EFFECT OF MODEST WEIGHT LOSS ON CARDIOVASCULAR INFLAMMATORY MARKERS IN OBESE WOMEN

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Abstract

INTRODUCTION: Obesity is associated with an increased risk of coronary heart disease. It is believed that adipose tissue inflammatory substances contribute to the pathogenesis of cardiovascular disease. To find out the metabolic benefits of weight loss in reducing cardiovascular risk, we assessed the effect of modest weight loss on plasma inflammatory markers in obese women.

METHODS: In a clinical trial, 42 obese women underwent a 10 week restricted diet program. Body weight, fasting glucose, insulin, total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c) and plasma inflammatory cytokines were measured at baseline and after 10 weeks.

RESULTS: Weight, BMI, fasting blood glucose, insulin, cholesterol and triglyceride had significant reductions. No significant changes were observed in HDL-c and LDL-c concentrations. All plasma inflammatory proteins improved significantly except CRP level.

CONCLUSIONS: Modest weight loss (≈5%) is associated with favorable changes in plasma inflammatory markers.

Keywords: Obesity, weight loss, inflammatory markers, cardiovascular disease.

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Introduction

Obesity is associated with an increased risk of coronary heart disease, stroke, hypertension, type 2 diabetes mellitus, and dyslipidemia. One mechanism of this relation might be the enhanced production of adipose tissue-derived proteins, such as interlukin-6 (IL-6), tumor necrosis factor-α (TNF-α), C-reactive protein (CRP) and leptin or decreased production of adiponectin.[12,13] Elevated levels of CRP and IL-6 indicating chronic subclinical inflammation, have been associated with features of insulin resistance[14,15] and incident cardiovascular disease, including myocardial infarction, stroke, and peripheral vascular disease.[16-20]

Adiponectin, a cytokine that is exclusively and abundantly expressed in adipose tissue is an anti-inflammatory protein that has a protective effect against atherosclerosis.[8] A number of observations correlate serum leptin with the pathogenesis of atherosclerotic vascular disease. TNF-α activates the transcription factor, which organizes inflammatory changes in vascular tissue.[9] Weight control is a widely accepted and recommended clinical goal in patient with type 2 diabetes and obesity.[1] The impact of weight loss on mortality and morbidity, in particular from cardiovascular disease, is still a matter of debate.[21] Investigating the effect of weight loss on the mentioned inflammatory markers might explain the role of weight reduction in reducing cardiovascular risk factors.

The aim of this study was to assess the effect of modest weight loss on plasma inflammatory markers in Iranian obese women for the first time.

Materials and methods

Forty-two obese women (BMI ≥ 30 kg/m^2) aged 20-47 years underwent a 10-week weight loss diet. All subjects were healthy, nonsmoking and not under treatment for coronary heart disease, diabetes, dyslipidemias, or endocrine disorders.

Most subjects were sedentary at baseline and were asked to continue their usual physical activity levels throughout the study. All participants gave their written consent to participate in the study.

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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.

Fasting blood samples were collected at baseline. Plasma or serum was isolated and frozen at -70 ºC until analyzed. Glucose, total cholesterol, HDL cholesterol, LDL cholesterol and triglyceride 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 as [1/ (log fasting insulin level) + (log fasting glucose level)].[9] Circulating plasma level of adiponectin was assessed by ELISA (Linco Research, Inc., St Charles, MO).

Plasma TNF-α and IL-6 were measured by ELISA (Bender MedSystem, Viena, Austria) and CRP was measured with a particle-enhanced immuno-turbidimetric assay with the use of commercially available enzymatic kits (Pars Azmoon , Tehran, Iran). Plasma leptin concentration was determined using ELISA (IBL Co, Gunma, Japan). Intra-assay and inter-assay coefficients of variation were 5.7% and 3.4% for adiponectin, 6.9% and 7.4% for TNF-α, 3.4 and 5.2 for IL-6, 10.1 and 6.4 for leptin, respectively. Baseline and final samples of all subjects were assayed in the same batch to minimize inter-assay variability.

Data are described as the mean ± SD in the case normal distribution. The logarithm of the CRP value was calculated for analysis, because the distribution of the variable was skewed. The effect of dietary intervention was tested by Student's paired t-test. The level of significance was set at $P<0.05$ for all analyses. The calculations were performed using SPSS version 10.0 (SPSS Chicago, IL).

Results

Following 10 weeks of restricted diet, the subjects had a 6.1±2.6% weight loss. Analysis revealed that the modest change of weight improved insulin sensitivity ($P<0.0001$), decreased fasting glucose by 6.7% ($P<0.0001$), cholesterol by 5.7% ($P<0.04$), and triglycerides by 15.7 % ($P<0.0001$). There were no significant changes in low-density lipoprotein cholesterol (LDL-c) and high-density lipoprotein cholesterol (HDL-c) concentrations (Table1).

We also observed statistically significant changes ($P<0.05$) in plasma adiponectin, leptin, TNF-α and IL-6, but the changes were not significant ($P>0.05$) in logCRP (Table 2).

