Original Article

Comparison of Adiponectin, Leptin and Blood lipid Levels in Normal and Obese postmenopausal women

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Abstract

Objective: To determine adiponectin, leptin and blood lipid levels in normal and obese postmenopausal women and to compare them.

Methods: Eighty postmenopausal women were selected which included 40 normal controls and 40 obese women matched for age and height. Adiponectin and leptin levels were determined by ELISA. Triglycerides, cholesterol, LDL cholesterol and HDL cholesterol were determined by standard kit methods using Clinicon 4010.

Results: Serum adiponectin level decreased and leptin level increased significantly ($P < 0.001$) in obese women compared to controls. Similarly triglycerides, cholesterol and LDL cholesterol were increased significantly ($P<0.001$) in obese subjects compared with controls. No significant change in HDL cholesterol was observed in both groups. Significant correlation of leptin with lipid profile was observed when both groups were combined.

Conclusion: Serum adiponectin level decreased and leptin level increased significantly in obese women compared to controls. Significant correlation exists between leptin and lipid profile in combined group (JPMA 56:391;2006).

Introduction

Adipose tissue is known to secrete various proteins that are recognized to play an important role in metabolism of carbohydrate, proteins and lipids.[1] Amongst them, leptin

and adiponectin play a key role in energy homeostasis and metabolism.

Leptin achieves most of its metabolic effects by the interacting with specific receptors located in the hypothalamus.[2] One candidate effectors molecule is the hypothalamic neuropeptide Y (NPY). Friedman[3] proposed that a loss of body fat leads to a decrease in leptin production and low circulating leptin levels stimulates neuropeptide Y (NPY) in the hypothalamus. NPY interacts with its hypothalamic receptors and induces a cascade of events that include increased food intake, decreased energy expenditure, decreased reproductive function, decreased body temperature and increased sympathomimetic activity. The net result is a state of positive energy balance, in which the food intake exceeds the energy expenditure. Conversely an increase in body fat results in an increase in the level of circulating leptin which induces melanocyte stimulating hormone to interact with its receptor. The interaction leads to decrease food intake, increased energy expenditure and increased sympathomimetic activity. The net result is a state of negative energy balance in which the energy expenditure exceeds the food intake. The settling point hypothesis of body weight regulation proposes that like a thermostat, the adipostat can be reset by factors in the environment.[4]

Adiponectin is 244 amino acid proteins and circulates at relatively high concentrations; its half life is several hours. Adiponectin increases tissue fat oxidation, leading to reduced levels of fatty acids and tissue triglyceride content, thus increases insulin sensitivity.[5] High fat feeding leads to decreased adiponectin secretion in rodents.[6] Similarly caloric restriction leads to higher circulating concentrations of adiponectin in mice and humans.[7] In vitro and vivo studies in rodents have shown that adiponectin prevents lipid accumulation in skeletal muscles in parallel to lowering blood glucose and improving insulin action.[8]

The objective of this study was to determine serum levels of adiponectin, leptin and lipid in obese postmenopausal women and compare them with normal subjects.

Subjects and Methods

Eighty postmenopausal women between 45 and 60 years were selected by convenient sampling including 40 normal controls and 40 obese women matched for age and height. Informed consent was obtained and study was approved by the Ethical Committee, Ziauddin Medical University, Karachi.

Obesity was classified on the basis of Body Mass Index (BMI Kg/m2) and Waist Hip Ratio. BMI is classified as under weight <19 (normal range is 19 to 24.9) overweight 25 to 29.9 and obese >30. On the basis of waist / hip ratio, women are classified as obese if the ratio is greater than 0.95.[9]

Individuals suffering from renal dysfunction, liver disease, congestive heart failure, retinopathy or cataract were excluded. Women on medications or hormone replacement therapy were also excluded from the study.

At first visit, height and weight of the participants were measured in light clothing. BMI was calculated as weight (in kilograms) divided by height (in meters) squared. Waist and hip circumference was measured in duplicate using a measuring tape. Each subject was called after overnight fast and 10 ml of the venous blood sample was taken, 5ml in sodium fluoride tube to check fasting blood glucose for the exclusion of diabetes mellitus and rest of 5 ml in plain tube which was centrifuged to obtain serum which was stored at -20 $\pm$ 5^{o}C for analysis of lipid profile, serum adiponectin and leptin levels.

Adiponectin and leptin levels were determined by ELISA by kits obtained from DRG Germany.[10,11] Triglycerides, cholesterol, LDL cholesterol and HDL cholesterol were determined by standard kit methods using Clinicon 4010.

Data was expressed as mean and standard deviation. Two groups were compared by Student's t- test to determine the significance. Correlations between adiponectin, leptin and blood lipids were assessed using Pearson's correlation coefficient. The data was significant if $P<0.05$ and highly significant if $P<0.001$.

