Indian Journal of Fundamental and Applied Life Sciences ISSN: 2231-6345 (Online)
An Online International Journal Available at http://www.cibtech.org/jls.htm
2011 Vol. 1 (4) October-December, pp.364-370/Eizadi et al.
Research Article

SERUM LEPTIN AND INSULIN RESISTANCE ARE NOT AFFECTED BY AN ACUTE CYCLING EXERCISE IN DIABETIC PATIENTS

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ABSTRACT
Review of research evidence shows that the adipocytokines secreted by adipose tissue have a key role in some chronic diseases such as diabetic and metabolic syndrome. The study objective was to investigate the effect a single bout exercise test on serum leptin and some indicator markers of type II diabetic disease. The baseline levels of serum leptin, insulin, glucose of seventeen middle-aged males with type II diabetic and healthy normal-weight subject matched for age were measured and compared with each other. Then, diabetic subjects were completed a cycling exercise test and blood sampling were collected immediately after exercise test for measuring above mentioned variables. Data were analyzed using by independent and paired T- test. The independent analysis showed that the Baseline level of leptin and insulin serum, glucose, triglyceride, and insulin resistance; in diabetic patients were significantly higher than healthy people's ($p < 0.05$). However, except in the blood glucose concentration, there was no significant change in any of the variables by exercise test in diabetic subjects ($p \geq 0.05$). These data suggest that 1) type II diabetic patients' have higher serum leptin compared to none diabetic subjects. 2) Acute exercise test appears to do not effect on systemic leptin levels and insulin resistance in these patients.

Key Words: *Insulin resistance, Leptin, Exercise, Type 2 diabetic*

Introduction
Diabetes is a chronic disease occurring when the pancreas cells are disabled to produce enough insulin or when the insulin sensitivity reduces (Wang *et al.,* 2010). In type 2 diabetes, the disability of functionality and the reduction of Beta cells mass accompanying the insulin resistance phenomenon usually lead to an increase in some cytokines of blood cycle and fatty acids and hyperglycemia (Stumvoll *et al.,* 2005). The research evidences clarify the potential role of the disturbance of the blood cycle inflammatory cytokines in hurting the secretion and function of insulin in diabetic patients. In the last decade, it has been clearly identified that inflammatory cytokines like Tumor factor necrosis alpha (TNF-α), leptin, resistin, and some interleukin play an important role in pathogens of diabetes (Kawasaki *et al.,* 2004). Since leptin and other hormones derived from adipose tissue were discovered, it has been clarified that adipose tissue as a giant source of fat storage plays an important role in the secretion of some peptide hormones effective in developing obesity and other relative diseases as an endocrine organ (Zhang *et al.,* 1994). Leptin is a peptide hormone with a 16 kilo Daltons molecule weight that is mainly secreted by adipose tissue. Some other tissues such as intestinal, skeletal muscle and liver (Green *et al.,* 1995), breast glands (Smith-Kirwin *et al.,* 1998), and epithelium (Buyse *et al.,* 2004), and some other tissues of body might secret it. This peptide hormone has a critical role in regulation the body weight, energy balance, and glucose homeostasis. Research findings claim that leptin has a positive correlation with fat level such as the body fatty mass and body mass index (BMI) (Unal *et al.,* 2004). Obesity leads to a systemic leptin increase, which will cause a disorder in insulin and hyperglycemia, specifically in type 2 diabetic patients (Fridman *et al.,* 1998, Kieffer *et al.,* 1996). Leptin Deficiency or its receptors will result in obesity or type 2 diabetic (Fridman *et al.,* 1998). Recently, it has been found that leptin directly effects on the process of insulin secretion from pancreas (Kieffer *et al.,* 1996). Besides its direct effect on beta cell function, leptin, also indirectly effects insulin secretion by activating sympathetic nervous system (Chwartz *et al.,* 1997, Garvey *et al.,* 1991). Some studies also remark the direct relation of leptin and insulin resistance and

fasting glucose concentration, particularly in diabetic type 2 diabetic, so that an increase in blood leptin level leads to insulin resistance and fasting glucose increase (Rudzka-Kocjan *et al.,* 2006).

