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Exercise-induced weigh loss in the absence of a control diet does not affect serum resistin or insulin resistance in obese males

Eizadi Mojtaba*, Ahmadi Pezhman, Nasiri Farsani Mokhtar, Torabi Mohsen

Department of Physical Education and Sport Science, Shahre Rey Branch, Islamic Azad University, Iran

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Abstract

To investigate effect a merely long time aerobic exercise program in the absence of a control diet on serum resistin and insulin resistance in obese males. A total thirty obese males aged 35 +/- 6 yr were randomly allocated into exercise and control groups. Serum resistin, insulin and glucose were measured after overnight fast before and after a supervised aerobic exercise for 3 month (3 sessions weekly) in exercise group or detraining in control group. Anthropometric assessments also were done in these conditions. Insulin resistance (HOMA-IR) was calculated using fasting insulin and glucose. Statistical analysis was performed using an independent paired t-test. A p-value < 0.05 was considered to be statistically significant. Despite all anthropometrical indexes and body weight were significantly decreased by aerobic exercise program training in exercise group ($p<0.05$), but serum resistin and insulin resistance remained without change ($p\geq0.05$). All variables remained without change in control group ($p\geq 0.05$). Based on this data, it was concluded that exercise program in the absence of a control diet does not affect circulation resistin or insulin resistance in obese subjects.

***Corresponding Author:** Eizadi Mojtaba ✉ izadimojtaba2006@yahoo.com

Introduction

Increased fat tissue mass has been identified as a key factor in the development of insulin resistance and type II diabetes that is associated with adipocyte-secreted signaling molecules that affect glucose homeostasis such as adiponectin, leptin and resistin (Park *et al.,* 2008). Meanwhile, resistin is a peptide hormone that is effective in the pathophysiology of obesity and insulin resistance (Stejskal *et al.,* 2003). Resistin levels in adipose tissue and blood circulation is increased in obese rodents (Steppan *et al.,* 2001). Studies have also suggested a possible role of resistin in the energy balance (Steppan *et al.,* 2001). Injection of resistin to lean animals leads to increased insulin resistance, while reducing systemic levels of resistin in insulin-resistant obese animals increases insulin sensitivity (Bastard *et al.*, 2006). Resistin delivery to the hypothalamus in mice stimulated changes in the circulating levels of hormones that help regulate glucose production, in a manner independent of glucose production itself, and is ultimately associated with increased blood glucose. Increased resistin reduces insulin-stimulated glucose transport which eventually leads to insulin resistance, while the use of anti-resistin antibodies increases glucose transport capacity by insulin (Kim *et al.,* 2001). Literature suggests that resistin is effective in association between adipose tissue, obesity and insulin resistance (Bastard *et al.*, 2006). Initial studies have shown that obesity is associated with increased circulation resistin concentration. These studies suggest that the there is a positive correlation between resistin and body mass index in obese people (Meier *et al.,* 2004). Recent reports indicate increased levels of resistin and TNF-alpha in obese and insulin resistant individuals (Hivert *et al.,* 2008). Some studies have suggested that the use of anti-resistin drug agents leads to reduction of the inhibiting effect on glucose uptake in muscle and other peripheral tissues (Bastard *et al.,* 2006; 5).

Some studies have also discussed the role of diet control in maintaining normal levels of resistin (Valsamakis *et al.,* 2004). On the other hand, the beneficial effects of exercise and regular physical activity on systemic levels of other adipokines secreted from adipose tissue such as leptin and adiponectin which somehow affect the function of insulin and blood glucose levels in obesity and related diseases have been reported repeatedly (Jung *et al.,* 2008; Kelly *et al.,* 2007). Longitudinal studies have shown that regular exercise has anti-inflammatory effects and leads to decreased levels of inflammatory markers (Moschen *et al.,* 2010). This question has also been raised whether exercise or weight loss as a non-pharmacologic therapy, can affect serum levels of this peptide hormone. In this regard, in a recent study, weight loss training program in obese individuals led to a decrease in resistin levels (Valsamakis *et al.,* 2004). In another study, long-term exercise program and diet led to a significant reduction in resistin and leptin in obese humans (Jung *et al.,* 2008).

