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Original Article

Relationship between Visceral Adiposity and Plasma Adiponectin Concentration: Effect of Weight Loss

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Abstract

Background: Adiponectin is an anti-inflammatory and antiatherogenic protein that has a protective effect against atherosclerosis and diabetes. It is exclusively secreted by adipose tissue. Serum adiponectin levels are inversely associated with parameters of overall adiposity including body mass index (BMI), fat mass, and percentage of body fat.

Methods: In a cross-sectional study of 76 women we sought to evaluate if adiponectin is associated primarily with central adiposity rather than overall adiposity. We also assessed adiponectin changes after weight loss in a subgroup of 42 obese subjects.

Results: Waist to hip ratio (WHR), an index of central obesity, was the only variable independently associated to adiponectin (Beta= 0.25, $P< 0.05$). A mean increase of 8.2±24.2% in adiponectin concentration was observed in response to the dietary restriction and weight loss ($P= 0.03$). Our findings provide evidence for association of serum adiponectin level with visceral fat, represented by waist to hip ratio index.

Conclusion: Moderate weight loss result in significant improvements in adiponectin concentration and provide another biological explanation for the beneficial effect of body weight loss on reducing cardiovascular and diabetes risks in obese patients.

Keywords: *Adiponectin, Visceral adiposity, Waist to hip ratio, Body mass index, Iran*

Introduction

It is well known that obesity is associated with metabolic cardiovascular disease (1). Until recently adipose tissue (AT) was commonly viewed as a rather specialized organ for fat storage and mobilization, but recent evidence has shown that AT expresses active proteins. Adiponectin is one of the proteins exclusively secreted by adipose tissue and circulate in high concentrations in blood (2). It is one of the most abundant AT-specific proteins that in contrast with other adipose derived proteins, is decreased in obese subjects (3). Accumulating evidence from animal and human studies shows that adiponectin has anti-inflammatory (4) and antiatherogenic effects (5) and may improve the lipid profile (6). Serum adiponectin levels are decreased in patients with obesity and type 2 diabetes (7) and are inversely associated with parameters of overall adiposity [eg. Body mass index (BMI), fat mass, and percentage of body fat] (8, 9). It is worth to evaluate whether adiponectin is associated primarily with central adiposity rather than overall adiposity and whether central fat affects insulin sensitivity by altering adiponectin levels.

Despite the increasing rate of obesity in our society, there is little information on circulating levels of adiponectin in our obese or normal weight population and its modulation after weight loss, so considering the potential role of adiponectin as a cardio-protective and anti-inflammatory agent, we sought to assess the association of adiponectin levels with several anthropometric and metabolic variables in a cross-sectional study of 76 women. In addition, to evaluate the effect of weight loss on adiponectin concentration, we measured adi-

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ponectin levels at baseline and 10 weeks after a restricted diet program in a subgroup of obese subjects.

Materials and Methods

The study sample included 76 women aged 20-55 yr. Participants were selected on purpose to cover a wide range of body mass index (BMI) values (19.9-40.9 kg/m²). All subjects were healthy, nonsmoking and were not under treatment for coronary heart diseases, diabetes, dyslipidemias, or endocrine disorders. All participants gave their written consent to participate in the study.

Measurements Body weight was recorded while the subjects were wearing light clothing without shoes to the nearest 0.1 kg. Height was measured to the nearest 0.5 cm, and BMI (kg/m²) was computed. WHR (waist to hip ratio) was defined as the minimal abdominal circumferences between the xiphoid process and the iliac crests (waist) with subjects standing and breathing normally, divided by the hip circumferences, measured on the greater tronchanters. Body composition was determined using Bioelectrical Impedance Analyzer (BIA). Measurements were obtained using the Human-IM Plus DS Medica instrument, current-source electrodes were placed on the base of the fingers and toes (10).

Fasting blood samples were collected at baseline. Plasma or serum was isolated and was frozen at -70 ºC until analyzed. Glucose, total cholesterol, HDL cholesterol, LDL cholesterol and triacylglycerol were measured on a Hitachi 717 auto analyzer (Boehringer Mannheim, Indianapolis, IN) with the use of commercially available enzymatic kits (Pars Azmoon, Tehran, Iran). Fasting insulin was measured with a radioimmunoassay kit (IRMA KIT, Prague, Czech Republic). Insulin sensitivity was derived from fasting glucose and insulin data and was calculated by (1/(log fasting insulin level) + (log fasting glucose level)) (11). Circulating plasma levels of adiponectin was assessed by ELISA (Linco Research, Inc., St Charles, MO). Intra-assay and inter-assay coefficients of variation for adiponectin were 5.7% and 3.4%. Baseline and final samples of all subjects were assayed in the same batch to minimize inter-assay variability.

