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Serum adiponectin response to a single heavy cycling in type II diabetic males

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ABSTRACT

Adiponectin is inflammatory peptide hormones that play a key role in glucose metabolism. The objective of this study was to assess the effect of single heavy exercises on adiponectin, insulin sensitivity in type 2 diabetic patients. For this purpose, sixteen type II diabetic men (age, 41 +/- 5 yr, BMI, 34 +/- 3 kg/m^2) and none-diabetic men with the matched age with normal weight (BMI, 24 +/- 3 kg/m^2) performed a single cycling exercise for 15 minute. Venous blood samples were obtained before and after (immediately) exercise test for measuring serum adiponectin, insulin and glucose. Statistical analysis used by Independent paired T-test. P<0.05 was considered significant. Diabetic patients have lower adiponectin and insulin sensitivity and higher insulin and glucose than none-diabetic subjects (P<0.05). There were no significant changes in all variables in control group by exercise test (P>0.05). In diabetic group, despite serum adiponectin significantly increased and glucose significantly decreased after exercise. But, insulin sensitivity were unchanged (P>0.05). This finding suggested that a single heavy exercise exercises stimulate serum production secretion in type II diabetic patients. But, it appears that adiponectin changes are not associated with insulin sensitivity after this exercise in these patients.

Keywords: Exercise, Adiponectin, Insulin Sensitivity, Diabetes.

INTRODUCTION

Scientific resources define obesity as a risk factor for the prevalence of cardiovascular disease, blood pressure and atherogenic diseases [1], although the molecular basis of this relationship is not yet fully known. Increased body fat percentage, especially visceral fat, affects insulin sensitivity and energy metabolism by releasing adipokines into blood [2]. Adiponectin is a 244 amino-acid protein that is synthesized and secreted exclusively by adipose tissue [3]. Today, due to its pharmacologic effects on insulin resistance and inflammatory diseases, adiponectin has received considerable attention as a potential pharmacological target for treatment of insulin resistance and great progress has been made in the understanding of the molecular mechanisms of adiponectin action [4]. This peptide hormone has anti-inflammatory, anti-atherogenic and anti-diabetic properties [5]. Plasma concentrations of adiponectin are lower in obesity and type 2 diabetes [6] and that adipose tissue Acrp30/adiponectin mRNA expression is decreased in obese ob/ob mice and obese humans [72]. Injection of adiponectin decreases plasma glucose level by inhibiting its production in the liver [8] and its consumption by diabetic rats leads to increased metabolism in skeletal muscle and decreased insulin resistance [9]. Plasma adiponectin concentration also shows negative correlation with TG [10] and intercellular fat deposits [11].

Among these some contradictory findings on adiponectin and its biological features can be seen; as the role of adiponectin in increasing fat-carbohydrate metabolism and its protective effect on the development of insulin resistance has been reported repeatedly [12]. But, some studies stated that acute increase in insulin sensitivity after exercise is not due to the increase of adiponectin levels [2].The findings of another study, however, would indicate no relationship of adiponectin with insulin resistance, fasting glucose and triglycerides [13]. In another study, adiponectin was introduced as a poor predictor of insulin resistance [14]. However, a recent study reports fasting plasma adiponectin and adipose tissue gene expression were not significantly different between obese diabetic, obese none diabetic and normal-weight control men [15].

Although exercise training combined with weight loss and diet leads to increased levels of adiponectin [16] it is still not entirely clear whether exercise in the absence of weight loss can change systemic levels of adiponectin. Some studies have suggested that exercise in the treadmill exercise training [17] or swimming [18] leads to delayed progression of type II diabetes in diabetic mice. Several short-term exercise protocols such as treadmill tests or ergometery have been conducted to determine changes in adiponectin levels caused by exercise in healthy subjects and patients [19, 20]. In this regard, the findings of a recent study showed that adiponectin concentration will increase significantly after 30 minutes running at 79% of VO2max. However, in this study, no significant changes in adiponectin levels, after walking on a treadmill with moderate to severe intensity were observed [21]. In another study, 45-minute exercise on the leg cycling led to reduced levels of insulin and increased insulin sensitivity immediately after the cessation of exercise which was not associated with changes in serum adiponectin [22]. In another study, 6 months of aerobic training did not lead to changes in levels of adiponectin in type II diabetic patients [23]. There are conflicting findings about the effect of exercise on adiponectin levels and other biochemical variables related to the implementation of new studies in this area creates. Therefore, the study attempts to compare the levels of this peptide hormone in type II diabetic patients and healthy subjects, and to the effect of a heavy ergometery exercise on serum levels in these patients.

