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Effects of Daily Exercise on Cholesterol and Hypertension in Diabetes and Non Diabetes Patients

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Abstract

The present study revealed that the relationship between HDL and CHD stresses the importance of finding ways to increase HDL. The majority of the exercise intervention studies that have been conducted in relation to lipoproteins have tried to uncover how exercise changes the blood lipid profile. The role of lipoproteins has been a major area of interest in relation to coronary heart disease (CHD) risk. It is evident that there exists a relationship between CHD risk and physical exercise. Possible alterations in lipoprotein fractionation due to exercise might be an important change that could explain the relationship between exercise and reduced CHD risk. High-density lipoprotein (HDL) is considered a major CHD risk factor and a low level of this lipoprotein is associated with increased CHD risk. Highly exercises exhibit higher levels of HDL cholesterol (HDL-C) than their low exercises therefore it is plausible to suggest that exercise induces these beneficial changes. Exercise training also improves cholesterol homeostasis. To examine this, we measured circulating levels of glucose, uric acid creatinine, AST, ALT ALP , whole blood CBC and lipids profile and hypertentiom systoloic blood pressure and diastolic blood pressure in 150 persons (average age 50 years; with at least one metabolic syndrome risk factor) before and after 6 months of exercise training. The blood glucose showed that high significant deccrease on blood glucose with increasing exercise. Also, there were significant decreases in blood elements (Na, K, Cl and Ca) in the population that increase exercise than other one. On the other hand there were a significant decrease on blood urea, creatinine and uricacid in the population that increase exercise than other one.The liver enzymes AST, ALT and ALP were a significant decrease in blood of human in the population that increase exercise than other one. Concerning lipid profile, we noted that variety induced low significant variation of different lipid parameters in the population that increase exercise than other one. Resuults generally showed that increase in exercise were always high significant decrease in their blood elements Na, K, Cl and Ca. Also, there is high significant decrease in liver functions and kidney functions in the population that increase exercise than other one and high significant variation of different lipid parameters in the population that increase exercise than other one.We suggest that ionic disturbance might be the missing link responsible for the frequent clinical coexistence of hypertension, atherosclerosis and metabolic disorders.

. These data indicate that exercise training reduces plasma cholesterol, glucose, uric acid creatinine, AST, ALT ALP and and hypertentiom systoloic blood pressure and diastolic blood pressure in patients with metabolic syndrome risk factors.

Key Words Exercise, Diabetes, Hypertention And Cholesterol Metabolism

Introduction

Human plasma contains small amounts of non- cholesterol sterols that provide information related to cholesterol homeostasis. For example, lathosterol, a precursor in the cholesterol synthetic pathway, is a marker for whole body cholesterol synthesis, while plant sterols, including campesterol and sitosterol, correlate with rates of cholesterol absorption (Miettinen et al. 1990). Furthermore, the ratio between campesterol and lathosterol is often used to indicate the ratio between cholesterol absorption and synthesis (Miettinen et al. 1990).

Individuals with type II diabetes, hyperlipidemia, and obesity have altered cholesterol homeostasis, indicated by low cholesterol absorption and/or elevated cholesterol synthesis (Chan et al. 2003, Gylling and Miettinen 1997, Miettinen et al. 2004, Simonen et al. 2000, Sutherland et al. 1992). Diet- induced weight loss improves many risk factors for the metabolic syndrome and was recently shown to increase cholesterol absorption in obese diabetics (Simonen et al. 2000). Furthermore, in this study the increase in cholesterol absorption was correlated with improvements in insulin resistance, leading to the suggestion that low cholesterol absorption should be considered a component of the metabolic syndrome (Simonen et al. 2000).

Endurance exercise training also improves traditional metabolic syndrome risk factors, but little is known about the effects of exercise training on cholesterol absorption or synthesis. Two recent studies by Varady et al. (2004, 2007) showed that 8 weeks of endurance exercise training had little mixed effects on markers of cholesterol absorption and synthesis. However, the relatively short exercise interventions used in these studies may have been insufficient to provide the metabolic adaptations necessary to promote significant changes in cholesterol homeostasis. The purpose of this study was to examine the effect of long-term endurance exercise training on cholesterol absorption and synthesis by measuring circulating plant sterol and lathosterol levels before and after a 6-month endurance exercise training intervention in individuals at risk for developing metabolic syndrome.

