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RESEARCH PAPER

Serum adiponectin predicts cardiovascular fitness in none-trained men

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Abstract

Accumulating evidence indicates that obesity and overweight are associated with systemic inflammation and low cardiovascular fitness. Although the pathophysiologic mechanisms of the relation between systemic inflammation and cardiovascular fitness are not fully understood. Therefore, in this study, we investigated the relationship between fasting serum adiponectin as an antiinflammatory cytokine with maximal oxygen consumption (VO2max) or heart rate as two physiological markers of cardiovascular fitness in 38 sedentary healthy adult overweight or obese men (Aged 36 to 46 years, body mass index = 30 ± 6 kg/m^2). Pearson correlations were used to establish the relationship between adiponectin concentrations with other variables on obese subjects. Serum adiponectin was highly negative associated with VO2max (r=0.54, p=0.000). Serum adiponectin concentrations were also independently associated with resting heart rate in studied subjects (r = 0.52, p = 0.000). On the basis of

these observational findings, it can be assumed that systemic inflammation affect cardiovascular fitness in obese human.

Key words: Adiponectin, Cardiovascular fitness, obesity, Heart rate .

Introduction

Obesity has emerged over the last decade as a high risk of coronary artery disease morbidity and mortality. Obesity leads to some chronic diseases including type 2 diabetes, dyslipidaemia, atherosclerosis and hypertension, which are major components of the metabolic syndrome (Moreno-Aliaga *et al.,* 2010). Adipose tissue -derived factors (fatty acids and adipokines) play an important role in the development of these metabolic disturbances a growing body of evidence supports the notion that deregulated adipokine secretion from the expanded White adipose tissue (WAT) of obese individuals contributes to the development of systemic low-grade inflammation and metabolic syndrome (Moreno-Aliaga *et al.,* 2010).

Enlargement of adipocytes, due to impaired adipocyte differentiation, leads to a chronic state of inflammation in the adipocytes and adipose tissue with increase in the secretion of proinflammatory cytokines such as interleukin (IL)-6, IL-8 and monocyte chemoattractant protein (MCP)-1 and a reduction in the secretion of adiponectin (Gustafson, 2010). Impaired secretion of these proinflammatory cytokines might also substantially affect cardiovascular function and morphology.

Adiponectin is one of several important metabolically active cytokines secreted from adipose tissue (Luo *et al.,* 2010). Adiponectin, a cytokine secreted by adipose tissue, has both metabolic and antiinflammatory properties. Although recently researchers have described the relationship between adiponectin and obesity in several human populations (Meilleur *et al.,* 2010), the precise mechanisms of any association between them are still not completely elucidated. This antiinflammatory cytokine stimulates nitric oxide production and may mediate associations between visceral obesity and vascular

dysfunction (Peña *et al.,* 2010). It was reported that its serum level is lower in obese children but its relationship with vascular function has not been clarified (Peña *et al.,* 2010). There is considerable evidence that circulating levels of adiponectin in obese human is lower than normal weight individuals (Galic *et al.,* 2010; Gnacińska *et al.,* 2010).

On the other hand, scientific resources support lower levels of cardiovascular fitness in non-trained individuals (Fattirolli *et al.,* 2003). Previous studies point to the fact that a sedentary lifestyle especially in obese individuals and chronic diseases related to obesity, reduces cardiovascular fitness (Lakka *et al.,* 2003; McGavock *et al.,* 2006). Despite numerous findings on decreased adiponectin levels in obese than in normal subjects on the one hand, and also lower levels of cardiovascular or cardiopulmonary fitness in some other studies, few studies so far has looked into the relationship between adiponectin levels and cardiovascular fitness in inactive obese individuals. Hence, this study aims to determine the relationship between baseline levels of serum adiponectin as an anti-inflammatory cytokine with VO2max and Heart rate as two determining physiological markers of cardiovascular fitness in non-athletic obese men.

