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Relationship of anti-inflammatory adiponectin with insulin resistance in smoker

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Abstract

Accumulating evidence indicates that smokers are at high risk compared to non-smokers for development of diabetes. The objective of this study was to determine relation of serum adiponectin with insulin resistance in cigarette smokers. For this purpose, fasting serum adiponectin, insulin and glucose concentration were measured in 37 healthy adult male smokers after an overnight fast. Insulin resistance was assessed using the homeostasis model assessment for insulin resistance formula derived from fasting insulin and glucose levels. A Pearson correlation was used to establish the relationship between serum adiponectin concentrations with insulin resistance in studied subjects. Although we did not observe any relationship between adiponectin with glucose concentration, but this anti-diabetic cytokine was inversely correlated with insulin resistance in smoker subjects. Based on this observation, we can say that each of insulin resistance or serum adiponectin directly can affect each other.

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Introduction

Adiponectin is one of the hormones secreted by adipose tissue, which comparing to other peptide hormones enters the bloodstream in higher concentrations (Fahim *et al.,* 2006). Lower concentrations of adiponectin are accompanied with obesity, dyslipidemia, hypertension, diabetes type 2, and other cardiovascular diseases (Hotta *et al.,* 2000; Weyer *et al.,* 2001; Kumada *et al.,* 2003). It has been found that clinical syndromes with hypoadiponectinemia always accompanied with insulin resistance syndrome or glucose resistance syndrome (Reaven, 2004). Besides, variation in plasma adiponectin concentrations or its different forms can affect the insulin sensitivity (Weyer et al., 2001; Hotta *et al.,* 2001; Chandran *et al.,* 2003; Pajvani *et al.,* 2004). Recently it has been found that adiponectin concentration decreases in smokers (Thamer *et al.,* 2005; Tsukinoki *et al.,* 2005). Experimental studies show that adiponectin and inflammatory markers are negatively related. Even some recent studies suggest that in obese people or type 2 diabetes patients the increase in plasma CRP levels always coincide with the decrease in adiponectin levels (Ouchi *et al.*, 2003; Engeli *et al.,* 2003). There is a hypothesis which states that the decrease in plasma adiponectin levels & its expression is due to the fact that pro-inflammatory cytokines like IL-6 have a negative effect on adiponectin secreting cells in adipose tissue (Fasshauer *et al.,* 2002; Suganami *et al.,* 2005). Some studies also say that smoking leads to the decrease in serum adiponectin levels (Miller *et al.,* 2003). In some other studies increased insulin resistance in smokers have also been reported (Attvall *et al.,* 1993).

Review of the findings shows that adiponectin levels decrease in smokers & some findings attribute this reduction of adiponectin levels to the increase of inflammatory markers like CRP, which is due to smoking (Wannamethee *et al.,* 2005). Some other investigations have also reported the increased insulin resistance in smokers (Facchini *et al.,* 1992). As studies on other cardiovascular diseases have indicated that the increased insulin resistance & any deficiency in factors which affect insulin resistance are important components playing an outstanding role in decreasing the adiponectin levels (Eizadi[a] *et al.,* 2011), they introduce insulin resistance as a predictive index for adiponectin levels. This raises the question of whether insulin resistance in smokers also leads to decreased adiponectin levels, or is it independent of decreased adiponectin levels and smoking or the increase of its related inflammatory markers independently leads to decreased serum and plasma adiponectin levels in these people. So to answer this question, the present study is performed among men who smoke, with this aim to identify the existing relation between adiponectin and insulin resistance index or blood glucose levels.

Material and methods

Thirty-five sedentary, healthy adult (42.6 ± 7.9 year of old) males smoker (BMI: 30.3 ± 2.1 kg/m2) were recruited through an accessible sampling in present study. This study aimed to determine serum adiponectin in relation to insulin resistance in mentioned smokers. The ethics approval was taken from Islamic Azad University of Iran ethical committee. After the nature of the study was explained in detail, informed consent was obtained from all participants.

Having history of at least 10 cigarettes a day for 5 years was the main criterion for inclusion. All subjects had not participated in regular exercise for the preceding 6 months, nor did all subjects have stable body weight. The exclusion criteria were infections, renal diseases, hepatic disorders, use of alcohol, having history of known hyperlipidemia, hypertension, coronary artery disease, cerebrovascular disease, and peripheral artery disease. Using medicine or hormone preparations that affect the carbohydrate and lipid metabolism was another exclusion criteria.

Anthropometric measurements of height, weight, percent body fat, and circumference measurements

were taken one day before study. Body weight was measured in duplicate in the morning following a 12-h fast. Height and body mass were measured using a wall- mounted stadiometer and a digital scale, respectively. Body mass index was calculated as body mass (in kilograms) divided by height squared (in square meters).

Subjects were asked to attend Hematology Lab between the hours of 8 to 9 am after an overnight 12-hour fast. Blood samples were obtained in order to measuring serum adiponectin, insulin and glucose concentration. Glucose was determined by the oxidase method (Pars Azmoon kit, Tehran). Serum adiponectin and insulin was determined by ELISA method. To estimate insulin resistance, the homeostasis model assessment (HOMA) index was calculated as fasting insulin concentration (μU/ml) × fasting glucose concentration (mmol/l)/22.5 (Molloy *et al.,* 1992).

Statistical analyses

All values are represented as mean ± SD. Data were analyzed by computer using SPSS software version 15.0. Normal distribution of data was analyzed by the Kolmogorov-Smirnov normality test. A Pearson correlation was used to establish the relationship between serum adiponectin concentrations with insulin resistance in studied subjects. P value of <0.05 was accepted as significant.

