Diabetes & Metabolic Syndrome: Clinical Research & Reviews 10S (2016) S131–S134

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Serum C1q and tumor necrosis factor (TNF)-related protein 9 in women with Polycystic Ovary Syndrome

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ARTICLE INFO

Keywords:
C1q/TNF-related protein 9
Polycystic Ovary Syndrome
Adipokine

ABSTRACT

Aims: To compare CTRP9 levels in women with Polycystic Ovary Syndrome (PCOS) and without PCOS. Furthermore, to determine the correlation between serum CTRP9 levels and some variety of anthropometric and biochemical parameters.
Methods: The study included 29 PCOS patients and 27 healthy volunteers of the same age and BMI. Body weight, height and waist circumference were assessed. Blood samples were taken for assessment of serum CTRP9 by enzyme-linked immunosorbent assay (ELISA) technique. In addition, blood samples were collected for fasting insulin, glucose, and lipid profiles, and homeostasis model of assessment-insulin resistance (HOMA-IR) values were calculated.
Results: Similar serum CTRP9 were found in PCOS subjects and controls (8.8 ± 19.9 vs 5.0 ± 7.6 ng/mL). Serum CTRP9 concentration positively correlated with serum LDL-C and total cholesterol in patient group. However, no correlation between CTRP9 and other biochemical and anthropometric variables was found.
Conclusion: Serum CTRP9 logs of PCOS participants exhibit a positive association with unfavorable lipid profile in this report.

1. Introduction

Polycystic ovary syndrome (PCOS), a common endocrine disorder, negatively impact women in reproductive age [1]. According to the European Society for Human Reproduction and Embryology/American Society for Repro ductive Medicine (ESHRE/ASRM) criteria, the prevalence of PCOS is estimated 15–20%. The manifestations of the disease include irregular menstrual cycles, anovulatory infertility, polycystic ovaries, biochemical and clinical hyperandrogenism such as hirsutism, to name but a few [2]. PCOS contributes to insulin resistance, resulting in impaired glucose intolerance (IGT), type 2 diabetes mellitus, hypertension, dyslipidemia, and metabolic syndrome [2,3].

PCOS and metabolic syndrome are similar in creating the conditions for abdominal obesity and dysregulation of adipose tissue function; the latter can induce an alternation in expression and secretion of adipose tissue products termed adipocytokines or adipokines. With regard to significant effects of altered adipokines on insulin sensitivity, these changes may contribute to metabolic disturbances in PCOS [4,5].

A recent family of adipokines named C1q and tumor necrosis factor (TNF)-related proteins (CTRPs) have been proposed to play a role in energy regulation and particularly glucose metabolism. In addition, CTRPs have displayed anti-inflammatory and insulin sensitivity promoting effects [6,7]. CTRP9, the closest paralog of adiponectin, is suggested to have a correlation with body weight by animal research [8,9]. Moreover, an increase in CTRP9 expression in mice caused a significant reduction in plasma glucose and insulin levels [8,10], through activating AMPK, Akt, and p44/42 MAPK signaling pathways [10].

Studies revealed that there are significant differences in serum CTRP9 concentrations in diabetic patients in comparison with

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http://dx.doi.org/10.1016/j.dsx.2016.03.012
1871-4021/

healthy controls. The association between serum CTRP9 with metabolic syndrome, homeostasis model assessment for insulin resistance (HOMA-IR), Body Mass Index (BMI), visceral fat amount, fasting serum glucose and some markers of lipid profile had been demonstrated in literature [11,12]. Due to a high prevalence of metabolic syndrome and diabetes in PCOS women [2], it is hypothesized that there would be a difference in serum CTRP9 of subjects with PCOS versus healthy controls. Therefore, we aimed to determine the difference between serum CTRP9 concentrations in PCOS patients and healthy controls. We also aimed to examine the probable relationship between serum CTRP9 levels and some metabolic and anthropometric parameters.

2. Materials and methods

2.1. Subjects

Twenty nine recently diagnosed PCOS women were recruited (age: 18–38 y) from a public clinic of Tehran University of Medical Sciences. These patients have not been under any pharmacological treatment for the disease. The PCOS patients were singled out by a gynecologist based on ESHRE/ASRM criteria [13]. The subjects were failed to participate, unless they would satisfied two of the three following criteria: Clinical and/or biochemical hyperandrogenism, Oligo-ovulation or anovulation, ultrasonographic polycystic ovaries. Patients with other androgen excess or related disorders (e.g., congenital adrenal hyperplasia, cushing syndrome) were also excluded.

Twenty seven age- and body mass index (BMI)-matched healthy control women with regular menstrual cycles were enrolled into the study through a public advertisement in the same clinic.

Women with autoimmune, systematic infectious, social and psychological, and endocrine disorders other than PCOS were excluded from both cases and controls. None of the participants were on medications for at least 3 months prior to the study, including oral hypoglycemic agents, reducing fat absorption drugs, anti-inflammatory medications, antioxidant supplements, and oral contraceptives. Other exclusion criteria for two groups were pregnancy and lactation, smoking and alcohol history for at least 6 months prior to the sample collection. The written informed consent forms were signed by all participants at the time of enrollment. Our study was approved by the Ethics Committee of Tehran University of Medical Sciences Vice Chancellor for Research (ID: 9211468014).