MATERIALS AND METHODS

The study was conducted with the approval of the Ethics Committee of Saveh Azad University. This semi-experimental study compared the baseline levels of serum adiponectin and insulin, glucose and insulin sensitivity in diabetic and non-diabetic subjects, and also studied the response of biochemical variables in a short session of heavy exercise in two groups.

Subjects: For this purpose, 16 adult obese males with type II diabetes from Saveh city volunteered to participate by accessible sampling in this study. Also, 16 healthy none- diabetic adult men with similar range of age participated in the study to compare the levels of serum adiponectin and insulin sensitivity with the diabetic patients. Informed consent was obtained from each subject after full explanation of the purpose, nature and risk of all procedures used.

Exclusion criteria: Neither the control or diabetic subjects had participated in exercise/diet for the preceding 6 months, nor did all subjects have stable body weight. All subjects were non-smokers. Subjects with a history or clinical evidence of recent myocardial infarction, coronary artery disease; tobacco use, congestive heart failure, active liver or kidney disease were excluded.

At baseline, anthropometric indexes such as weight, abdominal circumference, body mass index and body fat percentage were measured in diabetic and non diabetic groups. Then blood samples were taken pre- and post-exercise. As a venous blood sample was collected from all the subjects who came after a 12-h overnight fast to compare the biochemical variables between diabetic and non-diabetic groups (pretest). In the next step all participants performed the YMCA standard protocol on cycle ergometer. Immediately after exercise protocol, blood samplings repeated for to determine the response of serum adiponectin and insulin, fasting glucose, insulin sensitivity and serum level of triglyceride (TG) and High Density Lipoprotein (HDL) to exercise protocol (post-test).

Exercise protocol: Exercise test was a single cycling on leg ergometer (Tunturi, made in Finland) for 15 minutes consisting of 5 stages (each stage was 3 minute)[24]. Each test start with two minutes of no-load (no resistance) pedaling for warming up. They then performed the main step of the test in 3-minute consecutive stages of exercise with no rest intervals. The pedaling rate is 50 rpm and the initial workload (first stage) is 300 kpm•min-1 (50W) and

workload increases from each stage to the next step in accordance with protocol instructions (25 watt). The patients were advised to avoid any physical activity for two days before the test.

Biochemical analysis: Those patients unable to avoid taking hypoglycemic drugs or other therapeutic drugs within 12 hours before blood sampling or exercise were barred from participating in the study. It should be noted that not taking drugs in this period was carried out in accordance with physician approval. Insulin sensitivity was calculated using fasting glucose and insulin replacement in the related formula (25). Blood glucose was measured by glucose oxidase using Calorimetric method (Pars Azmoun, Tehran, Iran). Triglyceride, total cholesterol, HDL-cholesterol was measured directly with enzymatic methods (Randox direct kits) using Kobas Mira auto-analyzer made in Germany. Plasma insulin was determined by ELISA method (Demedite, German). The Intra- assay coefficient of variation and sensitivity of the method were 2.6% and 2.88 μg/L, respectively. Serum adiponectin was determined by ELISA method, using a Biovendor- Laboratorial kit made by Biovendor Company, Czech. The Intra- assay coefficient of variation and sensitivity of the method were 3.9% and 5-50 ng/mL, respectively.

Statistical analysis: Statistical analysis was performed with the SPSS software version 15.0 using an independent paired t-test. Pearson correlation method used to determine the relationship between adiponectin with lipid profiles in diabetic patients. A p-value < 0.05 was considered to be statistically significant. All values are represented as mean ± SD.