But contrary to the said findings, in study by Kelly et al, an 8-week aerobic exercise did not lead to a change in resistin levels in obese patients (Kelly *et al.,* 2007). In another study, in spite of the reduction of other cytokines, such as the 63-percent reduction of serum leptin followed by a long-term weight loss program, there was no change in serum resistin (Wolfe *et al.,* 2004). Also, in another study, after a weight loss program, no significant relationship was found between changes in resistin and changes in insulin resistance (Koebnick *et al.,* 2006). However, citing his findings, Marcel states that the decrease of insulin resistance due to weight reduction prompted by physical activity is independent of changes in adipocytokines or inflammatory factors (Marcell *et al.,* 2005). Hence, considering the contradictions between the findings on the effects of exercise on levels of blood resistin and insulin resistance, the present study aims to find the response of serum

resistin levels and insulin resistance in obese middle-aged men.

methods

This semi-experimental study was conducted in order to determine the effect of a merely weight loss exercise program in the absence of a control diet on serum resistin levels and insulin resistance in obese patients. The study protocol was approved by the ethics committee of Islamic Azad University, Saveh Branch (Iran). The study population consisted of 32 obese middle-aged men who were randomly placed in two experimental groups and control groups after measurement of anthropometric indexes. All participants gave informed consent before recruitment. The subjects of the study were non-smokers with no history of and controlled diet or regular exercise at least during the past 6 months. BMI measurements showed that all participants fell in obese category (BMI ≥ 30 kg/m^2). Apart from the phenomenon of obesity, all participants were in good health and those who had a history of chronic diseases such as cancer, gastrointestinal and respiratory diseases or diabetes and other metabolic and movement disorders were barred from participating in the study (Exclusion criteria). First, the anthropometric indices were measured with minimal clothing and without shoes on. BMI was calculated using standing height and body weight. Then, 5 ml of venous blood was taken from the participants in both experimental and control groups in the fasting state after an overnight fasting (12 hours fasting) between 8 am and 9 am to measure serum resistin as well as glucose and insulin (to calculate insulin resistance). All subjects were advised to avoid any serious exercise and taking dietary supplements 48 hours prior to blood sampling. The experimental group then participated in an aerobic exercise program for three months (three sessions per week) and control groups were barred from participating in any exercise training during this three-month period. Training sessions were performed in form of warm-up and exercise appropriate for weight loss, such as running on a flat surface and cycling and finally 5–10 min of cool down activity. Finally, 48 hours after the last training session, blood sample was retaken from both experimental and control groups to determine the effect of exercise on the intended variables. Insulin resistance was calculated using insulin and plasma glucose, according to homeostasis of minimal assessment of insulin resistance (HOMA-IR) [(fasting plasma insulin (μIU/mL) × fasting plasma glucose (mmol/L)) / 22.5] formula (Marita *et al.,* 2005). Serums were immediately separated and stored at -80° until the assays were performed. Fasting glucose was measured using glucose oxidase enzymatic method (Pars Azmoon, Tehran, Iran). Serum resistin and insulin were measured by ELIZA method respectively using (*Demeditec insulin ELIZA DE2935, Germany) and (Biovendor-Laboratoria medicina A.S. Czech)* laboratory kits. It should be noted that in this study the individuals' diets were not controlled either in pre-intervention time or during the three-month exercise activity. In fact the target of the study was simply the response of resistin and insulin resistance to a prolonged exercise in the absence of a control diet.

Statistical analysis

"T Student" test in SPSS software version 15 for was conducted for comparing the variables of the two groups in baseline conditions and to determine the effect of exercise program on each of the variables. P value of <0.05 was accepted as significant.