Results

Forty postmenopausal women classified as obese, based on BMI and waist hip ratio were compared with the age matched normal subjects. Table 1 shows levels of serum adiponectin, leptin, cholesterol, triglycerides, low density lipoproteins (LDL) and high density lipoproteins (HDL) in normal controls and obese subjects. Serum adiponectin level was significantly decreased ($P<0.001$) in obese subjects while serum leptin levels increased significantly

Table 1. Serum Adiponectin, Leptin, Cholesterol, Triglycerides, LDL and HDL in Normal and Obese subjects.

	Normal Control (n=40) Mean ± S.D	Obese (n=40) Mean ± S.D	P Value
Adiponectin (ng/ ml)	8.58±2.25	6.41±2.19416	0.001
Leptin(ng/ml)	8.99±2.23	32.63±10.071	0.001
Cholesterol (mmol/l)	4.18±0.44	5.24±0.551	0.001
Triglycerides (mmol/l)	1.26+0.15	1.78+0.281	0.001
LDL(mmol/l)	2.62+0.45	3.61 +0.731	0.001
HDL(mmol/l)	1.02+0.20	0.93+0.11	0.120

Table 2. Correlation of Adiponectin and Leptin versus Lipid Profile in Normal Controls and Obese subjects and combined.

	Adiponectin	Leptin
Normal Controls		
Cholesterol	0.295	- 0.077
Triglycerides	0.135	0.213
LDL Cholesterol	0.240	- 0.006
HDL Cholesterol	-0.018	0.005
Obese		
Cholesterol	0.073	- 0.115
Triglycerides	0.179	- 0.048
LDL Cholesterol	0.109	0.038
HDL Cholesterol	- 0.099	- 0.204
Normal and Obese combined		
Cholesterol	-0.22	0.59 *
Triglycerides	-0.24	0.64 *
LDL Cholesterol	0.14	-0.36 *
HDL Cholesterol	-0.17	0.56 *

* Significant correlation ($p<0.05$). The numbers shown are the r value

($P<0.001$) in obese group compared to controls. All the values of the lipid profile were significantly increased ($P<0.001$) in obese subjects compared with control subjects except for HDL cholesterol, which was not significantly decreased compared with controls.

In obese subjects non-significant correlation was found between adiponectin and lipid profile and leptin and lipid profile (Table 2). Significant correlation ($p<0.05$) was observed between leptin and lipid profile when the two groups (normal and obese) were combined together (Table 2).

Discussion

Obesity, defined as excess fat accumulation, is the most common cause of cardiovascular morbidity and mortality in industrialized countries. Excess body fat accumulation, is frequently accompanied by diabetes mellitus, dyslipidemia, and hypertension and finally results in atherosclerotic vascular diseases. Adipose tissue secretes various bioactive molecules like adiponectin, leptin and other hormones like peptides that may directly contribute to the development of obesity-related diseases.[1] This study confirms low adiponectin levels, increased leptin levels and lipid profile in obese postmenopausal women. Postmenopausal women were taken as hormones in reproductive age group may interfere with the adiponectin and leptin levels.

The results of present study confirmed that triglycerides, cholesterol and LDL cholesterol levels were significantly higher in obese group compared to controls while no significant difference was found in HDL levels in both groups. Blood cholesterol and triglycerides levels reflect plasma free fatty acid levels. Plasma levels of fatty acids are elevated in obesity primarily because a greater than normal amount of free fatty acid is released from expanded adipose tissue mass even though the rate of lipolysis from individual fat cells appear to be normal[12], In obesity increased free fatty acid induced insulin resistance may result in type 2 diabetes and other cardiovascular factors.[13] In the present study it was found out that serum adiponectin levels decrease and leptin levels increase significantly in obese compared with control subjects. Plasma leptin concentrations are significantly elevated in obese subjects in proportion to the degree of adiposity, suggesting that hyperleptinemia may play a role in the pathogenesis of obesity related complications.[14] Leptin receptors are present most abundantly in brain and are also present in various peripheral tissues. Mutation in the gene encoding the receptor results either impairment in the transport of leptin across blood brain barrier or impaired signal transduction. This results in leptin being unable to act on neuropeptides Y and therefore causes more food intake and less energy expenditure leading to obesity. The net result is leptin being unable to perform its functions despite being produced in excess. This phenomenon is called as leptin resistance.[15] Therefore leptin concentrations are increased in obese subjects. Adiponectin increases tissue fat oxidation, leading to reduced levels of fatty acids and tissue triglyceride content, thus increasing insulin sensitivity.[16] Paradoxically, plasma adiponectin concentrations are decreased in obese subjects[17], suggesting that hypoadiponectinemia is involved in the pathophysiology of obesity. Studies carried out by Shand et al.[17] and Matsubara et al.[18] have shown increased leptin levels and low adiponectin levels in overweight and obese subjects. Similar studies by Kondo et al.[19], Horta et al.[20] and Weyer et al.[21] also showed relationships of low adiponectin concentration and type 2 diabetes. Study by Faraj et al revealed adiponectin concentrations increase concomitantly with weight loss.[22] Therefore determination of leptin and adiponectin levels in obese individuals may guide us to the risk of developing insulin resistance and diabetes in these individuals. Preventive measures can be taken in such individuals, based on these determinations to prevent diabetes and its complications.

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