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Original article

Association of circulating adipokines with metabolic dyslipidemia in obese versus non-obese individuals

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ABSTRACT

Aim: Previous studies have shown that circulating adipokines may play an important role in the pathogenesis of some obesity related chronic disease such as dyslipidemia and type2 diabetes mellitus. The aim of the present study was to investigate the association between vaspin, omentin-1 and retinol binding protein-4 levels with metabolic dyslipidemia (MD) criteria in obese and non-obese individuals.
Method: The study was conducted on 170 obese and 81 non-obese individuals. After collecting the blood samples, serum levels metabolic parameters as well as three circulating adipokines and body composition were measured.
Results: No significant difference was noted regarding the mean serum levels of omentin-1 and vaspin between the obese and non-obese groups, while, serum level of RBP4 was significantly higher in the non-obese group. We found the 0.22 increased risk of MD in obese individuals with higher RBP4 concentration. After the adjustment for confounding factors, this association was still significant. No significant association was noted between MD and its components relative risks with omentin-1 and vaspin levels.
Conclusion: Our study demonstrated that circulating RBP4 was significantly higher in the obese individuals which may increase the risk of MD in them. Further researches are needed to address this association.

1. Introduction

In the recent decades, following the industrial developments of countries, various factors particularly sedentary life style and western dietary patterns have led to a rise in prevalence of obesity and obesity-related chronic diseases such as some kinds of cancers, type 2 diabetes and other metabolic disorders [1,2]. Based on the reports from World Health Organization (WHO), prevalence of obesity has doubled from 1980 to 2011 and also, about 312 million people are suffering from obesity [3].

Recent data has indicated that obesity and the adverse health consequences associated with it particularly type II diabetes mellitus and metabolic syndrome, are commonly associated with an imbalance in lipid profile. One of the most common abnormalities in obesity is metabolic dyslipidemia (MD) [4], which is characterized by increased triglyceride levels and decreased High-Density Lipoproteins (HDL) levels. This disorder is regarded as one of the important risk factors of cardiovascular diseases [5].

Among various factors involved in the pathogenesis of dyslipidemia, adipose tissue is a crucial that plays a major role in onset of this disorder. White adipose tissue (WAT) is an endocrine organ that secretes various factors called as "adipokines" [6]. Adipokines are variety groups of proteins that have been linked with homeostasis [7], insulin sensitivity [8]. appetite regulation and macronutrients metabolism [9]. Accordingly, several studies have demonstrated that impaired secretion of adipokines can cause obesity related diseases such as dyslipidemia [10]. Recent studies have been conducted on mostly vaspin, omentin-1 and RBP4 from the extended members of adipokines family.

Vaspin is one of the most important adipokines belonging to serin protease family secreted by visceral adipose tissue. This adipokine has been first found in visceral adipose tissue of OLTEF

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rats, a rodent model for insulin resistance and abdominal obesity [11]. Several studies have shown that vaspin concentration can be increased with obesity and insulin resistance and also, decreased with insulin therapy or pioglitazone treatment [12]. Furthermore, Esteghamati et al., previously reported that vaspin concentration was associated with some of the metabolic syndrome criteria in particular HDL, cholesterol and waist circumference [13]. Taken together, the association of vaspin concentration and obesity related disease such as metabolic syndrome and dyslipidemia was inconclusive [14].

Omentin is another family member of adipokines that secreted from visceral adipose tissue. Among the different isoforms of omentin, omentin-1 is a major isoform in human plasma [15]. Several studies have shown that omentin-1 plays an important role in some process such as insulin stimulated glucose uptake in human adipocytes, Akt/PKB phosphorylation and decrease the level of some inflammatory agents such as C-reactive protein (CRP) and TNF-α. Moreover, some data have indicated that plasma levels of omentin-1 may be decreased in metabolic syndrome, diabetes patients [16] and obese people [17].

RBP4, as a newly discovered adipokine is mostly known for having role in the transport of vitamin A, however, researches have shown diverse roles of RBP4 [18]. Compelling evidence suggests that elevated levels of RBP4 is associated with impaired insulin signaling pathway, [19] insulin resistance [20] and metabolic abnormalities particularly dyslipidemia [21].

It seems that these adipokines may be linked with developing of obesity related disorders such as dyslipidemia. Hence, the aim of this study was to investigate the association between vaspin, omentin-1 and RBP-4 levels with MD criteria in obese and non-obese participants.

