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RESEARCH ARTICLE

EFFECTS OF EXERCISE ON HOMOCYSTEINE LEVELS IN PATIENTS WITH OBESITY

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ABSTRACT

Background: Obesity is a chronic metabolic disease associated with cardiovascular and atherosclerotic changes. It is also a public health problem due to its related complications. High homocysteine levels are important markers for the development of atherothrombosis and atherosclerotic changes. Obesity with high homocysteine levels influences metabolic risk and makes individuals prone to comorbidities. In this study, we aimed to evaluate the effect of exercise on homocysteine levels in patients with obesity.

Methods: A total of 40 patients with obesity were included in this study; weights and heights were measured, and body mass indexes (BMIs) were calculated. A standard exercise program, which lasted 4 months, was applied to all patients. All of the patients walked regularly for 20 minutes before breakfast, and for 30 minutes two hours after dinner. The homocysteine levels at the baseline were compared with the values after 4 months.

Results: There were significant differences in the body weight, serum lipids and insulin levels ($p<0.05$) in these patients. The mean homocysteine level was 10.5±4.3 at the baseline, while it was 9.1±3.1 at the 4th month. Although there was a decrease in the homocysteine level, it did not reach statistical significance ($p>0.05$).

Conclusion: Obesity and high homocysteine levels are significant risk factors for cardiovascular disease. However, regular exercise can decrease body weight and homocysteine levels in patients with obesity.

INTRODUCTION

The prevalence of obesity is increasing rapidly throughout the world. It is generally caused by high caloric intake, lack of exercise, genetic susceptibility or psychiatric illness. According to the World Health Organization (WHO) report, there are 400 million obese and 1.6 billion overweight individuals around the world. Obesity has become a major public health problem due to its related complications, and it is strongly predictive of diabetes mellitus, hypertension, cardiovascular disease and other chronic medical conditions. The economic burden of obesity on individuals and societies is expensive due to the high direct and indirect medical costs of this disease (1-3). Homocysteine is a sulphur-containing amino acid which forms during the metabolism of methionine, and levels of homocysteine vary according to the population, but are generally high in males and in old age. Elevated serum levels of total homocysteine are toxic to the vascular endothelium, causing endothelial dysfunction, and contribute to the development of atherosclerosis (4,5). Additionally, homocysteine has been found to be significantly correlated with body mass index (BMI) and insulin resistance (IR), which are strongly associated with metabolic syndrome and obesity (6,7,8). Exercise is an important component to the overall approach of treating obesity. It can positively impact cardiovascular disease related risk factors, such as high blood pressure, as well as emerging disease risk factors, such as glycosylated haemoglobin, elevated homocysteine levels, insulin resistance and systemic oxidative stress (9,10). Homocysteine is disturbed in obesity because of a combination of dietary factors, lack of regular exercise, hypertrophic adipose tissue, low-grade inflammation, insulin resistance and other parameters under investigation. For the reduction of homocysteine, weight loss is probably necessary. It has been shown that certain well-balanced diets and regular exercise are important components of the overall approach to treating obesity. In this study, we aimed to evaluate the effects of exercise on homocysteine levels in patients with obesity.

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MATERIALS AND METHODS

This prospective observational study was carried out in the endocrinology clinics of a tertiary hospital in Turkey, from January of 2005 until June of 2005. The institutional review board of the hospital approved this experiment, and informed consent was obtained from all subjects. All procedures were followed in accordance with the Good Clinical Practice standards and ethical standards of the Responsible Committee on Human Experimentation, and with the Helsinki Declaration.

A total of 40 patients with obesity from both genders were included in this study. All subjects underwent a full medical history and complete physical examination. Patients with a diagnosis of diabetes, dyslipidaemia, coronary artery disease, renal failure, malignancies, vitamin B12 and/or folate deficiency, or other disease that could alter homocysteine levels, were excluded from this study. Breastfeeding and pregnant women, and smokers, were also excluded. All of the patients' weights and heights were measured, and body mass indexes (BMIs) were calculated. Obesity was defined as a BMI (weight in kg/height in m^2) of 30 or higher. All patients were recommended to consume 30 kcal/kg healthy diets each day for four months; a list of healthy foods was prepared and given to all of the patients. For this study, a healthy diet was characterized by a higher intake of fruit, vegetables, fish, whole grains and legumes. The subjects consumed these diets without any food or vitamin supplementation. All subjects walked regularly for twenty minutes in the morning, before breakfast, and for thirty minutes two hours after dinner. This exercise program lasted for 4 months.

A venous blood sample was collected in the morning after overnight fasting at the baseline and after 4 months. The measurements taken included: homocysteine, blood glucose, insulin, serum lipid concentrations, creatinine, vitamin B12 and folate levels. The serum homocysteine levels were determined by fluorescence polarization immunoassays (Siemens AG, Erlangen, Germany) (reference value of homocysteine is 5-15 µmol/L). The blood glucose, serum lipid concentrations and creatinine were analysed using a Hitachi 747 autoanalyzer, and the insulin levels were measured using an Abbott Architect I 2000 SR analyser system (Illinois, USA). The vitamin B12 and folate levels were measured with the Roche C-601 (Japan) analyser system using an electrochemiluminescence immunoassay. The smoking status of the subjects was also recorded.

The Statistical Package for the Social Sciences (SPSS) 11.0 was used for the statistical analyses. The variables were investigated using the Kolmogorov-Smirnov test to determine whether or not they were normally distributed. Descriptive analyses were presented using means and standard deviations, and the paired Student's t-test was used to compare the normally distributed measurements at two time points (baseline and 4 months). As a non-parametric test, the Wilcoxon test was conducted to compare the non-normally distributed parameters between the baseline and 4 months. The probability of making a type I error (alpha, significance) was 0.05 in all tests.