Materials and Methods

Blood samples were collected from 150 exercise persons that have Cholesterol, Hypertension and Diabetes and Non Diabetes. To show the effect of exercise on the persons that have Cholesterol, Hypertension and Diabetes and Non Diabetes. These samples were analyzed by using ICP emission instrument on Perkin Elmer ICP-400 at the University of Hail, KSA. Each hospital is represented by 50 blood samples for chemical and blood analysis with a total of 150 samples. Collect the blood samples to determine the Blood elements Na, K, Cl and Ca, liver functions and kidney functions in this population and different lipid parameters were measured. Blood sugar was measured in capillary blood samples with Lifescan One Touch II ® Glucometer, which has been tested for accuracy and precision against a Beckman Synchron CX7 analyzer of a laboratory that uses the glucose oxidase method.The assays of total cholesterol (TC), HDL-cholesterol, LDL cholesterol and triglycerides (TG) were performed by enzymatic colorimetric methods using kits marketed by Bio Systems, Spain. Reference values adopted are those given by the distributors of these kits. Liver functions and kidney functions in this population and different lipid parameters were measured were performed by enzymatic colorimetric methods using kits marketed by Bio Systems, Spain. Reference values adopted are those given by the distributors of these kits. The blood pressure measured by semi-automatic-blood-pressure- monitor-arm-67468-104993.

Statistical Analysis

Data were expressed as M ± SD. The SPSS program version 15 was used in analysis. One way analysis of Variance (ANOVA) followed by Duncan post hoc test and/or t-test were used in analysis. Pearson correlation Coefficient was used to study correlations. P-values less than 0.05 were significant.

Results

The present study showed that the effect of exercise on the persons that have Cholesterol, Hypertension and Diabetes and Non Diabetes on their blood glucose showed that high significant decrease on blood glucose with increasing exercise. Also, there were no significant decrease in blood elements (Na, K, Cl and Ca) in the population that increase in exercise than other one. On the other hand there was a significant decrease on blood pressure with increasing exercise as shown in Table 1. On the other hand there was no significant decrease in blood elements (Na, K, Cl and Ca) in the normal population before exercise than after exercise as shown table 1. Also, there was no significant decrease in blood glucose and blood pressure in the normal population before exercise than after exercise as shown table 1.

Table 1: Effect of exercise on the persons that have Cholesterol, Hypertension and Diabetes and Non Diabetes on the blood glucose and blood elements Na, K, Cl and Ca

Time	Normal before exercise	Normal after exercise	Patient before exercise	Patient after exercise
parameters	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE
Age	48 ± 2	48 ± 2	48 ± 2	48 ± 2
Hypertention	130 ± 0.23	125 ± 0.55	158 ± 0.22	130 ± 0.77
Glucose	6.0 ± 0.44	5.5 ± 0.33	7.63 ± 0.53	5.34 ± 0.55
Na	135.6 ± 0.54	133.6 ± 0.34	149 ± 0.1	125.1 ± 0. 11
K	3.35 ± 0.36	3.11 ± 0.16	5.52 ± 0.3	3.54 ± 0.43
Cl	73.62 ± 0.34	63.32 ± 0.44	114.6 ± 0.46	72.6 ± 0.23
Ca	1.41 ± 0.52	1.11 ± 0.12	2.86 ± 0.167	1.54 ± 0.31

Table 2 and table 3 showed that the urea, creatinine and uric acid in the population that decrease in exercise than other one. The liver enzymes AST, ALT and ALP were a significant decrease in blood of human in the population that increases in exercise than other one. Concerning lipid profile, we noted that variety induced high significant variation of different lipid parameters in the population that increase in exercise than other one. On the other hand there was no significant decrease in The liver enzymes AST, ALT and ALP in the normal population before exercise than after exercise as shown table 3. Also, there was no significant decrease in blood urea, creatinine and uric acid in the normal population before exercise than after exercise as shown table 2.