Various studies have been carried out on developing suitable strategies in order to prevent and cure type 2 diabetic and adjusting the systemic levels of come cytokines which are effective in obesity and type 2 diabetic, especially on blood leptin levels. Nevertheless, the role of physical exercises in adjusting the level of these peptide hormones secreted by fat tissues has been interesting for health researchers. Some studies have reported a decrease in leptin level (Landt *et al.,* 1997) and the others have announced no change in leptin levels by doing physical exercises (Levine *et al.,* 1999, Racette *et al.,* 1997). In addition, a study mentions that the level of plasma leptin has a direct relation with fat tissue and a negative relation with the level of physical fitness or physical activities (Courteix *et al.,* 2007). Another aerobic exercise program has resulted in an increase in leptin with an increase in maximum oxygen consumption (VO2max) in obese people (Kondo *et al.,* 2006). In another study, after a session of rowing, the leptin level decreased significantly immediately after exercise (Jurimae *et al.,* 2007). Moreover, findings of another research illustrated that the blood leptin concentration had a significant decrease, 24 and 48 hours after a maximum physical activity on tread mill; however, this reduction was independent from changes in insulin and glucose (Olive *et al.,* 2001). Nonetheless, in another study, despite a decrease in insulin and free fatty acid following a 60 minute activity on treadmill with a moderate intensity, no change was detected in leptin levels (Torjman *et al.,* 1999).

In spite of the fact that a wide range of studies have been carried out in this area, no similar findings and general conclusion has been obtained in terms of the role of exercise on blood leptin levels in obese or type 2 diabetic patients. Therefore, more studies are needed to take place. The present study aimed to determine serum and insulin resistance responses to a single bout relatively maximal cycling in middle-aged males with type 2 diabetic patients.

MATERIAL AND METHODS

The primary aim of this semi experimental study was to comparing baseline level of serum leptin and insulin resistance between middle-aged males with type II diabetic and healthy normal-weight subject matched for age. In addition, the secondary aim was to determine the effect of an acute heavy cycling exercise on serum leptin, insulin resistance, glucose, and insulin in diabetic's patients.

Subject: To achieve the above mentioned purposes, fifteen obese middle-aged males with type 2 diabetic and fifteen healthy normal-weight subject volunteered to participate in this study in order to compare the baseline level of above mentioned variables in the two groups. Written consent was obtained from each subject after the experimental procedures and possible risks and benefits were clearly explained.

Inclusion and exclusion criteria: Inclusion criteria for study group were determined as existing type 2 diabetic for at least five months, having a BMI of 30 or above. Cerebrovascular disease, kidney and liver disease, growth hormone deficiency and anemia were of exclusion criteria of the study. All subjects were non-smokers and had not participated in regular exercise/diet programs for the preceding 6 months.Those that were unable to avoid taking hypoglycemic drugs or insulin sensitivity-altering drugs for 12 hours before blood sampling were also barred from participating in the study.

Anthropometric measurements: The measurements for weight, height, abdominal and hip circumference and blood pressure were first performed. The weight and height of the participants were measured in the morning, in fasting condition, standing when the participant had thin clothes on and was wearing no shoes by using the standard hospital scales. Abdominal circumference and hip circumference were measured in the most condensed part using a non-elastic cloth meter. Also, Waist to hip circumference ratio (WHO) was calculated through dividing the abdominal circumference by hip circumference. The Body Mass index (BMI) was calculated using the formula body weight/height2 in terms of kg/m^2.

Blood sampling and exercise program: After anthropometric measurements, diabetic and none-diabetic subjects were asked to attend Hematology Lab following12 hours of overnight fasting, between the hours