RESULTS

The mean age was 45.0±3.4 years old, and the female to male ratio was 24:16 (60% vs. 40%) (Table 1). The mean body weight and BMI were 94.1±4.9 kg and 34.2±1.8 kg/m², respectively, at the baseline. The mean body weight and BMI were 87.7±3.8 kg and 31.9±1.4 kg/m², respectively, after four months (Table 2). There were statistically significant differences between the measurements at the baseline and at the 4th month ($p<0.01$). Table 3 shows the measurements of the patients. The mean homocysteine level was 10.5±4.3 at the baseline; however, it was 9.1±3.1 at the 4th month. Therefore, there was a statistically non-significant decrease in the level of homocysteine. The serum total cholesterol, LDL, triglyceride and insulin levels decreased; however, the HDL and folic acid levels increased after 4 months. The differences were statistically significant ($p<0.05$).

Table 1. Age, height and weight of the patients according to the gender

	Male N=16 (40%)	Female N=24 (60%)	Total N=40 (100%)
Age(year)	46.7±3.5	43.2±2.2	45.02±3.4
Height (cm)	170.9±6.8	161.3±5.7	166.5±7.7
Weight (kg)	100.4±5.1	88.6±4.1	94.1±4.9

Table 2. Weight, BMI, and waist circumference at the baseline and at 4th month

	At baseline	After 4 months	p
Weight(kg)	94.1±4.9 (75-120)	87.7±3.8 (72-114)	<0.01
BMI (kg/m²)	34.2±1.8 (31.25-39.52)	31.9±1.4 (30.1-38.11)	<0.01
Waist (cm)	108.6±7.3 (96-124)	104.5±6.9 (90-120)	>0.05

Table 3. Biochemical and clinical measurements of the patients

	At baseline	After 4 months	p
Homocysteine(µmol/L)	10.56±4.31	9.15±3.11	>0.05
Total cholesterol (mg/dL)	223±32.82	209±26.82	<0.01
HDL cholesterol (mg/dL)	43±11.36	48±10.52	<0.05
LDL cholesterol (mg/dL)	145±26.69	133±22.53	<0.05
Triglyceride (mg/dL)	175±51.1	140±40.0	<0.01
Glucose (mg/dL)	79±8.8	72±7.3	>0.05
Insulin (µU/mL)	17.96±3.87	13.56±3.51	<0.01
Systolic blood pressure (mmHg)	115.9±11.8	112.2±10.5	>0.05
Diastolic blood pressure (mmHg)	75.3±5.8	73.1±4.9	>0.05
Vitamin B12 (pg/mL)	445±112.34	471±123.56	>0.05
Folic acid (ng/mL)	10.3±2.3	13.2±3.98	<0.05

DISCUSSION

In this study, we have shown that regular exercise has beneficial effects on obese patients, and we found that regular exercise results in a decrease in body weight. Additionally, it also decreases the serum cholesterol, insulin and homocysteine levels. Obesity behaves as an independent and strong risk factor for cardiovascular disease. Apart from classical risk factors like insulin resistance, dyslipidaemia and hypertension, certain non-conventional risk factors, like high homocysteine, may enhance the risk of atherosclerosis and cardiovascular diseases in obese patients (11). Sanlier et al. found increased body weight to be associated with hyperhomocysteinaemia in their study (12). Furthermore, some previous studies have shown the association between increased concentrations of plasma homocysteine and premature coronary atherosclerosis, as well as carotid atherosclerosis (13,14). Homocysteine damages the inner linings of the arteries and promotes thrombosis through pathological collagen activation of the intrinsic pathway (15), impairment of thrombolysis, increased production of hydrogen peroxide, endothelial dysfunction, and increased oxidation of low-density lipoproteins (16). Boushey ***et al.*** estimated that 10% of the risk of coronary artery disease in the general population is attributable to homocysteine. They

reported that an increase of 5 µmol/litre of the plasma homocysteine concentration raises the risk of cardiovascular disease by 60% in men and 80% in women (17). In the current study, the type of exercise selected was regular walking, a cheap and socially acceptable form of activity that can be conducted frequently, without requiring special equipment or facilities. It carries a low risk of injury and has known health benefits (18). Regular exercise lowers homocysteine levels in obese persons by as much as 26% over the course of a 6-month brisk walking program (three to five times per week) (19). Smaller but significant reductions (6% to 8%) have been reported in healthy older adults after either a low or high-intensity 24-week resistance training program. They also reported that regular exercise has beneficial effects on serum lipids, and indirect effects on blood pressure and vascular endothelium (17). In this study, we have shown that regular exercise significantly lowers body weight, serum total cholesterol levels, triglycerides and insulin levels.

We also reported a slight decrease in homocysteine levels, which did not reach statistical significance. The level of folic acid decreased at 4th month in this study. This result can be associated with healthy foods. The subjects consumed healthy diets which were characterized by a higher intake of fruit, vegetables, fish, whole grains and legumes. These foods are rich in folate. Our study has some limitations. First, it would have been beneficial if the sample size had been larger. Second, the effects of exercise on homocysteine levels in healthy subjects were not investigated. Finally, the duration of the study could have been longer than four months. In conclusion, obesity and high homocysteine levels are significant cardiovascular disease risk factors. Regular exercise lowers the body weight, serum lipid, insulin and homocysteine levels. Therefore, obese individuals should engage in regular exercise to decrease cardiovascular risks.

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