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Evaluation of the Effect of Doing Eight Weeks of Aerobic Exercise Along with Vitamin Supplementation on Homocysteine and Insulin Levels of Obese Boys

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Abstract: *The purpose of the study: The objective of this research was to evaluate the effect of doing aerobic exercise along with vitamin C supplementation on Homocysteine and insulin levels of obese boys. Methodology: The method of current research was quasi-experimental. In this research, the researcher evaluated the relationship between variables which have not been manipulated by the researcher rather have occurred in the past which means that although they have happened in the past, they were under investigation in the current study. Quasi-experimental research is a systematic experimental study in which the researcher does not have direct control over the independent variables, since they have already occurred and have been studied. In this research, 40 obese boys aged 10 to 15 years old with a percentile of body mass index of 95% were selected and randomly assigned into control, exercise and vitamin C groups. The exercise group included performing the exercises at 50-70% of maximal heart rate for 3 sessions per week during 8 weeks. Data of the study were analyzed using ANOVA and t test. Results: The results showed that aerobic exercise along with vitamin C supplementation significantly decreased glucose, insulin and Homocysteine in obese boys ($p < 0.05$). Conclusion: Aerobic exercise and taking vitamin C might lead to negative adjustment of Homocysteine and insulin resistance in obese boys. Moreover, the combination of aerobic exercise and vitamin C supplementation is associated with the improvement of these effects.*

Keywords: *Aerobic Exercises, Homocysteine, Insulin, Vitamin*

INTRODUCTION

Obesity is one of the important factors in the development of insulin resistance (Habibian, Farzanegi and Asadi, 2017). Weight gain is one of the most important factors which can increase the risk of insulin resistance in individuals. Moreover, those who smoke regularly, do not exercise adequately, or have high blood pressure are at risk of obesity more than others. In addition, some cardiovascular problems are considered as risk factors for this disease. For example, insulin resistance is seen more than others in people with good blood cholesterol or low HDL or high blood glucose (triglycerides), history of myocardial infarction, or vascular problems in neck and leg. This complication can be problematic (Abacci et al., 2012).

The dysfunction of fat cells in lipid metabolism causes an increase in free fatty acids and, thus, it leads to the onset of inflammatory signalling cascade reactions in a number of filterable cells. This pathological state is exacerbated by creating a feedback loop through the secretion of the pre-inflammatory cytokines which is

caused by increased immune cell filtration as well as the interruption of insulin signalling cascades. This leads to an increase in insulin resistance following defect in glucose homeostasis in the skeletal and liver muscles, and finally, it leads to the development of Type 2 diabetes (Gallistl Sudi et al., 2000).

In addition, a significant relationship has been reported between total Homocysteine and body mass index and insulin resistance. As stated above, insulin resistance is directly associated with overweight and obesity and it is strongly dependent on our diet. Thus, we should reduce the use of sweets, chocolates, refined sugars and animal fats and increase the use of fruits, vegetables and non-refined grains (Kurto et al., 2010). In addition to regulating blood glucose, it can be useful in weight loss. One of the most popular diets recommended for insulin-resistant people is DASH (Dietary Approaches to Stop Hypertension) which is usually prescribed for people with cardiovascular disease and hypertension.

Reduction in sodium intake and an increase in daily intake of potassium, magnesium and calcium are the bases of the DASH diet. Hyper insulin is also involved in the increased level of Homocysteine , so that increased Homocysteine level, even in thin people, have been associated with insulin resistance (Feillet-Coudray et al., 1999). Homocysteine is an unnecessary amino acid produced in the liver through the metabolism of the essential amino acid of methionine. It is considered a risk factor for the development of cardiovascular disease. Homocysteine can damage vascular endothelial cells through producing inflammatory cytokines, increasing oxidative stress caused by free radical and reducing vascular expansion. In previous studies, higher levels of Homocysteine in obese children compared to children with normal BMI were reported (Bell et al., 2007; Diabetes Control and Complication Trial Research Group, 1993; Feillet-Coudray et al., 1999). Moreover, a significant relationship has been proven between total Homocysteine level and fasting glucose and insulin resistance (Giltay et al., 1998), and body mass index (Gallistl Sudi et al., 2000). Therefore, obesity and insulin resistance which were considered as a problem for older ages, is becoming a serious problem for children these days (King et al., 1996).

