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Correlation of Adipocyte-Derived Protein Adiponectin with Cardiovascular Risk Factors in Obese Men

Short Running title

Adiponectin in Relation to Lipid Profile

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ABSTRACT

Background and objective: Low levels of adipocyte-derived hormone adiponectin have been associated with metabolic risk factors (RF) and cardiac disease, although the molecular mechanisms for this are less understood. The aim of this study was to compare serum adiponectin between obese and normal weight middle-aged males, and also determination of adiponectin in relation to anthropometrical indexes and lipid profiles in obese subjects.

Methods: For this purpose, serum adiponectin, lipid profiles and anthropometrical indexes were measured in 45 obese and 40 none-obese middle-aged males after an overnight fasting. Comparison of variables between the obese and no obese groups was performed using independent samples test. Pearson correlations method was used to determine the relations of adiponectin with other variables in obese subjects. A p-value < 0.05 was considered to be statistically significant.

Results: Adiponectin level in none-obese subjects were significantly higher than those of obese subjects ($P < 0.05$). In obese participants, Serum adiponectin concentrations were negatively correlated with total cholesterol, low density lipoprotein, systolic and diastolic blood pressure and age of subjects ($P < 0.05$). But, this peptide hormone was not correlated with the anthropometrical indexes ($P \geq 0.05$).

Conclusion: Based on this data, it was concluded that serum adiponectin is a predictor index of cardiovascular risk factors and a reduction in systemic levels of this hormone is associated with cardiovascular diseases prevalence.

KEY WORDS: Obesity, Adiponectin, Cardiovascular risk factor.

INTRODUCTION

Obesity is the major health problem in developed countries and one of the significant problems in the developing countries. Epidemiological evidence is increasing regarding the increasing effect of obesity on many diseases such as asthma, diabetes, atopic, immune diseases and many cardiovascular and respiratory diseases [1, 2]. However the biological basis for these processes is not fully recognized yet.

White adipose tissue (WAT) is a major site of energy storage and is important for energy homeostasis. So that, it stores energy in the form of triglycerides during and releases it in the form of free fatty acids (FFA) when needed [3, 4].

Moreover, adipose tissue also plays a role as an important endocrine organ that secretes a number of biologically active "adipokines" such as leptin, resistin and adiponectin [5, 6]. Between them, adiponectin is an adipocyte-secreted protein which plays an important role in hyperglycemia and inflammatory mechanisms [7]. Low levels of this hormone are followed by obesity and insulin resistance [8]. Nowadays, adiponectin has been identified as a factor of promoting fat oxidation and glucose uptake in skeletal muscles and decrease of glucose release from the liver [9]. Studies suggest that obesity and increase of adiposity are associated with adiponectin reduction [10]. Despite the fact adiponectin is one of the most abundant peptide hormones secreted by adipose tissue, its levels is found to be lower in obese subjects than in lean subjects, and strong negative correlations between plasma adiponectin levels and body mass index (BMI) have been shown both in humans and in animals [11,12]. Moreover, close negative correlations have been shown between adiponectin levels and liver fat content [13]. Adiponectin levels were inversely correlated with anthropometric parameters of obesity and insulin resistance [14]. In a recent study, regression analysis revealed independent from body composition factors, role of adiponectin in determination of blood level of triglyceride [15]. Results show that serum adiponectin level is negatively correlated with insulin resistance, triglyceride, abdominal circumference, waist to hip ratio (WHO), low density lipoprotein (LDL), BMI and body fat mass and positively correlated high-density lipoprotein (HDL) [16,17].

One other study reveals that the relationship between adiponectin and TG, LDL and HDL will be maintained even after adjustment for age, sex and BMI [18]. But ccontrary to above mentioned results, the statistical result of a recent study showed that despite the direct relationship of adiponectin with HDL, there is no relationship between this peptide hormone and other body weight indices, total cholesterol (TC) TG LDL, insulin resistance and anthropometrical indices [19]. Disaffiliation between serum adiponectin levels and body fat levels has been also observed in some other studies [19]. A recent study showed significant relationship of adiponectin and lipid profile indices (TG, TC, LDL, and HDL) independently of BMI [20]. The study of Ram et al. also showed that there is no significant correlation between fasting adiponectin levels with abdominal fat volume [21]. Some other studies also suggest that the relationship of adiponectin with biochemical

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indicators of lipid profile (TG, TC, LDL, and HDL) is independent of adipose tissue levels [22, 23, 24]. Reviewing the research findings indicates contradiction in the findings regarding the relationship between adiponectin and lipid profile indicators and anthropometrical variables and there is still no general consensus regarding the relationship of this anti-inflammatory hormone with the mentioned indicators. Therefore, considering to the conflict findings of previous studies, this study was performed with aims to investigate the association among serum adiponectin and some cardiovascular risk factors such as lipid profiles and anthropometrical indexes in middle aged obese males.