Materials and methods

This semi-experimental study was conducted as part of ancillary study and was approved by Research Council and Ethics Committee of Islamic Azad University, Iran. Subjects were aged 36–46 years, sedentary, overweight, or obese (BMI 25–35 kg/m2, n=38) that participated in this study by accessible sampling. The subjects were given an oral and written description of the study and the possible risks and discomfort involved before giving their voluntary oral and written content to participate. Participants were non-athletes, non-smokers and non-alcoholics. Participants were included if they had not been involved in regular physical activity in the previous 6 months. Inclusion criteria were male, aged 35–50 years; BMI 26-35 kg/m2; body fat ≥ 23 %. Exclusion criteria included disease, use of medicine, daily smoking, heart failure, active liver or kidney disease, diabetes, neuroendocrine tumor and respiratory diseases. In addition,

exclusion criteria included inability to exercise and supplementations that alter carbohydrate-fat metabolism.

After obtaining written informed consent, Obesity was measured by body mass index (BMI) and body fat percentage. Body composition monitor (BF508-Omron made in Finland) with a precision error of less than 100 g was used to measure weight and body fat percentage of the subjects. Body mass index was calculated as body mass (in kilograms) divided by height squared (in square meters). Weight was measured by an electronic balance and height by a stadiometer. Height and body mass were measured using a wall- mounted stadiometer and a digital scale, respectively. Abdominal circumference and hip circumference were measured in the most condensed part using a non-elastic cloth meter.

Blood Samples and exercise protocol

After anthropometrical measurements the individuals were asked to attend Hematology Lab following 12 hours of overnight fasting, between the hours of 8 to 9 am for blood sampling in order to measuring serum adiponectin. The subjects were advised to avoid any physical activity or exercise 48 hours before the blood sampling. 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. Resting heart rate (HR) was measured after a 15-min rest in a sitting position and in a quiet environment. Cardiorespiratory fitness was assessed as VO2max (mL kg-1 min-1) was measured using a bicycle erogometer in a stepwise fashion according to YMCA instrucment. Seat height and handlebars were adjusted to fit the subject prior to each test. At first, Subjects completed two minutes of warm-up cycling with no resistance. The original YMCA protocol uses three or four consecutive 3-minute work loads without rest between stages. Subjects performed cycler ergometry at a cadence of 50 rev/min (Golding *et al.,* 1989).

Statistical analysis

Statistical analysis was performed with the SPSS software version 15.0. Normal distribution of data was analyzed by the Kolmogorov-Smirnov normality test. The bivariate associations between changes in serum adiponectin VO2max and resting heart rate were examined with the Pearson rank correlation analysis in studied subjects.

Results

In this study, we determined serum adiponectin in relation to cardiorespiratory fitness. Anthropometrical measurements showed all participants are obese with BMI=30 ± 6 kg/m^2 (26-35), body fat percentage=28.3 ± 5.22 (%); abdominal obesity= 105 ± 8.11 cm; visceral fat=13 ± 3.4 and weight = 99 ± 11 kg. The data of Kolmogorov-Smirnov test showed that all variables have a normal distribution. The data by Pearson method showed a significant positive correlation between serum adiponectin and Vo2max (r = 0.54, p=0.000, Fig 1). We also observed that serum adiponectin was negatively related resting heart rate in studied subject (r = 0.52, p = 0.000, Fig 2). Out data showed that serum adiponectin were correlated with VO2max and heart rate even after adjustment for body fat percentage, BMI and abdominal obesity in studied subjects.