Table 2: Effect of exercise on the persons that have Cholesterol, Hypertension and Diabetes and Non Diabetes on the liver functions enzymes AST, ALT and ALP

Time	Normal before exercise	Normal afterb exercise	Patient before exercise	Patient afterb exercise
parameters	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE
Creatinine	48.5 ± 0.42	22.5 ± 0.12	63.02 ± 0.11	22.70 ± 0.469
Uric	205.1 ± 0.26	265.1 ± 0.56	410.6 ± 0.667	201 ± 0.05
Urea	1.8 ± 0.92	1.1 ± 0.92	3.75 ± 0.6667	1.61 ± 0.252

Table 3: Effect of exercise on the persons that have Cholesterol, Hypertension and Diabetes and Non Diabetes on the kidney functions enzymes Creatinine, Uric acid and Urea

Time	Normal before exercise	Normal after exercise	Patient before exercise	Patient after exercise
parameters	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE
AST	17.01 ± 0.01	11.02 ± 0.012	21.16 ± 0.37	11.22 ± 0.5
ALT	20.14 ± 0.21	12.24 ± 0.131	48.26 ± 0.17	14.13 ± 0.011
ALP	40.28 ± 0.11	30.22 ± 0.121	85.2 ± 0.57	33.8 ± 0.12

Results generally showed that increase in exercise were always high significant decrease in their blood Cholesterol. Also, there is high significant decrease in Triglyceride and Albumin in the population that decrease in exercise than other one. and high significant increase in HDL but high significant decrease in LDL in the population that increase in exercise than other one as shown in Table 4. On the other hand there was no significant decrease in the blood Cholesterol in the normal population before exercise than after exercise as shown table 4. Also, there was no significant decrease in Triglyceride and Albumin in the normal population before exercise than after exercise as shown table 4. There was no significant increase The blood HDL in the normal population before exercise than after exercise as shown table 4.

Table 4: Effect of exercise on the persons that have Cholesterol, Hypertension and Diabetes and Non Diabetes on the total protein, albumin, triglycerides, LDL, HDL and cholesterol

Time	Normal before exercise	Normal after exercise	Patient before exercise	Patient after exercise
parameters	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE
T protine	7.42 ± 0.12	6.55 ± 0.32	8.88 ± 0.55	6.3 ± 0.63
Albumin	3.90 ± 0.22	3. 2 ± 0. 5	4.6 ± 0.7	3.1 ± 0.9
Cholesterol	4.9 ± 0.5	3.4 ± 0.5	7.6 ± 0.37	3.51 ± 0.11
Triglyceride	1. 2 ± 0. 1	1.1 ± 0. 1	2. 1 ± 0.22	1.1 ± 0.11
LDL	1.91± 0.15	1. 4 ± 0.45	3.1 ± 0.4	1.2 ± 0.36
HDL	1. 6 ± 0.01	1.9 ± 0.2	0.55 ± 0.5	1.93 ± 0.52

Data presented in table 5 are means ± S.E.M. *$p<0.05$ compared to baseline. Baseline and final testing are shown in Table 5. There was a modest (1.2 kg) reduction in total body weight ($p<0.001$). There was a small (1.3 %) increase in lean body mass (LBM) ($p=0.005$), and % body fat and intra-abdominal fat mass were reduced by 4 % ($p<0.001$) and 7 % ($p=0.002$), respectively. However, there was no significant change in subcutaneous fat mass ($p=0.10$). Plasma lipids improved in response to the exercise intervention, as TG, TC and LDL-C were each significantly reduced, while HDL-C increased after the intervention ($p < 0.05$ for each). In addition, fasting plasma insulin levels were reduced by 14 %, though plasma glucose levels paradoxically increased by ~ 10 % ($p<0.05$ for each).

Table 5: Effect of exercise on the persons that have Cholesterol, Hypertension and Diabetes and Non Diabetes on baseline and final testing.