MATERIALS AND METHODS

Subject: The purpose of this study was to compare serum adiponectin between obese and none-obese middle-aged men and also to examine its relationship with anthropometrical indexes and lipid profiles in obese subjects. For this purpose, 45 obese (BMI ≥ 30) and 40 none-obese middle-aged males aged 37 to 48 years participated in this study by randomly. The study was conducted with the approval of the Ethics Committee of the Islamic Azad University, Iran. Written informed consent was obtained from all participants.

Exclusion criteria: Subjects with a history or clinical evidence of impaired fasting glucose or diabetes, orthopedic abnormalities, recent myocardial infarction, congestive heart failure, active liver or kidney disease, growth hormone deficiency or excess, neuroendocrine tumor, anemia, or who were on medications known to alter insulin sensitivity were excluded. Subjects had neither used any medication 6 weeks prior to the study nor participated in any regular physical exercise.

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/m². The arterial systolic and diastolic blood pressures (BP) were calculated after they rested for 10 minutes with a mercury manometer with appropriate sleeves from the right and left arm, in sitting position on the condition that they had not eaten anything, had not taken any caffeine, had not smoked or exercised thirty minutes before the measurement, and then the averages were calculated.

Blood sampling: After anthropometric measurements, all participants were asked to attend Hematology Lab for blood sampling. Subjects were asked to avoid doing any heavy physical activity for 48 hours before blood sampling. A venous blood sample was collected from all the subjects who came after a 12-h overnight fast between the hours of 8 to 9 am. These blood samplings used for measuring of fasting serum adiponectin, total cholesterol, triglyceride, High Density Lipoprotein cholesterol, low density Lipoprotein cholesterol. Glucose was determined by the oxidase method (Pars Azmoon kit, Tehran). Total cholesterol, HDL cholesterol and triglycerides were measured using the colorimetric enzymatic method (Pars Azmoon kit, Tehran). 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: All values are represented as mean ± SD. Statistical analysis was performed with the SPSS software version 15.0 An Independent sample T-test was used to compare the serum levels of adiponectin between obese and none-obese subjects. Pearson correlations were used to establish the relationship between adiponectin concentration with lipid profiles and anthropometrical indexes on obese subjects. A p-value less than 0.05 were considered statistically significant.

RESULTS

Main objective of this study was to determine the correlation between antiserum adiponectin with anthropometrical indexes and lipid profile in obese males. Mean and standard deviation of anthropometrical characteristics and biochemical variables as well as significance levels of the studied variables with serum adiponectin in obese subject have been summarized in table 1. The findings of Independent sample T test showed that adiponectin level in obese subjects were significantly lower than those of none- obese group (5.68 ± 1.12 versus 7.69 – 1.88 μg /ml p = 0.009). The Pearson methods in obese subjects showed a positive significant correlation between serum adiponectin and total cholesterol (p = 0.037). A significant negative correlation also observed between adiponectin and fasting LDL levels (p = 0.031). However, the relationship between adiponectin with other lipid profile indicators such as HDL and triglyceride was not significant. But, our finding showed that adiponectin has a high negative correlation with TG/HDL ratio (p = 0.019). Also, decrease in adiponectin concentration was associated with increase of Systolic blood pressure (p = 0.005) and diastolic blood pressure (p = 0.019) of the studied subjects. Findings from Pearson analysis showed that although adiponectin has a negative linear correlation with each one of the anthropometrical indices, or in other words, an increase in these variables such as abdominal circumference, body mass index and waist to hip circumference ratio (WHO) is associated with decrease in serum adiponectin levels, but these relationships are not significantly from statistical perspective (p ≥ 0.05).

Table 1: Anthropometrical and laboratory characteristics, and their relation with serum adiponectin in middle-aged obese males.