of 8 to 9 am for a blood sampling. The subjects were advised to avoid any physical activity or exercise 48 hours before the blood sampling. These blood samplings used for measuring and to compare fasting serum leptin, insulin resistance and the other biochemical variables between two studied groups. In this stage, then diabetic patients were completed a YMCA standard test on leg ergometery cycle (Tunturi, made in Finland). This protocol was performed in 5 continues stage without rest between stages. Each stage lasted 3 minute (Mullis *et al.,* 1999). A blood sampling was also collected immediately after exercise test in order to determine the variables responses to exercise test in these patients. Insulin resistance was assessed using the homeostasis model assessment for insulin resistance formula derived from fasting insulin and glucose levels (Marita *et al.,* 2005). Glucose was determined by the oxidase method (Pars Azmoon kit, Tehran). Triglycerides were measured using the colorimetric enzymatic method (Pars Azmoon kit, Tehran). The intra-assay and inter-assay coefficient of variation of leptin (Biovendor Company, Czech) were 4.2% and 6.7% respectively. Serum insulin was determined by ELISA method (Demeditec, Germany) and the intra- assay and inter-assay coefficient of variation of the method were 2.6% and 2.88 respectively.

Statistical analyses: Independent t-test was used to compare the means of variables between diabetic and non-diabetic groups. Student's t-tests for paired samples were performed to determine significance of changes in variables by exercise test in diabetic patient. Significance was accepted at $P < 0.05$.

RESULTS

Baseline level of anthropometric and metabolic characteristics of the study participants in the diabetic and none-diabetic subjects groups are shown in Table 1. All values are represented as mean ± SD. Findings from independent t-test showed that baseline levels of serum leptin, insulin, glucose, triglyceride and insulin resistance in diabetic patients were significantly higher of none-diabetic subjects $P < 0.05$. Additionally, body weight, abdominal and hip circumference, BMI and body fat percentage in diabetic patients were higher than those without diabetic ($P < 0.05$. The data show that Leptin levels were not acutely affected by cycling exercise in diabetic patients (8.35 ± 2.11 versus 7.83 ± 1.68 ng/ml, $P = 0.111$). Also, the concentrations of insulin and triglyceride were unaltered during the exercise test (triglyceride: 178 ± 36 versus 186 ± 44 mg/dL, $P = 0.326$. Insulin: 8.55 ± 1.68 versus 9.11 ± 2.14 µIU/ml, $P = 0.144$). Moreover, insulin resistance was not signigcant change after cycling exercise compared to baseline (4.69 ± 1.38 versus 4.77 ± 1.32, $P = 0.221$). The only visible change in diabetic patients after the acute exercise was the reduction of the blood glucose (236 ± 42 versus 211 ± 35 mg/dL, $P = 0.113$). In other words, an acute heavy cycling test results in a significant decrease of blood glucose in diabetic patients ($P = 0.004$).

DISCUSSION

Leptin increase has been known as an important factor in developing diseases related to obesity (Fridman *et al.,* 1998, Kieffer *et al.,* 1996). The findings of the statistical tests of the present study have indicated that fasting serum leptin of the diabetic patients is significantly higher than healthy people with normal weight. An increase in leptin level has been witnessed in some other studies on obese or diabetic people (Rudzka-Kocjan *et al.,* 2006). In resting situation, the plasma leptin concentration is higher in diabetic patients even with the same fat mass than in healthy people (Kanaley *et al.,* 2001). Apart from the body fat levels, high level of serum leptin can be a sign of an increase in leptin resistance in obese and people with related diseases. The plasma leptin level has a direct relation with the fat tissue and a negative relation with the body fitness or physical activity (Courteix *et al.,* 2007). The result of another study showed that there is a reverse relation between the plasma leptin concentration and the resting energy expenditure and the carbohydrate oxidation and respiratory equivalence in obese people. Thus, these results reveal an increase in leptin resistance in obese people (Niskanen *et al.,* 1997). In comparison with the healthy group, an insulin resistance increase and a higher level of fasting glucose has also been seen in the diabetic patients of the present study. In addition, the findings of a recent study have clarified that in mice which their leptin receptors in hypothalamus and pancreas Beta cells are deleted, obesity and fasting

hyperinsulinemia is common, and glucose-dependent insulin release and glucose tolerance are disturbed (Covey *et al.,* 2006).