TABLE 1. Metabolic changes before and after weight loss in 42 obese women

	Baseline	Post-weight loss	Mean changes	P value
Weight (kg)	82.2±9.1	77.2±8.6	5.0±2.2	<0.0001
BMI (kg/m2)	32.9±3.0	30.9±2.8	2.0±0.9	<0.0001
FBS (mg/dl)	94.6±9.6	88.3±8.4	6.36±8.6	<0.0001
Insulin (mU/L)	7.2±4.1	4.5±2.7	2.7±3.6	<0.0001
Insulin sensitivity	0.36±0.02	0.39±0.03	-0.03±0.03	<0.0001
Total cholesterol (mg/dl)	201.4±33.7	189.9±44.4	11.5±34.17	<0.04
HDL-C (mg/dl)	50.0±8.8	49.4±7.8	0.6±5.2	NS
LDL-C (mg/dl)	94.5±17.2	96.3±19.8	-1.8±9.7	NS
Triglyceride (mg/dl)	133.6±55.8	112.6±43.0	21.0±35.8	<0.0001

All values are Mean±SD, NS: Non-significant, BMI: Body mass index, FBS: Fasting blood sugar

TABLE2. Inflammatory markers changes before and after weight loss in 42 obese women

	Baseline	Post-weight loss	Mean changes	P value
Adiponectin (µg/ml)	9.9±3.9	10.7±4.9	-0.8±2.3	0.03
Leptin (ng/ml)	26.1±8.2	21.6±7.7	4.5±7.7	0.0001
logCRP	0.22±0.4	0.17±0.3	0.05±0.4	NS
IL-6 (pg/ml)	3.4±1.5	2.8±1.6	0.6±1.3	0.005
TNF-α (pg/ml)	4.1±1.3	3.9±1.1	0.2±0.8	0.05

All values are Mean±SD, NS: non-significant, logCRP: logarithm C-reactive protein, IL-6: interlukin-6, TNF-α: tumor necrosis factor alpha

Discussion

The present study suggests that modest weight loss (≈6%) after a restricted diet in obese women is associated with improvement in fasting glucose, insulin, insulin sensitivity and lipid profile. Modest weight loss is also associated with potentially favorable changes in serum inflammatory markers.

This is contrary to some reports.[15] There is some evidence from the literature that only reduction in body weight above the threshold of 10% is likely to result in a significant decrease in circulating leptin levels.[1,10,11] In present study, however, moderate weight loss with a low-calorie diet in obese subjects led to a significant reduction in leptin concentration. It is suggested that leptin may contribute to the pathophysiology of atherosclerosis by promoting vascular inflammation, proliferation and calcification, and by increasing oxidative stress. These prothrombotic actions of leptin could potentially increase the risk of obese subjects for developing acute coronary events and venous thrombosis.[15]

Several studies suggest that adiponectin is protective against atherosclerosis, and increasing adiponectin may be helpful in decreasing the risk of coronary artery disease.[8-11,23] Adiponectin has been reported as the strongest independent variable for predicting carotid IMT in early atherosclerosis in obese juveniles.[17]. The vasoprotective effect of adiponectin is also supported by in vitro studies showing that adiponectin decreases the expression of adhesion molecules on endothelial cells,[29] suppresses foam cell formation by macrophages,[30] and inhibits vascular smooth muscle migration.[31] In the present study we realized the significant increase of plasma adiponectin concentration accompanied by weight loss. This finding is in agreement with other studies,[83] while some studies have failed to show any significant improvement in adiponectin concentration after moderate weight loss. Giannopoulou showed that weight loss program including exercise alone caused just small changes in body weight.[25] This study, in contrast with our results suggested that dramatic weight loss or clinical interventions for inflammatory changes including adiponectin are needed. In Rochlitz study, weight loss caused significant changes in some metabolic syndrome markers such as waist circumference, fasting blood glucose and HDL-c, but adiponectin changes did not reach statistical significance.[24]

Some studies suggest a discordant effect of moderate body weight loss on inflammatory markers. Manigrasso[20] suggested that CRP and IL-6 were the most sensitive for energy restriction, whereas adiponectin was not affected by a moderate weight decrease and might require prolonged periods of energy restricted diet to revert to normal. Antonios reported a marked improvement in glucose, insulin, leptin, and triglycerides after 4-6 weeks of weight loss, whereas adiponectin and TNF-α concentration did not change.[13] In our study, CRP was the least sensitive to weight reduction. Marcell[22] also reported that moderate to intense exercise was not associated with improved measures of chronic inflammation markers, as measured by CRP.

In the present study, there was a significant reduction in the level of IL-6 compared with baseline level. Interestingly, doubling of IL-6 level was found to be associated with a two-fold increase in the risk for myocardial infarction in apparently healthy men.[14] By analogy, it seems likely that a significant reduction in IL-6 level associated with weight loss could also reduce the cardiovascular risk in obese patients.

In conclusion, the present study suggests that the modest weight loss provides a protective cardiovascular effect in the obese subjects. Its effect is beyond the favorable changes in traditional cardiovascular risk factors such as lipid profile, but with improvement in sub-clinical inflammation. However, Longer-term studies are needed to show whether the improvement observed in inflammatory markers will eventually translate into a significant clinical benefit, i.e. delaying and/or reversing cardiovascular morbidity and mortality.

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