2.2. Anthropometric measurements

Anthropometric measurements including body weight, height, and waist circumference were performed. Body weight and height were measured to the accuracies of 0.1 kg and 0.1 cm respectively. Body mass index was computed as weight divided by height squared (kg/m^2). Waist circumference was measured to an accuracy of 0.1 at midpoint between the lowest rib and the iliac crest.

2.3. Clinical and biochemical analysis

After a 10 h overnight fast, blood samples which drawn from the veins of adult female subjects were immediately centrifuged. Aliquots of plasma and serum samples were stored at −80 °C until biochemical analysis.

Serum CTRP9 concentrations were measured using commercial ELISA kit manufactured by Biovendor (Bio Vendor LM, Brno, Czech Republic) according to the instruction of manufacturer. The kit had intra- and inter-assay coefficients of variations of 5.5% and 7.9% respectively. Limitation of detection for the assay was 9 pg/mL. We measured fasting serum glucose concentrations by the glucose oxidase method (Pars Azmoon Inc.; Tehran, Iran) and serum insulin by ELISA kit (Insulin ELISA kit; DiaMetra; Milan, Italy). The HOMA-IR indexes were calculated by the following formula: HOMA-IR = fasting glucose (mg/dL) × fasting insulin (μU/mL)/405 [14]. Total cholesterol, triglyceride (TG), high-density lipoprotein (HDL)-cholesterol, and low-density lipoprotein (LDL)-cholesterol levels were analyzed respectively using the cholesterol oxidase-phenol + aminophenazone (CHOD PAP), the glycerol-3-phosphate oxidase-phenol + aminophenazone (GPO PAP), immuno, and enzymatic kits on a BIOLIS 24i premium auto-analyzer (Tokyo, Japan).

2.4. Statistical analysis

All statistical analyses were performed using the SPSS statistical package compatible with Windows, version 18 (SPSS Inc. IBM CO). We used Kolmogrov–Smirnov test in order to explore the normality distribution of variables. Log transformation was conducted for skewed distributed variables. The differences in the mean of the variables were compared using a parametric and non-parametric tests; independent student *t*-test and Mann–Whitney *U*-test, respectively, according to their distribution. To find the relationships between log transformation of CTRP9 levels and other parameters, Simple Linear Regression model was used. $P < 0.05$ was regarded as statistically significant. All data are presented as mean ± standard deviation.

3. Results

The demographic, clinical, and anthropometric characteristics of participants are provided in Table 1. The means of CTRP9 levels were 8.8 ± 19.9 ng/mL in PCOS and 5.0 ± 7.6 ng/mL in control groups, respectively. These levels ranged from 0.025 to 82.3 ng/mL in patients and 0.025 to 31.1 ng/mL in control subjects.

Fasting serum CTRP9 concentration differences were not significant in two groups ($P > 0.05$). Among other biochemical parameters, serum levels of triglycerides were significantly higher ($P = 0.01$) and HDL-C levels were significantly lower ($P = 0.01$) in PCOS subjects than controls.

Age and BMI did not statistically differ between PCOS and control groups. However, PCOS women had significantly higher waist circumstances than healthy controls ($P < 0.001$).

Using linear regression, serum CTRP9 levels showed no significant correlation with age and anthropometric variables. Serum concentrations of CTRP9 positively correlated with serum LDL-C ($B = 0.019$; $P = 0.03$) and total cholesterol in PCOS group

Table 1
Basic, anthropometric and biochemical characteristics of patients and controls.

	PCOS	Control	*P* value
N	29	27	
Age (year)	26.2 ± 4.1	27.1 ± 5.0	0.46
Height (cm)	162.5 ± 6.2	161.9 ± 5.9	0.83
Weight (kg)	71.4 ± 13.5	67.3 ± 10.4	0.21
Waist Circumstance (cm)	93.5 ± 8.2	80.6 ± 9.9	<0.001
BMI	26.9 ± 4.2	25.6 ± 3.8	0.23
Triglycerides (mg/dL)	134.3 ± 81.0	91.5 ± 43.9	0.01
Total cholesterol (mg/dL)	184.2 ± 35.2	179.7 ± 35.0	0.63
LDL-C (mg/dL)	100.7 ± 23.7	96.4 ± 22.6	0.49
HDL-C (mg/dL)	41.7 ± 7.0	48.7 ± 12.4	0.01
Fasting blood sugar (mg/dL)	87.7 ± 11.1	73.5 ± 27.1	0.10
Fasting insulin (μU/mL)	8.6 ± 1.6	18.4 ± 26.2	0.43
HOMA-IR	1.1 ± 0.18	1.4 ± 1.1	0.61
CTRP9 (ng/mL)	8.8 ± 19.9	5.0 ± 7.6	0.74

PCOS: Polycystic Ovary Syndrome; BMI: body mass index; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; HOMA-IR: Homeostasis Model Assessment of Insulin Resistance; CTRP9: C1q and tumor necrosis factor (TNF)-related protein 9.