Results

In this study, the effect of aerobic exercise training, three sessions a week, for three months on serum resistin levels and insulin resistance in obese middle-aged men were studied. The baseline anthropometric and metabolic characteristics of the study participants in control and experimental groups are shown in Table 1. Data are presented as mean ± SD. Initial measurements showed that baseline levels of

anthropometric variables are identical in the experimental and control groups ($p \geq 0.05$).

Table 1. Mean and Standard deviation of anthropometrical and biomedical indexes in baseline condition of two groups.

Variable	Experimental group	Control group
Age (years)	35 ± 6	36 ± 7
Weight (kg)	101 ± 9.44	100 ± 8.32
Height (cm)	177 ± 8	176 ± 7
Abdominal circumference(cm)	107 ± 9	106 ± 10
Body mass index (kg/m2)	32.23 ± 3.11	32.28 ± 4.23
Systolic blood pressure (mmHg)	13 ± 1.64	13 ± 2.11
Diastole blood pressure (mmHg)	8.85 ± 1.01	8.44 ± 0.98
Fasting blood glucose (mg / dl)	103 ± 24	106 ± 19
Insulin (µIU / ml)	7.69 ± 2.14	8.01 ± 1.86
Insulin Resistance index (HOMA-IR)	1.95 ± 0.31	2.09 ± 0.28
Resistin (ng/ml)	2.88 ± 0.35	2.94 ± 0.36

No significant change was observed in any anthropometric and biochemical indexes in the control group subsequent to three months of detraining ($p \geq 0.05$). Table 2 shows all changes after exercise program condition in compare to baseline condition in experimental group. Data table shows the body fat percentage, one of the determinants of body fat levels has significantly decreased in the experimental group as a result of the three-month physical activity ($p < 0.05$). BMI, abdominal circumference, and body weight significantly decreased following the exercise intervention in the experimental group ($p < 0.05$).

Table 2. Mean and Standard deviation of all variables in before and after exercise program in experimental group.

Variable	Pre-Exercise	Post-Exercise
Weight (kg)	101 ± 9.44 *	96.44 ± 9.68
Abdominal circumference(cm)	107 ± 9 *	102 ± 8.11
Body mass index (kg/m2)	32.23 ± 3.11 *	30.78 ± 4.11
Fasting blood glucose (mg / dl)	103 ± 24 *	92 ± 19.48
Insulin (µIU / ml)	7.69 ± 2.14	8.13 ± 3.24
Insulin Resistance index (HOMA-IR)	1.95 ± 0.31	1.84 ± 0.36
Resistin (ng/ml)	2.88 ± 0.35	2.68 ± 0.56

* represent significant changes ($p < 0.05$)

Despite the reduction in anthropometric indices, serum resistin levels did not change significantly in response to exercise program in the experimental group ($p \geq 0.05$, Fig 1). In addition, there were no significant changes in insulin resistance in all participants after exercise program ($p \geq 0.05$).

Discussion

In this study, the response of serum resistin and insulin resistance to three-month exercise training was not significant in the studied obese men. In other words, no significant change was observed in serum resistin after three months aerobic exercise in obese subjects. Generally resistin is synthesized in fat tissue and belongs to the family of proteins rich in cysteine (Athyros *et al.,* 2010). The systemic increase of this peptide hormone is associated with inflammation symptoms in obese individuals or with related diseases (Weikert *et al.,* 2008). Its increased secretion is associated with amplified secretion of certain inflammatory hormones and is precise predictor factor of cardiovascular diseases (Weikert *et al.,* 2008; Kadoglou *et al.,* 2003; Reilly *et al.,* 2005).

