disease is the major cause of death in developing and developed countries. Age, gender, blood lipids, hypertension, genetics and life style all have affects in the pathogenesis of atherosclerosis. Low HDL-Cholesterol (HDL-c), high LDL-cholesterol (LDL-c), and oxidized-LDL (ox-LDL) are considered important among the many other risk factors of atherosclerosis. Elevated blood lipid concentrations lead to elevated blood lipid peroxides which contribute to endothelial injury and start the process of atherogenesis. Excess free radicals are thought to initiate atherosclerosis by impairing endotelial function and oxidizing LDL and HDL. Oxidized LDL attract macrophages which in turn scavenge the ox-LDL and turn into foam cells (1). Ox-HDL is no longer efficient in reverse cholesterol transport (2). It is suggested that lipid peroxidation products can exchange between lipoproteins and the interaction of lipid

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peroxidation products among the lipoproteins and cells will enhance atherogenesis.

Genetic, hormonal and environmental factors determine serum lipid and HDL levels (3-6) . Turkish people are known to have low HDL-c levels compared to other Caucasians (7). This low HDL-c seems to be independent of obesity markers and sex steroid hormones (8) and continues to be low even when Turkish people migrate to other countries (9). Dietary interventions and weight loss are known to have beneficial effects on the blood lipids and blood pressure (10). Regular exercise is known to prevent cardiovascular disease by increasing the HDL-c and decreasing fibrinogen and body weight (11,12). However, during exercise, body O_2 consumption is greatly increased and more superoxide anion and hydrogen peroxide form in vivo (13,14).

We investigated the effects of exercise on blood lipids and especially HDL-c and oxidant–antioxidant status in healthy young non-smoker Turkish males. Erythrocyte superoxide dismutase (eSOD), a major antioxidant enzyme that dismutases superoxide anion to hydrogen peroxide (H_2O_2) and oxygen, erythrocyte glutathione peroxidase (eGpX) that removes the H_2O_2 and other hydroperoxides, antioxidant molecules like albumin, uric acid and, total bilirubin and total antioxidant status (TAS) were measured. Thiobarbituricacid-reactive substances (TBARS) were determined as an indicator of lipid peroxidation.

SUBJECTS AND METHODS

Healthy non-smoker young men volunteers from the navy with no diabetes, coronary artery disease, hypertension , systemic disease, overt obesity, hyperlipidemia were included in this study. The participants had been in the navy for at least a year. The participants were divided into two groups; Group A: 34 sedentary men that make no exercise and Group B: 79 men that exercise regularly. After a statistical analysis, the participants were classified into three groups according to their weekly exercise hours: 34 people who did no exercise were put in Group A, 44 people with weekly exercise of 7-14 hours in the moderate-exercise group (BI) and, 35 people with 42 hours weekly exercise and heavy work in the intense-exercise group (BII).

Blood was taken after 14 hours of fasting in the morning. Systolic and diastolic blood pressures (SBP and DBP) were measured by standard mercury sphygmomanometer and venous blood was taken after 10 minutes of resting. Sera and plasma were separated within 30 minutes by centrifugation at 3000g for 10 minutes. Samples were kept at -80 °C when not assayed immediately. Waist and hip measurements were taken to the nearest 0.1 cm and body mass index (BMI) was calculated by dividing the weight in kg by square of height in meters, waist to hip ratios (w/h) were also calculated. eSOD, eGpX , and total antioxidant status were measured in heparinised blood, Lp(a), and TBARS were measured in EDTA plasma, glucose, total cholesterol, triglycerides, apo AI, apo B, uric acid, total bilirubin, albumin were assayed in serum. HDL-c was quantitated by the same enzymatic cholesterol method after precipitation of the apo B containing lipoproteins by phosphotungstic acid/MgCl2. LDL-c was calculated according to the Friedewald formula. Biochemical parameters were measured by Biotrol kits in Bayer-Opera autoanalyzer. The laboratory participated in external quality assurance programs for the routine biochemistry parameters.