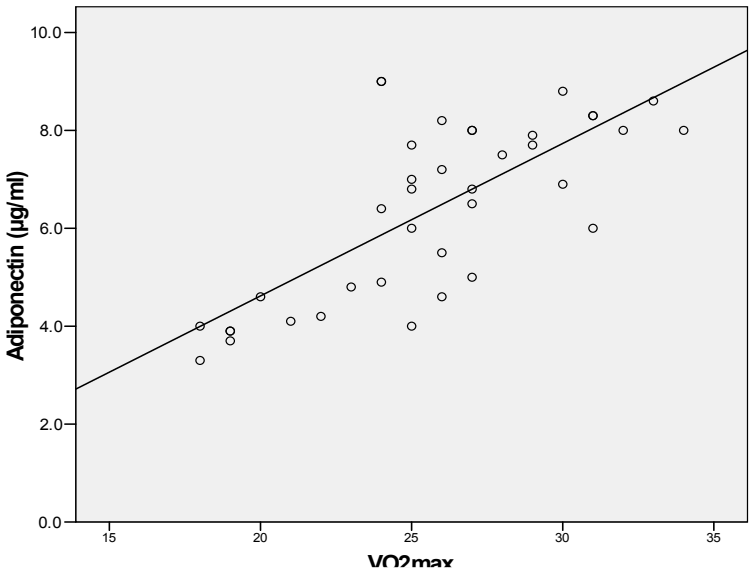

Fig 1. The correlation pattern between serum adiponectin and VO2max in studied subjects. A significant positive liner correlation is present.

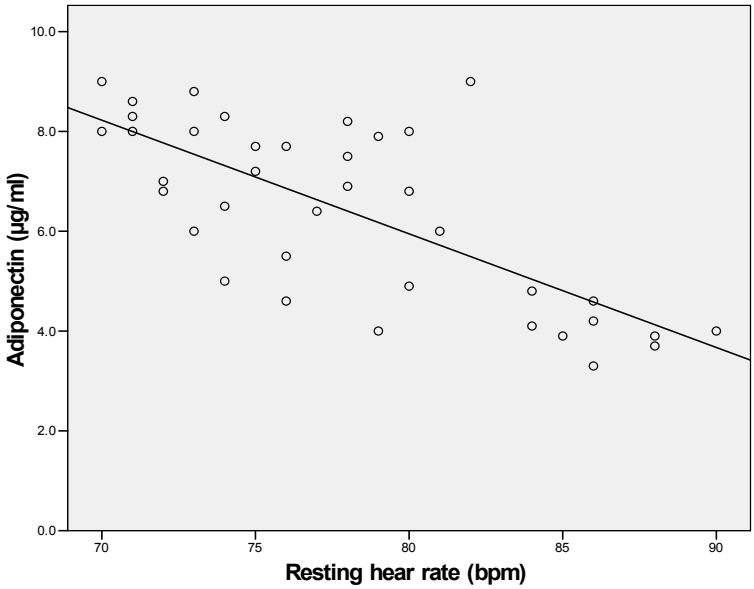

Fig 2. The correlation pattern between serum adiponectin and resting heart rate in studied subjects. A significant negative liner correlation is present.

Discussion

In this study, we observed significant positive relation between serum adiponectin and VO2max as an important determining factor of cardiovascular fitness. Also, our study clearly showed that serum adiponectin was negatively associated resting heart rate as other cardiovascular fitness markers. Recent findings demonstrate that adipose tissue, a major regulator of the metabolic adaptation to stored energy availability (Shuldiner *et al.,* 2001; Spiegelman *et al.,* 2001), exerts these functions through the secretion of different hormone-like peptides, named adipocytokines include leptin, resistin and TNF-α (Zhang *et al.,* 1994; Steppan *et al.,* 2001). Recent evidence has shown that adiponectin has antidiabetic and antiatherogenic properties (Maeda *et al.,* 2002; Yamauchi *et al.,* 2003) that are believed to be related to its inverse relationship with body fat mass and insulin resistance. Although, some recent studies suggest that adiponectin's biological effect may be independent of fat mass (Yamauchi *et al.,* 2003; Tschritter *et al.,* 2003).