Change in the life style is the most important medical treatment to relieve insulin resistance. The drug should be also prescribed by physicians to improve the use of cells from insulin. Metformin is the most commonly prescribed drug to reduce the risk of diabetes and weight loss in obese people. Reducing the type 2 diabetes in women with a history of gestational diabetes is one of the benefits of metformin (UK Prospective Diabetes Study Group, 1998). Nowadays, the use of life style interventions such as diet, exercise and educational programs are recommended to reduce obesity and prevent its caused diseases (Kurtoglu et al., 2010; Habibian, Farzanegi and Asadi, 2017). However, improved insulin sensitivity, reduced insulin resistance, or reduced visceral fat accumulation as well as exercise have been reported for children and adolescents (Perez-de-Arce, Foncea and Leighton, 2005). However, ineffectiveness of exercise on insulin sensitivity in obese or overweight children was also observed by other researchers (Savini et al., 2013; De Silva Ade, da Mota, 2014).

Moreover, owing to confounding factors and potential effects such as age and maturity of subjects, duration, intensity and type of exercise, and diet control before and after blood tests, the role of exercise on Homocysteine levels and insulin resistance in obese children has not been well recognized (Habibian, Farzanegi and Asadi, 2017; Soori et al., 2016; Van der Heijden et al., 2010). Some dietary supplements can cope with some of the high blood glucose losses, and some others can have a supportive role in controlling blood glucose. Owing to disease or malnourished nutritional habits, diabetic people might suffer from the deficiency of vitamins and minerals (Watts et al., 2004; Zhu et al., 2006). Vitamin C is one of the essential vitamins which should be used with caution in diabetics. The level of this vitamin required daily by the body is about 90 mg. People using high doses of vitamin C might be at increased risk for vascular complications, which means that this drug should be used with caution. Homocysteine is a substance produced by the body. Homocysteine is a metabolite to produce other substances. This substance should not remain in blood more than few seconds and should not be seen in the blood and urine. Observing metabolite in the urine and blood is a warning sign. Homocysteine has been widely recognized as a classic risk factor for cardiovascular diseases and myocardial infarctions and strokes (Welch and Loscalzo, 1998).

Homocysteine is a sulfur-containing metabolite produced from methionine amino acid. As stated above, it should not be observed in the blood (a waste substance). Homocysteine is the only intermediate substance in the production of cysteine and turin from methionine. While Homocysteine is a harmful substance, it produces an important substance called L-carnitine, in addition to producing two cysteine and turin substances mentioned above. In other words, L-carnitine is produced from methionine in the presence of different vitamins (Yilmaz et al., 2008). Previous studies have confirmed a negative correlation between the levels of Homocysteine and vitamin C in the blood (Soori et al., 2016) .They have also reported a reduction of insulin and fasting glucose levels after 6 weeks of daily intake of vitamin C in patients with type 2 diabetes (Kovács et al., 2009). Although many studies have been conducted on the effects of different types of exercises on insulin resistance (Kandil et al., 2010) and Homocysteine levels (McArdle et al., 2013) on obese subjects, no study was found to evaluate the effects of taking this vitamin or its interactions with aerobic exercises on the levels of Homocysteine, insulin, and fasting glucose on obese children. Given the studies conducted, the present research was conducted to evaluate the effect of aerobic exercise and taking vitamin C on the level of Homocysteine and insulin of obese boys.

Methodology

The current research was a quasi-experimental study conducted by using a pre-test and post-test design with control group. Although many of the natural and social situations cannot be completely controlled, the researcher used a research method similar to the real experimental research method to study the situation. In other words, there are some situations, in which the researcher cannot study the characteristics of real experimental research, such as "What factors are influenced, when they are influenced, and to what extent they are influenced". The term "quasi-experimental" was first introduced to educational and behavioral sciences for the first time by Compel in 1957.

The strongest motivation to invent this experimental method might be the "inappropriateness" of the real experimental research method to study the human beings in natural situations, since, as stated before, if the experimental and studied situation is fully controlled and the subject is human, he or she would rarely show the real behavior. The subjects of this research included inactive male obese students with the age range of 10 to 15 years in Tehran. They were selected based on the derived information from health questionnaire, which was used to obtain information about their age, history of diseases, used drugs and their history of exercising. They were selected using convenient sampling method after physician`s examining of their height and weight, body fat percentage and maximal oxygen consumption.

In the next step, the subjects were randomly assigned to two control, exercise and vitamin C groups. They were included into the research after providing explanations on the way of conducting the research. The all filled the content form to be included in the study.