Variable	M ± SD	Range	p-value	R
Age (years)	44 ± 7	38 - 49	0.011	**0.511**
Weight (kg)	100 ± 12	86 - 113	0.112	**0.192**
Height (cm)	175 ± 11	168 - 186	0.521	**0.223**
Systolic blood pressure (mmHg)	127 ± 9	110 - 140	0.005	**0.584**
Diastolic blood pressure (mmHg)	89 ± 9	70 - 100	0.019	**0.411**
Abdominal circumference	106 ± 18	101 - 125	0.086	**0.231**
hip circumference	104 ± 14	102 - 121	0.123	**0.245**
Abdominal to hip circumference ratio (WHO)	1.02 ± 0.08	0.97 - 1.09	0.211	**0.214**
Body mass index (kg/m2)	32.65 ± 3.14	30 - 36	0.188	**0.231**
Body fat Percentage (%)	33 ± 4	28 - 36	0.123	**0.236**
Visceral obesity	14 ± 4	13 - 17	0.236	**0.257**
Total cholesterol (mg/dl)	187 ± 31	119 - 228	0.037	**0.521**
Triglyceride (mg/dl)	168 ± 38	114 - 242	0.201	**0.218**
Low density lipoprotein (mg/dl)	141 ± 33	103 - 161	0.031	**0.196**
high density lipoprotein (mg/dl)	44 ± 5	38 - 48	0.074	**0.238**
TG/HDL	3.81 ± 1.03	2.44 - 5.14	0.019	**0.534**
Adiponectin (µg /ml)	**5.68 ± 1.12**	**4.14 - 6.63**	**---**	**----**

DISCUSSION

Our study shows that serum adiponectin levels were significantly decreased in obese males compared to those with none- obese. The role of adiponectin has been repeatedly reported to promote lipid oxidation and glucose uptake in skeletal muscles as well as reduction of hepatic glucose production by inhibiting hepatic gluconeogenesis [25, 26]. Hence, extensive studies have been carried out or are conducting on factors affecting determination of systemic levels of this hormone and its secretion from adipose tissue. This 247 amino acid peptide hormone has antiatherogenic and anti-diabetic features [27, 28]. In this study, the role of anthropometrical factors and blood lipid levels on serum adiponectin concentration was studied in obese males.

The findings of present study demonstrate that obesity is accompanied with low adiponectin. This finding indicates the independent impact of obesity on this peptide hormone. Although, this study confirms the reduction of adiponectin levels in obese subjects, once the independent relation of each one of anthropometrical indexes such as BMI or abdominal circumference was examined with serum adiponectin separately, these relationships are not significantly from statistically perspective. In other words, although increase of the levels of anthropometrical indices is accompanied with decrease in serum adiponectin levels, but this relationship was not statistically significant. Based on this data, so we can probably conclude that increase in combination of a set of determinants of obesity with one another leads to reduction of adiponectin levels in obese subjects. Overall, relying on the serum adiponectin levels being lower in obese individuals than subjects with normal weight in this study, it can be concluded that obesity has been a decisive factor in adiponectin reduction in the studied subjects.

In other studies, reduction circulating adiponectin levels has been also observed in obese populations [10, 29]. Another major aim of this study is to determine the relationship between lipid profile indices and adiponectin levels in the studied subjects. In this regard, the study results showed that despite the inverse linear relationship between serum adiponectin and fasting triglyceride levels, this relationship is not significant. These finding state that TG and HDL are not precise predictors of serum adiponectin. In fact, although HDL tended to be negatively correlated with the serum adiponectin level, this did not reach statistical significance. In this area, some study did not found any correlation between adiponectin and lipid profile markers (TG, TC, and LDL) or anthropometrical indexes [19, 21]. In another study, adiponectin were significantly correlated with circulating levels of TG, TC, LDL, and HDL independent of BMI or adiposity [20, 24). It should also be noted that low number of participants is a one of the limitations of this study. On the other hand, it is probably that lack a significant relation between adiponectin with TG or HDL in this study to be due to low number of participants who have participated in this study.

Despite the lack of significant relationship between serum adiponectin with HDL and triglyceride levels in these individuals, the statistical data indicated a negative significant relationship between serum adiponectin concentration with total cholesterol and LDL levels. So that increase in circulating TG level as an index of lipid profile leads to reduction of serum adiponectin. Confirm the findings in our study; Rubin et al observed that increase of TG concentration is associated with decrease in adiponectin levels [30]. In addition, our study findings showed a significant negative correlation between serum adiponectin and TG/HDL ratio in these subjects which is of the determinants of cardiovascular disease [31]. These findings support the hypothesis that low adiponectin is associated with prevalence of cardiovascular disease. The findings of this study also showed that decrease in serum adiponectin levels is associated with increase of blood pressure and fasting glucose level of the studied subjects. The Inverse relationship of adiponectin with blood pressure in obese patients has also been observed in the study of Lee et al [32].

Conclusion

In summary, the findings of this study along with most previous findings indicate decrease adiponectin levels in obese subjects compared with those with normal weight. Based on our findings, it was concluded that although in the present study on obese subjects, obesity and high levels of some lipid profile markers such as TC, LDL and TG/HDL ratio is

accompanied with decrease in serum adiponectin. These findings support the hypothesis that low systemic adiponectin is a appreciate predictor of cardiovascular disease prevalence. Nevertheless, the specific mechanisms responsible for these observations are not fully understood and require further studies in this field.

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