Lipid peroxidation was monitored by measuring the malondialdehyde, a breakdown product of lipid peroxides (15). eGpx was assayed by using t-butyl hydroperoxide as substrate and the method was applied to Technicon RA -XT auto analyzer (16). eSOD was determined by the method developed by Sun Yi (17). Both eGpX and eSOD activity were expressed as units per gram hemoglobin. TAS was measured with a Randox kit. Fibrinogen, Apo AI and Apo B were quantitated in Behring nephelometer. Lp(a) was assayed with Tint Elize-Biopool Elisa kit (Umea Sweden).

Statistical Analysis was performed with the SPSS program. Logarithmic transformations before statistical comparisons were done for parameters that did not show normal distribution . Student t Test for continuous variables and Mann Whitney U test for the nonparametric parameters were utilized in comparison of the groups A and B. Comparison of the means of the groups A, BI,

and BII were done with Kruskall-Wallis test. Univariate regression analysis were performed by Pearson test.

RESULTS

Of the 113 subjects, 84 had their blood lipids measured for the first time in their lives, 12 had cardiovascular disease in their families and, 20 had BMI greater than 25 kg/m^2. They all had the same diet and saturated fatty acid (butter) - monounsaturated fatty acid (olive oil)- polyunsaturated fatty acid (sunflower oil) combination in their diets. Their daily calorie intake was 3800-4000 cal. The mean age of all the participants was 21.5±2.0, 5 and 95 percentile values were 20 and 25 respectively. Mean value for BMI was 23.3±2.6 kg/m^2 and w/h was 0.84±0.06. HDL-c and apo AI mean values were strikingly low (35.9±9.2 mg/dl and 130.5±18.9 mg/dl respectively), and the median value for Lp(a) was 16.2 mg/dl. Total cholesterol and LDL-c mean values were rather low (152.8±73.7 and 91.3±28.2 mg/dl), total cholesterol/ HDL-c ratio (4.4±1.7) and LDL-c/ HDL-c (2.3±1.49) did not indicate cardiovascular risk. eSOD and TAS levels were higher than the expected normal range whereas eGpX was in the normal range-though borderline low when the study group was taken as a whole . Waist circumference, BMI, w/h, SBP and DBP were all in the favorable range.

When the mean values of the parameters measured were compared between the sedentary and the exercising group as a whole, significant differences were found only in the mean blood glucose ($p<0.01$), TBARS ($p<0.05$), eGpX ($p<0.001$) , and eSOD($p<0.01$). Glucose and eSOD were lower and TBARS and eGpX were higher in the exercising (B) group compared to the sedentary (A) group. There were no significant differences in the antioxidant molecules albumin, total bilirubin, uric acid. Hb decreased favorably though insignificantly and TAS increased only insignificantly. When the participants were divided into three groups according to increasing exercise hours eSOD activities of the sedentary group (A) and moderate activity group (BI), eGpX activity of the intense activity group (BII), and TAS of all the three groups were found above the normal range. eSOD activities decreased sharply as the exercise hours increased. The eSOD decrease in the Group BII was accompanied by almost 50% increase in GpX values. Mean Hb values also decreased with the increasing exercise hours. Mean fibrinogen, apo AI, apoB mean, albumin, uric acid, total bilirubin values were normal in each group. Fibrinogen and eSOD were lowest in the intense activity group (BII) whereas eGpX was highest in the same group. (Table I).

When the mean values of the variables were compared between the three groups: there was no significant difference in age, BMI, SBP, DBP, w/h, total cholesterol, HDL-c, LDL-c, triglycerides, albumin, total bilirubin, uric acid, TBARS, Hb, apo AI, apo B, total cholesterol/HDL-c, LDL-c/ HDL-c and, TAS (Table I). Differences in the mean levels of the erythrocyte antioxidant enzymes (eGpX; $p<0.05$, eSOD; $p<0.01$) among the three groups were significant. Serum glucose was significantly lower in the moderate exercise group BI compared to the sedentary (A) group and the intense activity (BII) group ($p<0.05$).