RESULTS

Table 1 show that anthropometrical indexes in diabetic and none diabetic subjects. Preliminary findings based on the comparison of anthropometric and biochemical variables show that weight, BMI and body fat percentage in the diabetic group are much higher than those of non-diabetics ($p < 0.05$). The baseline levels of serum adiponectin and insulin sensitivity are lower in diabetic patients than in non-diabetics subjects ($p < 0.05$). The baseline level glucose, insulin, triglyceride and high density lipoproteins to triglyceride ratio in diabetic patients is significantly higher than those in non-diabetics ($p < 0.05$). Pearson correlation test showed significant negative correlation between adiponectin levels with each of the indices of lipid profile, triglyceride ($p = 0.02$, $r = -0.326$), total cholesterol ($p = 0.009$, $r = -0.391$) and low density lipoprotein ($p = -0.006$, $r = -0.518$) in diabetic patients. The baseline and changes of all biochemical data in the diabetic and none-diabetic groups are shown in Table 2. However, Paired T-test results showed that serum adiponectin concentration in diabetic patients increases significantly in response to a single session of exercise ($p = 0.01$) (Fig 1). But this exercise brought about no significant change in insulin sensitivity in patients ($p = 0.21$, Fig 2). In addition, blood triglyceride levels also remained unchanged in response to exercise ($p = 0.31$). These findings were observed while the concentration of blood glucose ($p = 0.005$), TG/HDL ($p = 0.039$) and TC/HDL ($p = 0.019$) after exercise significantly decreased in diabetic patients. All variables remained without any change in none-diabetic group by exercise test ($p \geq 0.05$).

DISCUSSION

Initial findings of this study showed that serum adiponectin levels in diabetic patients were significantly lower than those in healthy individuals. Lower levels of adiponectin concentration in obese and type II diabetics than those with normal weight have also been reported in some other studies [7]. Inflammation plays an important role in the spread of type II diabetes, although clinical studies in this area are limited [26]. Recent epidemiological studies have showed the relation between baseline levels of adiponectin with metabolic abnormalities including obesity, insulin resistance and type II diabetes and cardiovascular diseases [27]. Some studies have reported the concentration of less than 6 micrograms per milliliter (μg / ml) in obese individuals [28]. Inverse relationship between serum adiponectin with anthropometric indices of obesity, especially abdominal fat, as well as of each of the indicators lipid profile such as triglyceride, total cholesterol and low density lipoproteins of the patients were among the other findings of this study. This means that systemic adiponectin levels in those patients who have a higher lipid profile are much lower than others. The research data suggest that subcutaneous adipose tissue may play an important role in modulating adiponectin expression in diabetes and obesity [29]. Adiponectin circulates at relatively high (mg/L) concentrations, and its half-life is in the range of several hours [10] and this amount of time is appropriate for its role in regulating metabolic processes such as body fat analysis and glucose homeostasis.

Administration of adiponectin and/or its globular head portion stimulates free fatty acid oxidation in skeletal muscle [30]. Administration of adiponectin in mice consuming a high-fat diet leads to improved insulin sensitivity which

was associated reduced liver and muscle triglyceride content and increased fat oxidation in muscles [30]. A recent study pointed to the fact that 52% of changes in plasma adiponectin levels are affected by blood triglyceride levels [31]. The findings of this study have been reported repeatedly in some other studies on obesity and diabetes, but the mechanisms accounting for the relationship between them are still remain unexplored [9]. This study also showed that exercise leads to reduced TG/HDL and TC/HDL ratio in these patients. Increased adiponectin and reduced concentrations of glucose are among the main findings of this study. In fact, in this study; one session of relatively maximal cycling led to significant increase of serum adiponectin together with decreased blood glucose. In this regard, some recent studies have suggested that the acute increase in plasma adiponectin levels reduces circulation glucose by inhibiting both the expression of hepatic gluconeogenic enzymes and the rate of endogenous glucose production in both wild-type and type 2 diabetic mice, and finally led to reduced blood glucose levels together with increased hepatic insulin action and they proposed that adiponectin sensitizes the body to insulin [32]. In another study, injection of adiponectin to insulin-resistant mice resulted in immediate reduction of plasma glucose levels [8].