Measure	Baseline	Final
Body weight (kg)	100.6±2	85.5±2.0
Body fat (%)	34.4±2.2	31.1±2.1
IA fat (cm2)	132±2.4	124±5.5
SC fat (cm2)	300±9.6	275±11.1
LBM (kg)	45.5±2.5	47.5±2.5
Systolic BP (mm Hg)	141.1±1.2	130.0±1.0
Diastolic BP (mm Hg)	90.1±2.3	80.8±2.4
Fasting glucose (mmol/l)	5.01±0.1	5.1±0.2
Fasting insulin (pmol/l)	70.1±2.4	60.2±4.2
Triglycerides (mmol/l)	1.6±0.5	1.3±0.2
Total cholesterol (mmol/l)	6. 6±0.3	4.50±0.3
HDL-C (mmol/l)	1.2±0.1	1.5±0.2
LDL-C mmol/l)	3.1±0.1	2.2±0.1

Discussion

This study include 6 months of exercise training increased plasma levels of cholesterol absorption (Miettinen et al. 1990). Thus these data suggests that exercise training increases cholesterol absorption and the ratio of cholesterol absorption to synthesis, whereas there was no significant change in cholesterol synthesis with training. Despite the increase in markers of cholesterol absorption, the plasma lipoprotein profile improved, as total and LDL-C levels were reduced, and HDL-C levels increased. This study to demonstrate that long-term exercise training is associated with changes in these markers of cholesterol metabolism. Recently, Varady et al. (2004) showed that a shorter 8-week endurance exercise program increased plasma lathosterol, but not plant sterol levels, and a follow-up study by the same group found that same 8 weeks of endurance exercise training had no effect on either cholesterol absorption or synthesis measured by the single stable isotope tracer method (Varady et al. 2007). There were several differences between our study and the studies by Varady et al. that may account for these discrepant findings. First, the length of the exercise intervention was significantly shorter in the studies by Varady et al. (8 weeks) compared to our study (24 weeks). It is possible that the adaptations that promote significant changes in cholesterol metabolism may not manifest themselves until after several months of exercise training. A second primary difference between these studies was the dietary control. In our study, all subjects were stabilized on an AHA step I diet prior to beginning the exercise intervention, while in the studies by Varady et al. subjects were only asked to maintain their current dietary regimens. It is possible that significant diet variations between subjects may have masked the effects of the exercise intervention on plant sterol levels or cholesterol absorption in their studies.Another significant finding in our study was the correlations between plasma markers of cholesterol absorption with factors associated with the metabolic syndrome. At baseline, there was an inverse correlation between exercise and fasting plasma insulin levels, and a trend for a correlation between these variables at final testing ($p = 0.08$). Furthermore, we found an inverse correlation between exercise and TG levels at baseline, and an inverse correlation between % body fat and after the exercise training intervention. This is similar to the data of Simonen et al. (2000) who found a positive correlation between plant sterol levels and serum sex hormone binding globulin (SBHG), a marker of insulin sensitivity (Haffner 1996), and an inverse correlation between campesterol and TG levels after diet-induced weight loss. Several other studies have also noted inverse correlations between markers of cholesterol absorption and various metabolic syndrome risk factors (Elsayed shokr et al. 2016 & 2017; Gylling et al. 2004, Pihlajamaki et al. 2004), leading to speculation that low cholesterol absorption may be a component of the metabolic syndrome (Simonen et al. 2000). We believe our data provide additional support for this hypothesis. Simonen et al. (2000) also found that the diet- induced change in plant sterols was inversely correlated to the change in body weight. This correlation was independent of changes in other metabolic syndrome risk factors in a multiple regression analysis (Table 5). Many of the beneficial effects of exercise on risk factors for chronic disease are often attributed to weight loss induced by the increase in physical activity. Our data