Correlation analysis (Table II) within the sedentary (A) and the exercising (B) group revealed significant positive relations between TBARS and Lp(a) , and eGpX; between log^e triglycerides and uric acid; between total bilirubin and BMI, glucose in the sedentary group; between Lp(a) and albumin, between apo AI and Hb, between uric acid and weight, between eGpX and TAS; between apo B and triglycerides, BMI, weight; between triglycerides and BMI; between waist circumference and triglycerides in group B. Significant negative correlation was found between triglycerides and DBP; between w/h and DBP in the sedentary group; between fibrinogen and albumin; between eGpX and eSOD , between TAS and Hb, w/h; between TBARS and glucose , SOD, triglycerides , Lp(a) ; between waist circumference and albumin ; between BMI and Lp(a) in the exercising group.

The expected significant positive correlations between apo AI and HDL-c and between apo B and LDL-c were found in all the groups; other well-known associations between the lipids and obesity, age are not mentioned.

Table I: Mean values ± Standard Deviations of the parameters measured

PARAMETERS n	Sedentary Grp (A) 34	Exercising Grp (B) 79	Exercising Grp BI (BI) 44	Exercising Grp BII (BII) 35	Expected Value
Glucose (mg/dl)	99.2 ± 12.3**	90.3 ± 14.3	85.0 ± 13.2*	94.0 ± 15.4	70-110
T Chol(mg/dl)	151.8 ± 30.5	152.8 ± 28.3	156.0 ± 25.7	149.3 ± 31.6	140-200
Triglyceride (mg/dl)	138.6 ± 81.4	129.7 ± 73.4	132.9 ± 86.1	125.5 ± 52.5	<150
HDL- Chol (mg/dl)	35.7 ± 7.3	36.1 ± 9.5	36.7 ± 9.6	35.3 ± 9.7	>35
LDL- Chol (mg/dl)	84.9 ± 34.1	92.5 ± 26.4	92.4 ± 24.7	91.9 ± 29.9	<130
VLDL- Chol (mg/dl)	33.9 ± 26.0	24.9 ± 14.2	24.8 ± 17.0	25.1 ± 10.6	<30
Albumin (mg/dl)	4.4 ± 0.7	4.4 ± 0.2	4.4 ± 0.3	4.5 ± 0.2	3.5-5.5
T Bilirubin (mg/dl)	0.99 ± 0.72	0.74 ± 0.35	0.73 ± 0.29	0.75 ± 0.44	0.2-1.1
Uric acid (mg/d)	3.9 ± 0.9	4.1 ± 0.94	3.0 ± 0.8	4.0 ± 1.0	2.6-7.2
TBARS (nmol/lt)	0.48 ± 0.16*	0.74 ± 0.63	0.83 ± 0.57	0.63 ± 0.08	0.5-1.5
GpX (U/gHb)	17.4 ± 7.9***	25.5 ± 8.3	22.2 ± 7.6***	29.1 ± 7.6	27.5-73.6
SOD (U/gHb)	2249 .6 ± 1263**	1730.0 ± 624	1835 ± 689**	1594 ± 510	1100-1600
TAS (mmol/lt)	1.8 ± 0.46	2.0 ± 0.85	2.0 ± 0.9	1.9 ± 0.4	1.3-1.8
Hb (mg/dl)	17.0 ± 3.4	15.7 ± 3.2	16.0 ± 3.4	15.4 ± 2.9	14-18
Fibrinogen (mg/dl)	248.3 ± 46.1	227.3 ± 87.2**	266.0 ± 83.6**	188.0 ± 72.9	180-350
Apo AI (mg/dl)	135.1 ± 20.7	129.6 ± 18.5	125.6 ± 18.1	133.9 ± 18.3	120-220
Apo B (mg/dl)	110.0 ± 29.1	97.2 ± 24.7	92.9 ± 22.5	102.1 ± 26.4	65-165
Lp (a) (mg/dl)	22.5 ± 23.8	25.3 ± 24.9	20.6 ± 21.9	31.2 ± 27.3	<30
Apo AI/B	1.3 ± 0.4	1.4 ± 0.4	1.4 ± 0.4	1.4 ± 0.3	1.2-1.5
T. Chol/HDL-c	4.5 ± 1.3	4.4 ± 1.7	4.3 ± 1.1	4.6 ± 2.3	<4.5
LDL-c/HDL-c	2.1 ± 1.3	2.6 ± 1.2	2.7 ± 1.2	2.4 ± 1.5	<3.5
BMI	23.2 ± 1.5	23.4 ± 2.8	23.4 ± 3.0	23.4 ± 2.6	<25
Waist circumference (cm)	85.0 ± 5.8	85.0 ± 8.0	85.0 ± 8.0	85.2 ± 8.4	<102
Waist/hip	0.86 ± 0.06	0.83 ± 0.05	0.83 ± 0.05	0.85 ± 0.07	<0.9
SBP (mmHg)	112 ± 8	111 ± 7	111 ± 7	112 ± 7	<140
DBP (mmHg)	69 ± 5	72 ± 0.6	72 ± 6	71 ± 6	<85
Age	21.3 ± 5.6	21.8 ± 3.0	21.9 ± 2.7	21.7 ± 3.2	