Adiponectin by binding to two subtypes of adiponectin receptors which are designated as AdipoR1 and AdipoR2 exerts its physiological functions. AdipoR1 is abundantly expressed in muscle, and AdipoR2 is mainly expressed in liver [33]. The finding of a recent study showed that globular adiponectin increased glucose uptake in skeletal muscle cells via GLUT4 translocation and lead to decrease to glycogen synthesis and shifted glucose metabolism toward lactate production [34]. The researcher reported that globular adiponectin, increases muscle fat oxidation, decreases circulation glucose, and causes weight loss [30].

Although some studies have reported that exercise training has no effect on adipokines or their secretion, but other studies have reported a reduction of inflammatory cytokines and increased adiponectin by short or long-term exercise [35]. Most current researcher have pointed to the fact that only those short-term activities affect the blood adiponectin levels in which the cost of the activity leads to negative energy balance or the exercise lasts more than 60 minutes [36]. Some studies have also suggested that adiponectin has a delayed response to the exercise. As in a recent study, adiponectin concentration significantly increased after a 30-minute recovery following exercise [36]. However, some researchers have attributed the slim changes in adiponectin levels immediately after exercise to plasma volume changes rather than changes in release of adiponectin [21]. Thus, it appears that determining the proportion of adiponectin to plasma volume before and after exercise would clarify certain vague points in this area which underlines the need for further study in this field. Adiponectin increased in response to short-term exercise in this study may be attributed to high intensity of the exercise.

Scientific resources state that insulin sensitivity increases after exercise, and researchers believe that the response of insulin sensitivity to exercise is dependent on the expression of adiponectin receptors in skeletal muscles [2]. These results indicate direct correlation of changes in adiponectin with insulin sensitivity after exercise [2, 37]. But in the present study, in spite of the significant increase in adiponectin in response to exercise, insulin sensitivity remained unchanged. These findings are confirmed by some other studies on diabetic and non-diabetic subjects that have reported no change in insulin sensitivity in response to exercise in spite of changes in adiponectin serum or the independent correlation of their changes in response to exercise [38, 39]. The lack of an effect of adiponectin on insulin sensitivity in the lean state has been noted in adiponectin knockout mice [40]. In another study, adiponectin changes after weight loss correlated with triglyceride decrease and HDL-C increase but, surprisingly, not with insulin sensitivity changes, although insulin sensitivity improvement was directly correlated with weight loss [36]. It must be mentioned that most studies that have reported a simultaneous increase of adiponectin or insulin sensitivity or a significant relationship between them, in response exercise have to do with long-term exercise program together with weight loss not; short-term and one-session exercise. Therefore, it seems that the response of insulin sensitivity to exercise-induced increase in adiponectin is more related to long-term exercise with weight loss than to acute exercise.

Table 1: Mean and standard deviation of Anthropometrical indexes of diabetic and none diabetic

Variables	Diabetic	None-diabetic
Age (years)	41 ± 5	40 ± 5
Height (cm)	175 ± 6.14	176 ± 7
Weight (kg)	103 ± 9	73 ± 6
Abdominal circumference (cm)	105 ± 11	90 ± 7
Body fat (%)	31 ± 3.11	22 ± 3
Body Mass Index (m/kg)	33.63 ± 3	23.56 ± 3.14

Table 2: The baseline and changes of all biochemical data in the diabetic and none-diabetic groups