The obesity criterion for the subjects of this study was a percentile equal to 95 percent (body mass index for age and sex) or more than it which was equivalent to the obesity of adolescents (Habibian, Farzanegi and Asadi, 2017). The body fat percentage was determined using caliper and the measurement of three-head and leg skinfold and the two-point formula. The maximum oxygen consumption (VO2max) was determined using the submaximal shuttle run test. All measurements were performed in the morning .The exercise program for exercise and vitamin C groups included 8 weeks of increasing submaximal exercise with an intensity of 50% to 70% of maximal heart rate, 45 minutes of main exercise per session, for 3 sessions per week. Each exercise session included 10 minutes of warm-up, main exercises and 10 minutes of cooling down. The main exercise was performed for 30 minutes with the intensity of 50% -55% of maximal heart rate in the first and second weeks. Through the increase of 5% and the intensity of 2 minutes every two weeks, it reached to the intensity of 65 % 70% maximal heart rate for 45 minutes at the end of the eighth week (Habibian, Farzanegi and Asadi, 2017).

The subjects of the combined and supplement group received a 500-mg vitamin C tablet after meals along with a glass of water (once per two days) for 8 weeks. Two days after the last exercise session and after 12-days of fasting period, the blood samples of subjects were collected in two stages of pre-test and post-test. The blood samples were collected from their left ventricle vein after 15 minutes of resting at 8-10 am (5 cc). Then they were centrifuged at 3000 rpm/ min at 4 ° C for 15 minutes. Later on, the resulting serum was frozen at -80 ° C. Homocysteine levels were measured using the kit (manufactured by Belgium country) and based on the manufacturer's guidelines.

The fasting glucose levels were measured by the enzyme colorimetric method and glucose oxidase technology through using the Pars Azmoon kit and Selectra-E biochemical auto-analyzer. Insulin levels were measured using Sandwich ELISA method and a human kit (Mercodia Insulin ELISA) manufactured by Sweden. Homeostatic assessment (HOMA-IR) model was used to calculate the index of insulin resistance. In this method, the insulin concentration and fasting glucose were measured and the insulin resistance was calculated by dividing the multiplication of fasting insulin (micro unit / ml) to fasting glucose concentration (mmol / L) by the constant number of 22.5 (Habibian, Farzanegi and Asadi, 2017). To examine the intergroup and intragroup variations, T-test and ANOVA along with Tukey's post hoc test were used at the significance level of $P < 0.05$. All statistical analyses were performed using SPSS, 18 version, software.

Results

Results of ANOVA test indicated no significant difference in the anthropometric characteristics of the subjects and the levels of Homocysteine, glucose, insulin and insulin resistance in the pre-test stage ($P = 0.997$, $P = 0.980$, and $P=0.976$), respectively. The results of intragroup variations revealed that after 8 weeks of exercise and taking vitamin C significantly reduced the levels of Homocysteine, glucose, insulin and insulin resistance in obese boys. Moreover, a significant difference was found in the means of Homocysteine, insulin and insulin resistance in study groups after 8 weeks.

The findings of the Tukey's test revealed that the means of Homocysteine, insulin resistance and insulin resistance in the subjects of aerobic exercise group ($P = 0.013$, $P = 0.009$, $P = 0.101$, respectively) and vitamin C group ($P = 0.16$, $P = 0.011$, and $P = 0.098$, respectively) were lower than those in control group.

Table 1: Mean and standard deviation of body composition indices of the subjects

Variable	Control	exercise	Supplement	F value
Height	143.4±61.85	136.10±71.98	126.5±00.73	0.890
Age	10.0±00.81	10.1±00.05	10.1±28.76	1.124
Weight before 8 weeks (kg)	51.4±85.30	47.9±00.15	55.03±14.49	0.745
Fat percentage	39.1±13.97	42.6±32.02	44.3±41.87	2.302
Maximal oxygen consumption	36.01±74.59	35.1±59.92	45.2±68.21	0.875

Table 2: Intergroup and intragroup variations in research variables

control	groups	Pre-test	posttest	% Percentage of variations
Homocysteine	control	9.2±87.05	11.2±6.39	1.2±2.71
	exercise	9.2±74.11	8.2±6.69	-28.2±68.$_{79}$
	Vitamin c	9.2±80.29	9.2±9.47	-19.2±33.22
Fasting glucose	control	90.12±63.41	89.18±17.06	-1.0±80.75
	exercise	90.11±16.21	65.60±56.21	-4.1±79.90
	Vitamin c	88.10±45.45	99.12±84.45	-3.0±59.41
insulin	control	10.34±70.03	11.23±1.01	0.80±4.48
	exercise	10.73±3.48	6.32±1.79	-29.71±3.90