Results

Anthropometric and metabolic characteristics of the study participants in smoker subjects are shown in Table 1. All values are given as mean and standard deviation.

Serum adiponectin concentrations were negatively correlated with body weight in studied subjects ($p = 0.000$, $r = - 0.61$). The main objective of present study was to determine relation between serum adiponectin and insulin resistance in smoker subjects. In this regard, a high negative significant association was observed between these variables in smokers studied ($p = 0.015$, $r = - 0.39$, Fig 1). Determine relation between adiponectin and insulin was a Secondary objective of the study. Despite the strong association of adiponectin with insulin resistance, but this anti-inflammatory cytokine was not related with serum insulin in studied subjects ($p = 0.39$, $r = 0.15$).

Discussion

In present study, we observed that serum adiponectin was strongly associated with insulin resistance in middle-aged smoker men. In other word, increased serum adiponectin is negatively correlated with insulin functional in this population. Relationship between insulin resistance with adiponectin or other anti and inflammatory cytokines was reported in some previous studies (Eizadi[a] et al., 2011; Eizadi[b] *et al.,* 2011).

Table 1. The descriptive anthropometric and biochemical features of studied subjects.

Variable	Mean	Standard deviation
Age (years)	42.6	7.9
Weight (kg)	92.5	5.81
Height (cm)	174.6	3
Body mass index (kg/m^2)	30.30	2.1
Body Fat (%)	28.9	2.3
Serum adiponectin (μg/m)	5.7	2.4
Insulin (μIU/m)	11.4	5.1
Insulin resistance (HOMA-IR)	3.47	1.3
Glucose (mg/dL)	107	45.9

Adiponectin is produced in large amounts from adipose tissue and is present in relatively high concentration in the blood. It has been demonstrated that Low circulating concentrations of adiponectin have been associated with obesity, dyslipidemia, essential hypertension, type 2 diabetes, and cardiovascular disease (Hotta *et al.,* 2000; Weyer *et al.,* 2001; Kumada *et al.,* 2003). On the other hand, the clinical syndromes in which hypoadiponectinemia occurs are all associated with peripheral resistance to insulin-mediated glucose uptake (Reaven, 2004).

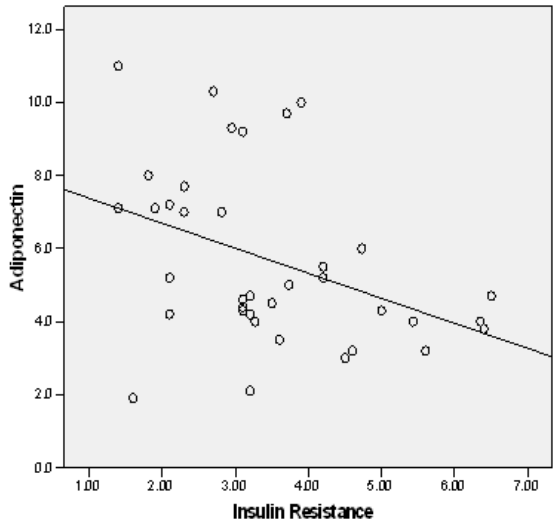

Fig. 1. The correlation pattern between serum adiponectin and insulin resistance in smoker subjects.

It is probably that the relationship between smoking and lower adiponectin concentrations results from inflammation-mediated down-regulation of adiponectin expression in adipose tissue (Fahim *et al.,* 2006). It is well known that smokers are at high risk for development of diabetes compared to non-smokers and a strong relationship between tobacco smoke and metabolic syndrome among adolescents has been observed (Weitzman *et al.,* 2005). On the other hand, some previous studies have been reported higher insulin resistance in smoker than non-smokers (Gupta *et al.,* 2006; Facchini *et al.,* 1992; Attvall *et al.,* 1993). But it is not clear whether hypoadiponectinemia in cigarette smoker is due to smoking, and possibly the associated inflammation, or to the coexistence of insulin resistance. In reply to this question, our study finding showed a strong negative correlation between fasting serum adiponectin and insulin resistance in this population. Higher fasting serum insulin, glucose and insulin resistance in smokers as compared to nonsmokers have been also reported by some previous study (Gupta *et al.,* 2006). Increased fasting glucose in smokers could be due to decrease in cellular glucose uptake and utilization, thereby suggesting that smoking affects a mechanism involving early steps in insulin action or by mechanisms operating simultaneously on different biochemical pathways (Silvia *et al.,* 2011). It is likely that a lower adiponectin concentration in smokers is not related to smoking, but to the concomitant presence of insulin resistance in smokers (Miyazaki *et al.,* 2003; Iwashima *et al.,* 2005). Some previous study also has been suggested that lower adiponectin concentration in smoker is independent of insulin functional or insulin resistance (Fahim *et al.,* 2006).

It has been demonstrated that some inflammatory factors such as TNF-α and IL-6 have been associated with lower adiponectin levels (Kern *et al.,* 2003; Bruun *et al.,* 2003) and may directly reduce adiponectin secretion of adipose tissue (Fasshauer *et al.,* 2002; Suganami *et al.,* 2005); It is important to make a note here that cigarette smoke contains thousands of potentially bioactive constituents, including free radicals, therefore, it is probably that one or more of these factors may lower adiponectin production or release from adipocytes (Silvia *et al.,* 2011). In an aggregation, based on our data, we can say cigarette smoke can be affect both adiponectin and insulin resistance. On the other hand, each of insulin resistance or serum adiponectin directly can affect each other.

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