Intervention study Forty-two obese subjects (BMI ≥ 30 kg/m²) underwent a 10 week energy restriction program. The diets were prescriptive fixed-menu plans. Each subject had to complete daily checklists of all foods consumed and was assessed by a dietitian every 2 weeks. The composition of the diets consumed by the subjects and their compliance throughout the study were assessed through analyzing the three consecutive days (one weekend and two weekdays) of the checklist from each 2-week visit with the use of Food Processor II software. At week 10 body weight and body composition measurement were performed. At the same time points single blood sample was also taken in the morning after the subjects had fasted overnight for measurement of serum glucose, insulin, lipids and adiponectin concentration.

Statistical Analysis Data are presented as Mean±SD. Differences at baseline were analyzed using a one-way analysis of variance. Linear relationships among variables were computed by spearsman's correlation coefficients. Regression with a step-type backward elimination procedure was used to determine the relative contribution of statistically significant predictors of adiponectin concentration. The effect of diet intervention in obese group was tested by student-paired *t* test. The level of significance was set at $P< 0.05$ for all analysis. The calculations were performed using SPSS version 10.0 (SPSS Chicago, IL).

Results

General characteristics of the 76 subjects are presented in Table 1. Adiponectin concentration was significantly lower in obese group in comparison with that of the non-obese group (Table 2). In the overall samples adiponectin levels were negatively correlated with BMI, WC (waist circumference), WHR (waist to hip ratio), total body fat and positively with insulin sensitivity (Table 3).

Step-type multiple regression analysis based on backward elimination criterion involving predictor variables (BMI, WC, WHR and total body fat) showed that WHR was the only variable independently associated to adiponectin (Beta= 0.25, $P< 0.05$). The non-obese group was studied only once at baseline and the data were used only for baseline comparison.

Obese vs. nonobese subjects When subjects were grouped according to BMI into nonobese (BMI< 30 kg/m²) and obese (BMI ≥ 30 kg/m²) groups, plasma adiponectin was inversely correlated with fasting insulin level in obese subjects (r= - 0.33, $P= 0.03$), but not in nonobese subjects.

Intervention study data At 10 week of restricted diet, the subjects lost 6.1± 2.6% of their initial weights. Values at baseline and after weight loss for all measured variables are displayed in Table 3. All variables except HDL-C improved significantly. A mean increase of 8.2±24.2% in adiponectin concentration was observed in response to the dietary restriction and weight loss ($P= 0.03$). When adiponectin changes were calculated as Δ values (plasma concentration after weight loss minus baseline level), Δ-adiponectin was correlated with changes in HDL-C (r= 0.38, $P< 0.02$). (Table 4)

Table 1: Cross-sectional study, general characteristics at baseline[1]

	Total n=76	Non obese n=34	Obese n=42	Between groups *P* value
Age (yr)	37.3±8.44	39.2±9.4	35.7±7.3	0.07
Weight (kg)	72.9±13.1	61.4±6.2	82.2±9.1	<0.001
BMI(kg/m²)	29.2±5.0	24.6±2.4	32.9±3.0	<0.001
WHR	0.77±0.06	0.74±0.04	0.79±0.06	<0.001
Body fat (kg)	25.6±9.3	17.6±4.9	32.0±6.6	<0.002
Body fat (%)	38.7±4.3	27.9±6.3	10.8±1.2	<0.001
SBP (mmHg)	10.8±1.2	10.5±0.8	11.1±1.4	0.032
DBP (mmHg)	7.1±1.5	6.5±1.0	7.7±1.6	<0.001

[1]All values are Mean±SD. BMI: body mass index, WHR: waist to hip ratio, SBP: systolic blood pressure, DBP: diastolic blood pressure.

Table 2: Cross-sectional study. metabolic characteristics of the two study groups at baseline[1]

	Non obese n=34	Obese n=42	*P* value
Glucose (mg/dl)	89.2 ± 12. 7	94.6 ± 9.6	0.04
Insulin (mU/L)	6.7 ± 6.2	7.1 ± 4.1	0.68
Insulin sensitivity	0.40 ± 0.08	0.37 ± 0.03	0.02
Total Cholesterol (mg/dl)	184.8± 30.9	201.4 ± 33.7	0.03
HDL-C (mg/dl)	50.8 ± 11.2	50.1 ± 8.8	0.75
LDL-C (mg/dl)	96.3 ± 21.3	94.4 ± 17.2	0.67
LDL/HDL	2.0 ± 0.65	1.9 ± 0.45	0.72
Triacylglycerol (mg/dl)	114.1 ± 40.9	133.6 ± 55.8	0.09
Adiponectin (µg/ml)	11.9 ± 1.6	9.9 ± 3.9	0.006

[1]All values are Mean±SD. HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, LDL/HDL, LDL to HDL ratio, logCRP: logarithmic CRP.