Variable	Diabetic		None-diabetic	
	Pretest	post-test	Pretest	post-test
Total cholesterol (mg/dl)	203 ± 36	195 ± 31	153 ± 21	149 ± 28
Triglyceride (mg/dl)	164 ± 33	153 ± 27	142 ± 26	140 ± 28
High Density Lipoprotein (mg/dl)	45 ± 4	49 ± 5	49 ± 9	50 ± 11
TG / HDL	4.51 ± 1.02	3.97 ± 0.68	3.12 ± 0.56	2.98 ± 1.12
TC / HDL	3.64 ± 3.	3.14 ± 0.68	2.90 ± 0.68	2.80 ± 0.41
Fasting glucose (mg/dl)	224 ± 43	211 ± 31	94 ± 14	92 ± 18
Fasting insulin(μIU/ml)	8.38 ± 3.11	9 ± 2.56	6.92 ± 2.14	7.06 ± 1.43
Insulin sensitivity(HOMA-IR)	0.50 ± 0.07	0.51 ± 0.09	0.66 ± 0.11	0.65 ± 0.12
Adiponectin (ng/ml)	5.84 ± 0.98	8.06 ± 2.14	8 ± 1.68	9.1 ± 2.65

Values are means ±SD.
** represent significant changes (p < 0.05).*

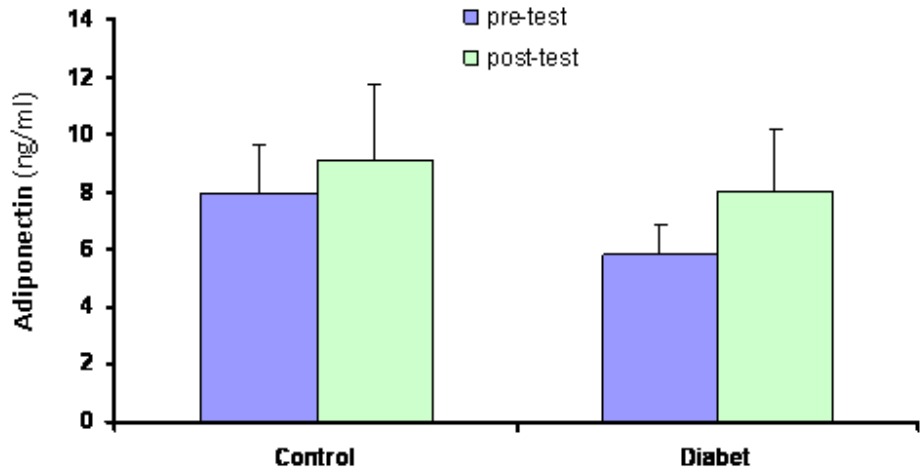

Figure 1; The changes pattern of serum adiponectin in two groups. Adiponectin levels increased significantly in response to exercise program in diabetic group.

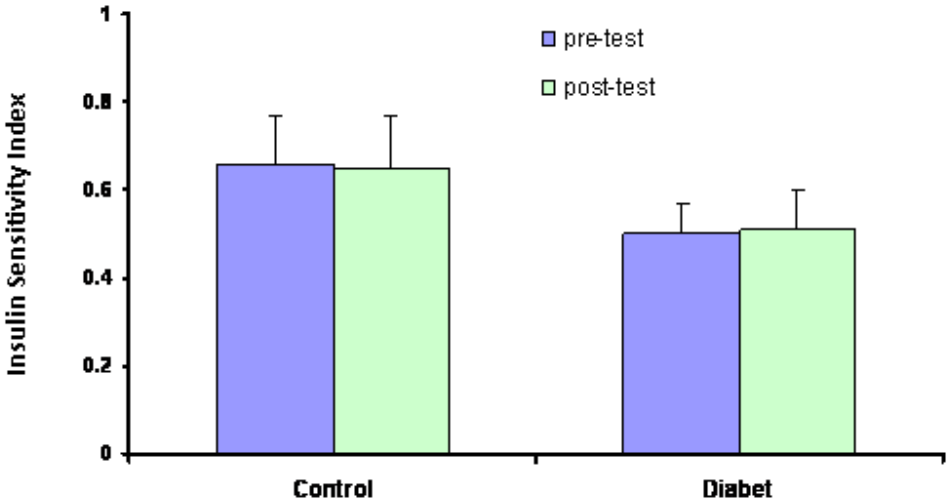

Figure 2: The changes pattern of insulin sensitivity in two groups. Insulin sensitivity levels did not change significantly in response to exercise program in two groups.

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