2. Materials and methods

2.1. Subjects

The present study was conducted as a comparative cross sectional study. The study protocol was approved by the local ethical committee of Endocrinology and Metabolism Research Institute of Tehran University of Medical Sciences. Individuals were included if they met following criteria: having $30 \leq BMI \leq 39.9$ kg/m^2 for the obese group and $18.5 \leq BMI \leq 24.9$ kg/m^2 for non-obese group. Individuals with the exclusion criteria namely were having morbid obesity (BMI ≥ 40 kg/m^2), being overweight ($24.9 \leq BMI \leq 29.9$ kg/m^2), suffering from diabetes, hypothyroidism, history of acute or chronic inflammation and consumption of any pharmaceutical drugs as well as dietary supplements that can influence lipid profile.

MD was diagnosed as having two features: TG levels ≥ 150 mg/dl and reduced HDL levels (<40 mg/dl in men and <50 mg/dl in women) [5]. All participants were provided written and informed consent forms and completed a self-administered questionnaire regarding demographic characteristics, health status, history of smoking and participants' current medications.

2.2. Body composition analysis

Body composition of all participants was assessed through BODY COMPOSITION ANALYZER BC-418MA-Tanita device (United Kingdom). To increase the accuracy of measurement, individuals were advised to avoid exercise and intensive activity on the day of body composition measurement and analyzing the body composition was started only if the participants had sufficient resting. To prevent inaccurately low body fat percentage measurements as well as other measurement errors, participants were asked to hold both arms straight down while taking measurements. Body composition analysis was performed in the morning while participants having a fasting condition due to the fact that distribution of total body water can be affected by body temperature and food intake. Body fat percentage, fat mass, fat free mass and predicts muscle mass were assessed on the basis of data that obtained by Dual Energy X-ray Absorptiometry (DXA) using Bioelectrical Impedance Analysis (BIA). Electrical signals that send out by device passes from the fat mass, fat free mass and body water with a different speed and rate, so that amount of signals that passes from the fat free mass and body water is more than the fat mass. This difference is determined by a phrase which named "electrical resistance". The percentage of fat and other body constituents can be inferred by the measurements of this resistance.

2.3. Measurement of anthropometric and blood parameters

Height and weight were measured at baseline. Height was measured by Seca stadiometer, with accuracy about 0.5 cm and weight was measured by Seca scale in light clothing and barefoot with accuracy nearest to 100 g.

Blood samples were obtained from all individuals in early morning after having the 12 h fasting state at the beginning of study. Serum concentrations of triglyceride and fasting glucose were measured by GPO-PAP and GOD/PAP methods, respectively, Total cholesterol level was measured by Enzymatic Endpoint method and direct HDL-C was measured using enzymatic clearance assay. Insulin, fasting serum glucose and lipid profile measurements were analyzed by Randox laboratories kit (Hitachi 902). Serum vaspin concentration was measured by Human visceral adipose specific serine protease inhibitor (vaspin) ELIZA kit (CUSABIO BIOTECH, Wuhan, China), with the sensitivity of 0.8 pg/ml and an intra-assay and inter-assay variability of 1.3–3.8 and 3.3–9.1%, according to the manufacturer. Serum concentration of RBP4 was measured by competitive enzyme-linked immunosorbent assay (ELISA) (AdipoGen, Seoul, Korea) and inter and intra-assay variability were 4.2% and 4.5%, respectively. Finally, omentin-1 concentration was assayed through ELISA (Enzo Life Sciences; sensitivity: 0.4 ng/ml; reference range: 0.5–32 ng/ml inter-assay variability: 4.61%; intra-assay variability: 5.2%) (Cat. No. APO-54 N-034).

2.4. Statistical analysis

Statistical analysis was performed using SPSS version 19 (IBM Corp., New York, NY, USA). Normal distribution of data was assured using Kolmogrov–Smirnov. Normally distributed variables are reported as Mean ± standard deviation. Baseline characteristics of variables were compared among two groups using independent sample *t*-test, Mann–Whitney test and Chi-square test, whenever, to determine the association between normally distributed variables, partial correlation test was used and the level of significance was set to <0.05 for all tests. Logistic regression models were incorporated to assess the associations between circulation adipokines and each MD criterion, adjusting for weight, age and sex. In all regression models, odds ratios (OR) with 95% confidence intervals (95% CI) were calculated.

3. Results

3.1. Baseline characteristics of obese and non-obese participants

A total of two hundred fifty-one participants (obese group: $n = 170$ and non-obese group: $n = 81$) were included in this study. The mean age of obese and non-obese groups was 38.78 ± 12.2 and 33.3 ± 10.96 years, respectively. Study population, body composition, biochemical and anthropometric characteristics of two groups are