	Vitamin c	10.2±67.54	8.85±1.64	-43.91±1..58
Insulin resistance	control	2.38±1.10	3.92±1.89	-2.82±6.16
	exercise	2.45±10.86	2.86±1.05	-37.15±5.96
	Vitamin c	2.0±47.85	1.78±1.73	-31.71±4.22

Discussion and Conclusion

The results of this research showed that aerobic exercise along with vitamin C was effective in preventing the complications of obesity in obese boys. Given the normal levels of Homocysteine and insulin resistance greater than 2.5 micro unit / ml for adolescents as insulin resistance status (Habibian, Farzanegi and Asadi, 2017), it seems that obese boys were at increased risk for insulin resistance. This status was improved with aerobic exercise interventions and taking vitamin C. In line with the results of this study, increased insulin resistance (Van der Heijden et al., 2010; Perez-de-Arce K, Foncea R, Leighton, 2005) and Homocysteine (Kovács et al., 2009) was reported in obese children by other researchers. Watz et al reported the lack of change in Homocysteine levels after 8 weeks of circular exercises, including exercising on fixed bike (with an intensity of 65-85% maximal heart rate) along with resistance exercise (with an intensity of 55-70% maximal heart rate) on obese adolescents.

In addition, Subasi et al examined the effect of two types of three-month submaximal aerobic exercise program (with an intensity of 55-75% of heart rate) or resistance exercise (with an intensity of 70% of one maximal repetition) on the plasma levels of Homocysteine in non-exercised young people. However, they did not observe significant changes due to the normalization of folic acid levels in these people. Thus, the possible cause of the inconsistencies of these results with those of this study may be related to the type of exercise, age range, intensity and duration of exercise, and the level of folic acid and vitamins B6 and B12 (Habibian, Farzanegi and Asadi, 2017). Homocysteine and insulin resistance are among the most important cardiovascular risk factors. Homocysteine levels can be reduced by insulin and it can be increased due to insulin resistance conditions. Exercise and physical activity can contribute to the elimination of insulin resistance.

There are conflicting results about the effects of exercise and proper diet on controlling cardiovascular risk factors, metabolic disorders; increased prevalence of impaired glucose tolerance, diabetes and blood fat disorders and the positive effects of regular exercise programs on improving and regulating endocrine status (King et al., 1996). Although the precise mechanisms for reducing Homocysteine following exercises have not been recognized well, one of the possible pathways for reducing Homocysteine in the present research might be to reduce the insulin, glucose and insulin resistance, as well as weight loss following exercise interventions (unreported) or taking vitamins C. Hyper Homocysteineemia through the induction of insulin can result in compensatory hyperinsulinemia (Habibian, Farzanegi and Asadi, 2017). Insulin might also lead to Homocysteine accumulation in the blood by a damage to the activity of the methylene teratophyllature reductase enzyme. In addition, insulin acts as a modifying agent for Homocysteine owing to its inhibitory effect on the activity of the liver cystatin beta synthase enzyme (Kurto et al., 2010).

In fact, the aerobic program stimulates the liver glutathione synthesis, leading to a reduction in Homocysteine (Kandil et al., 2010). In a research conducted by Bruham et al. (2016), the effects of exercise using climbing stairs test with moderate intensity on Homocysteine of inactive young women showed that these exercises could cause desirable changes in cardiovascular disease risk factors and blood fat profiles of them. The results revealed that increasing Homocysteine in diabetes was associated with endothelial malformation, insulin resistance, and dyslipidemia, poor control of the disease, nephropathy, macroangiopathy, and oxidative stress. Vitamin C can prevent the formation of Homocysteine-induced free radicals, which affect blood vessels and cause cardiovascular diseases (Ramezani et al., 2016; Lepkin, 1999).

While a study was found regarding the effects of using vitamin C on the levels of research variables (which is one of the research limitations), a negative relationship between Homocysteine and vitamin C levels in adults was confirmed by the researchers (McArdle et al., 2013). Nowadays, the use of lifestyle interventions such as diet, exercise, and educational programs are recommended to reduce obesity and prevent diseases caused by it. While improvements in insulin sensitivity, reduced insulin resistance, or reduced visceral fat accumulation following exercise have been reported in children and adolescents, the lack of exercise effect on insulin sensitivity in obese or overweight adolescents was also observed by other researchers. In addition, the role of exercise on Homocysteine levels and insulin resistance in obese adolescents has not been well described owing to the presence of confounding factors and potential effects such as age and maturity of subjects, duration, intensity and type of exercise, and diet control before and after blood tests. Given the results of this research, the use of vitamin C and regular aerobic exercise is recommended as a strategy for modifying the lifestyle to control childhood obesity and prevent its side effects.

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