Some previous studies have mentioned the impact of a balanced diet and regular exercise in reducing levels of blood resistin. These studies have also pointed out that weight loss by reducing body fat mass in response to diet or exercise leads to a reduction in resistin serum. The three-month exercise training programs in this study led to significant reduction of anthropometric indices such as abdominal circumference, BMI and body fat percentage together with a significant reduction in body weight. In this regard, the study's findings of Jang et al (2008) showed that a weight-loss caused by exercise combined with diet significantly improved lipid profile, serum resistin and leptin (Jung *et al.,* 2008). In another study, the reduction of abdominal circumference with weight loss was associated with decreased levels of blood resistin (Valsamakis *et al.,* 2004). A recent study also showed that resistin levels and insulin resistance in obese individuals was reduced following a weight loss program (Wolfe *et al.,* 2004). But despite these findings, in a recent study, low-calorie diet which brought about a significant decrease of BMI, glucose and serum leptin levels did not lead to a change in serum resistin (Anderlová *et al.,* 2006). Also in some other studies, responses of resistin and other adipokines such as adiponectin, leptin, and some interleukin to a long-term exercise intervention was not significant (Kelly *et al.,* 2007). Increased resistin is associated with increased insulin resistance, although the exact mechanisms remain unknown (Kopff *et al.,* 2005). Most studies have pointed to the fact that serum resistin changes due to exercise or dietary interventions in humans and animal models is associated with similar changes in insulin resistance (Valsamakis *et al.,* 2004; Kopff *et al.,* 2005). In confirmation of these findings, our study showed that prolonged exercise intervention, leads to changes in neither resistin serum nor insulin resistance. Serum resistin levels remaining unchanged despite weight loss in obese individuals has also been observed in some other studies (Jung *et al.,* 2008). In this regard, Reinehr et al (2006), citing his findings, does not support the association between resistin and insulin resistance with changes in body weight (Reinehr *et al.,* 2006). On the other hand, a recent study showed that unlike other adipokines, resistin has a weak relation with body fat level and is not a good indicator for predicting insulin resistance or metabolic syndrome in humans (Utzschneider *et al.,* 2005).

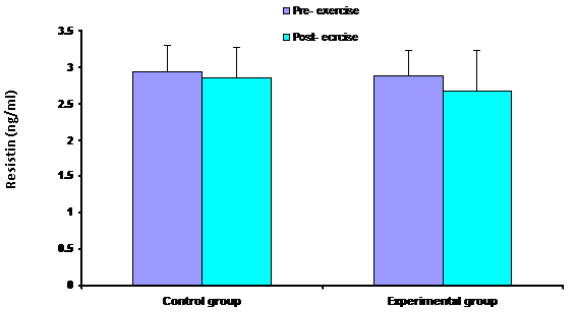

Figure 1; The changes pattern of serum resistin in two groups. Resistin levels did not change significantly in response to exercise program.

Fig. 1. The changes pattern of serum resistin in two groups. Resistin levels did not change significantly in response to exercise program.

These variables remaining unchanged by exercise, despite a significant reduction in body weight in the study subjects is controversial. Lack of a control group that is people with normal body weight has been one of the main limitations of the study. It is possible that baseline levels of resistin serum in obese subjects are similar to those of individuals of normal weight. In this case, no change in resistin levels by the exercise intervention may be attributed to it. In this regard, the findings of some recent studies have shown that there is no significant difference in levels of resistin in lean, obese and insulin resistant persons (Utzschneider *et al.,* 2005). Reinher et al (2006) did not find any significant differences in baseline levels of serum resistin between lean and obese subjects either (Reinehr *et al.,* 2006). The similarity of baseline resistin between lean and obese subjects was also reported in the study of Zhu and colleagues (Zou *et al.,* 2007). The lack of dietary control during the

exercise program has probably contributed to the non-significant changes in these variables.

Conclusion

Despite the reduction in resistin serum levels and insulin resistance in response to the controlled diet and physical activity in most studies, our study in line with findings of some other studies showed that three-month exercise training in obese individuals led to no significant change in these variables. These variables remaining unchanged may be attributed to the severity or duration of exercise, uncontrolled diet or other unknown molecular mechanisms. In the end, citing the findings of this study; it be can concluded that prolonged exercise in the absence of controlled diet does not lead to any changes in resistin serum levels of insulin resistant and obese individuals. Presence of a healthy control group to eliminate non-sports confounding factors is strongly recommended in future studies.

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