Table 1: Mean and standard deviation of Baseline level of anthropometric and metabolic characteristics of studied subjects

Variables	Diabetic group	None-diabetic group
Age (year)	45 ± 5	44 ± 6
Weight (kg)	98 ± 8	71 ± 6
Height (cm)	174 ± 7	175 ± 9
Body Fat (%)	32.01 ± 3.11	22 ± 3.12
Body mass index (kg/m^2)	31.75 ± 3.12	23.18 ± 2.44
Abdominal circumference (cm)	106 ± 11	88 ± 8
Triglyceride (mg / dl)	178 ± 36	152 ± 25
Glucose (mg/dL)	236 ± 42	97 ± 11
Insulin (μIU/ml)	8.55 ± 1.68	6.35 ± 2.11
Insulin resistance	4.69 ± 1.38	1.53 ± 0.21
Leptin (ng/ml)	8.35 ± 2.11	4.11 ± 1.32

Physical exercise is considered as one of the main cures for controlling blood sugar and for weight loss of the type 2 diabetic patients. Although clinical studies on the effect of exercise on these patients have shown contrastive results, the statistical findings of this study clarified that a acute exercise on an ergometery cycle for 15 minutes does not lead to a significant change in serum leptin level and insulin resistance. In this regard, some other studies have reported no change in serum leptin level immediately after a one-session exercising test. Besides, after a one-session walking on treadmill (45 minute) with a 60 to 80 percent maximum heart rate by obese women, despite a reduction in insulin resistance, there has been no change in serum leptin level (Karbowska *et al.,* 2006). Furthermore, other reaches have not found any changes in serum leptin and insulin levels through a single bout maximal exercise (Bouassida *et al.,* 2004).

Apparently, in the present study, the amount of the consuming calorie of the performed physical activity has not been enough so that it can make a balance of the negative energy in the participants, since the negative energy balance due to a physical exercise is one of the factors in reducing the blood leptin level (Hilton *et al.,* 2000). Because in a recent study, long one-session endurance exercise with a high energy cost caused a significant reduction in leptin serum (Zaccaria *et al.,* 2002). Some researches, in this regard, state that the blood leptin concentration decreases after one-session exercises with more than 60 minutes of activity which stimulates the release of free fatty acids or after the activities which cause an energy cost of over 800 kilo calories and such decrease can be attributed to the increase of lipolysis (Bouassida *et al.,* 2006, Bouassida *et al.,* 2010, Bouassida *et al.,* 2006).

It is remarkable that, in the present study, absence of change of serum leptin concentration has been seen while the cycling exercise had led to a significant reduction of blood glucose. On the other hand, some studies declare that beside the balance of the negative energy, a reduction in the blood leptin levels in diabetic patients after an exercise might be due to the reduction of glucose existence (Kanaley *et al.,*

2001). These researchers believe that the reduction of glucose transfer to the adipose tissue is because of a more glucose transference to the muscles after exercise and they think it is an important factor in the reduction of leptin secretion in the recovery period after exercise test. In fact, some studies support the delayed reduction of serum leptin after exercise. Moreover, another research points out that despite a lack change in serum leptin after an acute exercise, its level decreased significantly after 24 hour recovery. The researchers believe that this delayed reduction in leptin serum is because of the time needed for a change in ob gene of the adipose tissue (Meuller *et al.,* 1998). The above mentioned findings could bring about a justification for the serum leptin not changing immediately after exercise (Dirlewanger et al., 1999, Kraemer *et al.,* 1999). Furthermore, some other studies have stated that the decrease in leptin concentration after an exercise is not immediate and they have reported a reduction of leptin after 24 and 48 hours following the exercise (Essig *et al.,* 2000, Duclos *et al.,* 1999). Additionally, a 20 minute intense running done by obese diabetic and non-diabetic men and women resulted in a significant reduction of leptin (Legakis et al., 2004). In this regard, the study of Gordon *et al* (2066) indicated that leptin response depends on the intensity of exercise. One of the major limitations of the present study is not repeating the blood sample during the recovery period following exercise.

Conclusion

Type 2 diabetic patients have a higher level of serum leptin in comparison with healthy people. Results of the present study confirm some other studies that acute exercise with a low energy cost does not lead to a reduction of serum leptin levels in type 2 diabetic patients. However, based on some other sources, it is possible that the changes or reduction in serum leptin occurs with a delay subsequent to the exercise which needs further studies with more blood sample repetitions in the recovery period after exercise.

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