*: p<0.05 **: p<0.01 ***: p<0.001 *(Significance Level): placed between the groups compared
T.Chol:Total cholesterol, TAS: total antioxidant status, BMI: body mass index, GpX: glutathione peroxidase, SOD: superoxide dismutase

Table II: Results of the Correlation Analysis (Pearson)

GROUP A		r	p
TBARS	Lp(a)	0.5308	0.05
	eGpX	0.5777	0.05
ln triglycerides	uric acid	0.5092	0.05
total bilirubin	BMI	0.7777	0.001
	glucose	0.7962	0.001
triglycerides	DBP	-0.8136	0.001
w/h	DBP	-06983	0.001
GROUP B			
Lp(a)	albumin	0.2343	0.05
apo AI	Hb	0.3168	0.05
uric acid	weight	0.2919	0.05
GpX	TAS	0.3646	0.05
apo B	triglycerides	0.2848	0.05
	BMI	0.3408	0.001
	weight	0.4126	0.001
triglycerides	BMI	0.4119	0.001
waist cir.	triglycerides	0.3628	0.05
fibrinogen	albumin	-0.3016	0.05
eGpX	eSOD	-0.2909	0.05
TAS	Hb	-0.3865	0.05
	w/h	-0.4477	0.05
TBARS	glucose	-0.3809	0.001
	SOD	-0.3257	0.05
	triglycerides	-0.3280	0.01
	Lp(a)	-0.3115	0.05
waist circumference	albumin	-0.2878	0.05
BMI	Lp(a)	-0.2924	0.05

T.Chol: Total cholesterol, TAS: total antioxidant status, BMI: body mass index, GpX: glutathione peroxidase, SOD: superoxide dismutase

DISCUSSION

The most striking result of the comparison of the exercising group with the sedentary group was that there was no change in HDL-c values, significant increases in eGpX and TBARS and decrease in eSOD and blood glucose when the exercising group was compared with the sedentary group. Decrease in fibrinogen levels and increase in TAS levels were not significant. We expected to find higher HDL-c values in the exercising group. Exercise is among the very few interventions used to increase HDL values. Persistence of low HDL levels puts the Turkish population in quite a critical situation. Life style, age, and environmental factors influence the antioxidant enzyme activities as well as blood lipids. We have tried to eliminate various effects on the blood lipid parameters and erythrocyte enzyme activities by choosing young healthy non-smoker male subjects who were doing their military service and were under a uniform diet.

In Turkey and especially in the Kocaeli region there is considerable air pollution. Chronic

exposure to air pollution has also been shown to decrease SOD activity (18). As the eSOD decreased, TBARS increased in the exercising group. In fact we found significant negative correlation between eSOD and TBARS (19) Increase in lipid peroxidation was most probably a result of decreased SOD activity. Inverse relationship between TBARS monitored lipoperoxidation and eGpX points out the fact that antioxidant enzymes have a fine control of intracellular lipoperoxide concentration and the balance between antioxidant and prooxidant factors in free radical metabolism shifts towards increased lipid peroxidation (20).