In accordance with these observations, in a recent study, the plasma adiponectin relationship with insulin sensitivity and serum lipid profile (total cholesterol/HDL-C ratio, HDL-C, and triglyceride levels) was statistically independent of body fat mass (Baratta *et al.,* 2004). In our study, serum adiponectin concentrations were positively correlated with VO2max. Out data showed after adjustment for body fat percentage, BMI and abdominal obesity, fasting serum adiponectin levels still correlated significantly with VO2max in studied subjects. These data support the role of adiponectin as an antiinflammatory and antiatherogenic cytokine in cardiovascular fitness. Plasma adiponectin concentrations are also positively associated with decreased concentrations of inflammatory markers and favorable plasma lipid profiles, suggesting that adiponectin may affect cardiovascular disease by modulation of plasma lipids and low-grade, chronic inflammation (Kantartzis *et al.,* 2006). It was reported that low adiponectin plasma concentrations are associated with triglyceride as a lipid profile index (Chan *et al.,* 2005; Tschritter *et al.,* 2003). Our study also showed that serum adiponectin were negatively correlated with total cholesterol and low density lipoprotein cholesterol. Low adiponectin plasma concentrations are predictive of type 2 diabetes onset (Lindsay *et al.,* 2002), and are related to increased risk for the development of cardiovascular disease (Pischon *et al.,* 2004). Underlying mechanisms include direct effects of adiponectin on fat oxidation and vasculature (Chandran *et al.,* 2003).

Accumulating evidence indicates that individuals with obesity have low adiponectin levels, suggesting that decreased adiponectin levels may contribute to the increased inflammatory state in obesity (Medoff *et al.,* 2009). Despite the close relationship between serum adiponectin levels and VO2max as a physiological indicator of cardiopulmonary fitness in the present study, the main mechanisms responsible for this relationship are still obscure. It is possible that by impact on respiratory performance or vascular mechanisms of the body, low levels of adiponectin influences cardiopulmonary fitness levels especially in obese individuals. In this area, recent studies have suggested that adiponectin can influence the development of lung inflammation and, possibly, pulmonary hypertension (Medoff *et al.,* 2009).

Recent studies demonstrate that adiponectin-deficiency, which mimics one component of the obese state, enhances allergic airway inflammation in a murine model of chronic asthma (Medoff *et al.,* 2009). It is also possible that the through expanding vascular network or affecting the levels of smooth muscle cells, adiponectin increases oxygen transport to active muscles especially during exercise. .In the light of this hypothesis, adiponectin seems to affect aspects of organ tissue remodeling and vascular SMC proliferation in disease (Maeda *et al.,* 2002; Weyer *et al.,* 2001). Adiponectin has also been found to inhibit vascular smooth muscle cell proliferation (Fernández-Real *et al.,* 2004). It has also been reported that adiponectin deficiency can lead to vascular ischemic and diseases (Shibata *et al.,* 2005). Supporting these observations, mice with a deletion of the adiponectin gene (APN2/2) are predisposed to inflammatory diseases, such as diabetes and atherosclerosis (Shibata *et al.,* 2005; Okamoto *et al.,* 2006), and develop enhanced organ remodeling and vascular smooth muscle cell (SMC) proliferation in disease (Shibata *et al.,* 2005; Maeda *et al.,* 2002). In addition, adiponectin inhibits proliferation and migration of cultured vascular smooth muscle cells induced by mitogens (Kondo *et al.,* 2002; Okamoto *et al.,* 2002; Ouchi *et al.,* 1999) and may have similar effects on murine airway smooth muscle (Shore *et al.,* 2006).

Recent sources suggest that adiponectin reduces the proliferation of smooth muscle cells of vascular network. Undoubtedly, the effect of adiponectin on vascular network and the respiratory pathways somehow influences the relationship between adiponectin and cardiopulmonary fitness levels and can be an important factors influencing the relationship between VO2max and adiponectin. The decrease in smooth muscles cell of airway caused by adiponectin prevents the narrowing of respiratory pathways which is associated with reduced airway resistance, which ultimately increases oxygen supply especially to muscles active during exercise.

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