Table 3: Cross-sectional study. Correlation (r) among BMI, WC, WHR, body fat(kg), body fat percent, insulin sensitivity and circulating concentration of adiponectin

	Before weight loss	**After weight loss**	**Difference**	***P***
Weight (kg)	82.2±9.1	77.2±8.6	5.01±2.2	<0.001
BMI(kg/m²)	32.9±3.0	30.9±2.8	1.99±0.94	<0.001
WHR	0.79±0.06	0.71±0.05	0.08±0.06	<0.001
Body fat(kg)	32.0±6.6	28.4±6.6	3.6±2.2	<0.001
Body fat(%)	38.7±4.3	36.6±4.9	2.1±2.1	<0.001
FBS(mg/dl)	94.6±9.6	88.3±8.4	6.4±8.6	<0.001
Insulin sensitivity	0.37±0.03	0.40±0.03	-0.03±0.03	<0.001
Cholesterol(mg/dl)	201.4±33.7	189.9±44.4	11.5±34.2	0.035
HDL(mg/dl)	50.1±8.8	47.9±7.4	2.1±6.9	0.052
TG (mg/dl)	133.6±55.8	112.6±43.0	21.0±35.8	<0.001
Adiponectin(µg/ml)	9.9±3.9	10.7±4.9	-0.81±2.3	0.03

Table 4: Interventional study. anthropometric and metabolic characteristics of obese subjects at baseline and after weight loss diet[1]

	Adiponectin (r)	***P*-value**
BMI(kg/m²)	-0.34	< 0.005
WC (cm)	-0.38	0.002
WHR	-0.30	<0.009
Body fat (kg)	-0.32	<0.005
Body fat (%)	-0.21	0.065
Insulin sensitivity	0.27	<0.02

BMI: body mass index, WC: waist circumference, WHR: waist to hip ratio.

[1]All values are Mean±SD. BMI: body mass index, WHR: waist to hip ratio, FBS: fasting blood sugar, HDL: high density lipoprotein, TG: triacylglycerol.

Discussion

The relationship between obesity, insulin resistance, and type 2 diabetes is well known (1). The mechanisms of this relationship, however, are still unclear. In particular, the role of adipose tissue and the role of substances it secretes, in determining insulin resistance requires a better understanding.

In the present study, we have investigated the specific role of adiponectin by analyzing the correlation of its plasma level with a variety of metabolic and anthropometric parameters. First we studied nondiabetic subjects spanning a wide range of BMI (from normal weight to severe obesity) and found that adiponectin concentrations correlated with BMI, total body fat, waist circumference, waist to hip ratio and insulin sensitivity. The multiple regression analysis revealed that among all adiposity variables studied, waist to hip ratio as an index of visceral fat accumulation was the only independent predictor of adiponectin levels. Indeed our study has shown that waist to hip ratio could explain 12% of the variation in adiponectin concentrations, suggesting that adiponectin may represent a link between central obesity and insulin sensitivity. The relationship of adiponectin with adiposity (BMI, fat mass, percentage of fat mass) has been previously reported to be inversely associated with

serum adiponectin in Japanese people (3, 8, 9, 12, 13), Pima Indians (14), and Caucasians (15). But recently similar to our findings, Gavrila et al. (16) have reported that intra abdominal fat (but not BMI) was significantly and independently associated with adiponectin, whereas a Japanese study (9) has reported an inverse association between adiponectin and WHR just in morbidly obese patients but not in overweight and moderately obese patients. The associations of visceral fat accumulation with variables of the plasma lipoprotein and lipid profiles have been reported previously. The present study shows that low plasma adiponectin concentration is also added to other risk factors associated with visceral fat.

Our data indicating the correlation between adiponectin levels and insulin sensitivity is in agreement with observation having already been reported (7, 17, 18). Interestingly, changes in insulin sensitivity and adiponectin levels were not correlated after weight loss. Although our findings is in agreement with Manigrasso and et al. (19), but some previous studies have shown this correlation after weigh reduction (20). Those reasons that we were unable to demonstrate this relationship, possibly related to small sample size or differences in the method of determining insulin sensitivity. For example, our study measured insulin sensitivity by estimating method (11), whereas those studies mentioned used euglycemic-hyperinsulinemic clamp procedure (17). However this finding may have different explanations that demand further studies.

Weight loss was associated with favorable changes in adiponectin concentrations in obese subjects. This finding is in agreement with previous observation (16, 21, 22), and in contrast with those that reported no significant changes of plasma adiponectin after weight loss (23, 24). The mechanisms of regulating plasma adiponectin levels by body weight changes are still unknown and merit further studies. Our observation that changes in adiponectin levels after weight loss were correlated with HDL-C changes is similar to data reported by Xydakis and et al. (25). This correlation may be secondary to modulation of HDL metabolism by adiponectin (26).

In summary our findings provide evidence for association of serum adiponectin level with visceral fat, represented by waist to hip ratio index. Our results also indicate that moderate weight loss result in significant improvements in adiponectin concentration. This provides another biological explanation for the beneficial effect of body weight loss on reducing cardiovascular and diabetes risks in obese patients.

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The authors declare that they have no Conflict of Interests.

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