Previous studies have shown eGpX values to be lower in current smokers, higher in users of oral antioxidant-supplements (21). Life style and environmental factors seem to affect eGpX most clearly (22). GpX is an unstable enzyme easily inactivated (23). High eSOD and low eGpX in the sedentary group, and decrease of eSOD and increase of eGpX with increasing exercise hours is hard to interpret. Air pollution may have lowered the eGpX levels and eSOD may have increased as a response to balance the antioxidant enzyme levels. Although parallel increases and decreases of the erythrocyte antioxidant enzymes would be expected to occur, increase of H_2O_2 as a result of exercise may have led to the destruction of eSOD and induction of the eGpX at the same time.

GpX is the main enzyme that deals with the H_2O_2 produced by SOD both in the cytosol and the mitochondria. The activities of the antioxidant enzymes must also be balanced . Too much SOD in relation to H_2O_2 metabolizing enzymes can damage the cells. H_2O_2, when it accumulates, inactivates SOD (21). SOD has also been shown to effectively reduce NO derived peroxynitrite formation thereby decreases cytotoxicity and LDL oxidation and prolongs the half life of NO (24,25) and as a result inhibit a number of events involved in atherogenesis. However experiments made by fat fed mice expressing human copper-zinc SOD do not support this antiatherogenic effect (26). eSOD activities expressed per g Hb are found to be similar or constant for a wide range of animal species whereas eGpX and catalase activities vary widely. However lack of standardization in the measurements of these enzymes poses a great problem in the comparison and interpretation of the results of different studies.

Although exercise programs may improve plasma lipids and lipoprotein patterns (27,28), many studies show that severe exercise increases levels of lipid peroxidation markers (29). It is now clear that exercise may initiate oxidative stress (30). Increase of pentane exhaled in humans after training also confirms this (23). Protection against oxidative damage could be achieved by careful endurance training. There are findings suggesting that a chronic exercise of aerobic type decreases susceptibility of the individual's LDL to undergo oxidation whereas exercise of shorter time span creates a more oxidative environment in the body (13). The remarkable decrease in eSOD and increase in eGpX in the B Group or only in the BII group when the participants were classified according to exercise hours are in partial agreement with other studies that found increases in both of the erythrocyte or organ specific antioxidant activities (31-33). Other studies found either no increase or CuZn SOD decreases (34,35). Trained young rats showed 62% and 27 % higher GpX and SOD activity in skeletal muscle compared to controls (36). In our exercising group, decrease in eSOD and increase in TBARS did not indicate favorable antioxidant status while increase in eGpX may counter balance the situation because the overall antioxidant capacity TAS had slightly but insignificantly increased. The heavy air pollution may have been even harder to cope with for the exercising group. Hb can stimulate lipid peroxidation while albumin and uric acid show protective effects (23, 36). Contribution of insignificant increases in albumin and uric acid and decrease in Hb and total bilirubin may also be important for the antioxidant status of the organism.

In our study group, exercise had no favorable effect on the blood lipids, however its beneficial effect was clearly observed in fibrinogen. The same result was also confirmed by Zmuda et al in men with initially low HDL-c (37). No increase in HDL-c was observed probably because exercise failed to alter the triglyceride metabolism. However studies showing the favorable effects of exercise along with diet in men and in postmenopausal women with low

levels of HDL-c and high levels of LDL-c are also present (38). Ferguson et al indicated that in healthy trained men, 1100 kcal of energy expenditure is necessary to elicit increased HDL concentrations (39). Regular exercise training lower resting and submaximal exercise heart rates, increase oxidative enzyme capacity, lower SBP, DBP, LDL-c, increase HDL-c, reduce body weight, improve mood and hence favorably modify risk factors. Epidemiological studies indicate that a sedentary lifestyle is associated with twice the risk of developing coronary artery disease. Many studies assess the cardiovascular benefits of physical exercise in men, women, elderly, children and youth (40). Preventions to reduce coronary heart disease generally address middle aged and elderly people, however considerations for the younger group would be much more beneficial. Daily physical exercise may be an important prevention for cardiovascular diseases in later life (41).

Although no favorable effects of exercise on HDL-c and other blood lipid levels were detected in young Turkish soldiers, beneficial effects were observed on fibrinogen levels while those on erythrocyte antioxidant enzymes were contradictory.

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