indicate that both weight loss and increases in cardiorespiratory fitness may have independent effects on cholesterol absorption. The mechanisms responsible for the changes in markers of cholesterol absorption found in this study are uncertain. Elsayed shokr et al. 2016 & 2017; Simonen et al. (2000) hypothesized that increasing insulin resistance and obesity may change the intestinal cholesterol pool or the absorption mechanism of the intestinal mucosa. Thus the exercise could exert its effects on intestinal cholesterol absorption by improving insulin sensitivity. However, while insulin sensitivity was not measured in this study, we did not find a correlation between changes in plasma sterol levels and fasting insulin or glucose levels. Another possibility is that changes in cholesterol metabolism could be due to alterations in the expression of genes involved in intestinal cholesterol transport. Cholesterol absorption is regulated by multiple genes expressed by enterocytes, including Niemann-Pick C1- like1 (NPC1L1), which induces the influx of dietary cholesterol and plant sterols from the intestinal lumen into the enterocyte (Davis et al. 2004; Elsayed shokr et al. 2016;), and the ATP binding cassette transporters (ABC) G5 and G8, which limit sterol absorption by selectively pumping them back into the intestinal lumen (Yu et al. 2004). Several studies have shown that genetic polymorphisms in the ABCG5, ABCG8, and NPC1L1 genes affect cholesterol absorption in humans (Cohen et al. 2006, Elsayed shokr et al. 2016 & 2017; Gylling et al. 2004), and the variable expression of these genes may explain the differences in rates of cholesterol absorption between inbred strains of mice (Duan et al. 2004, 2006). Consequently, one way in which exercise may affect cholesterol absorption is by altering directly the intestinal expression of the ABCG5, ABCG8 or NPC-1L1 genes. In mice, we have shown that 3 months of endurance exercise training (treadmill running) reduced the expression of ABCG5, ABCG8, and NPC1L1 by ~60 % (Wilund et al. 2008). However, we are uncertain if exercise training modifies the expression of these genes in a similar manner in humans. A positive correlation between cholesterol absorption and LDL-C levels has been seen in population studies (Kesaniemi and Miettinen 1987), suggesting that reducing cholesterol absorption may have therapeutic benefits. Furthermore, ezetemibe, bile acid sequestrants and dietary plant sterol intake are commonly used as therapies for reducing cholesterol absorption and lowering LDL-C levels. However, Simonen et al. (2000) showed that diet-induced weight loss increases cholesterol absorption, without increasing LDL-C levels, and our data presented here indicate that exercise training with modest weight loss also increases markers of cholesterol absorption, while decreasing LDL-C levels. This apparent paradox may be explained by data from earlier animal studies showing that endurance exercise training may increase the catabolism of cholesterol into bile acids (Elsayed shokr et al. 2016 & 2017; Hebbelinck and Casier 1966, Malinow et al. 1968) and the excretion of cholesterol and bile acids in the feces (Fukuda et al. 1979, Ostlund and Reaban 1989). As a result, increases in cholesterol absorption may be offset by increased catabolism and excretion of cholesterol, resulting in no change or the modest reductions in LDL-C seen in many exercise training studies. There are several limitations to this study. The first is the absence of a non-exercising control group. The subjects analyzed here were part of a larger trial in which subjects with polymorphic variations at specific gene loci served as the comparison groups, so a sedentary control group was not included. Second, we did not measure plasma variables prior to beginning the 6-week dietary stabilization period, so we cannot exclude the possibility that the changes in plasma sterols were influenced by the change in diet prior to beginning the exercise intervention. However, we believe that the 6-week lead-in-period for the dietary changes makes this unlikely. Future studies using randomized controlled trial designs should be conducted to confirm the results presented here. A third limitation of this study was that we estimated cholesterol absorption and synthesis using plasma markers

In conclusion, we found that exercise training increased markers of cholesterol absorption, but did not affect markers of cholesterol synthesis, in elderly individuals with at least one metabolic syndrome risk factor. Despite this, the lipoprotein-lipid profile was improved, as there was a reduction in TG, TC, and LDL- C, and an increase in HDL-C following the intervention. This exercise-induced increase in cholesterol absorption may indicate a correction in cholesterol metabolism in this population and highlights the complex relationship between chronic physical activity and cholesterol homeostasis.

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