PLASMA LEVELS OF NESFATIN-1 IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Introduction. Polycystic ovary syndrome (PCOS) is an important disorder in women of reproductive age which is characterised with menstrual dysfunction, anovulation and hyperandrogenism. 5-10% of the female population affected by this syndrome (1,2). Clinical, biological and ultrasonographic criteria play role for diagnosis of the PCOS. Nesfatin-1 is a new anorexigenic hormone which is expressed from several regions of hypothalamus and peripheral tissues. Nesfatin-1 is related with obesity, insulin resistance and appetite. We aimed to evaluated the nesfatin-1 levels in patients with PCOS.

Material and methods: Sixty-five patients (37 patients with PCOS and 28 healthy control subjects) were enrolled in the study. We included newly diagnosed patients with PCOS in our study. Diagnosis of PCOS was based on the 2003 ESHRE/ASRM diagnostic criteria.

Results: The patients with PCOS and controls were similar in terms of mean age body mass index (BMI), waist/hip (W/H) ratio and homeostasis model assessment-insulin resistance (HOMA-IR) index. Plasma Nesfatin-1 levels were similar between groups. There was no correlation between plasma Nesfatin-1 levels and other parameters.

Conclusion: In conclusion nesfatin-1 may be play important role in glucose metabolism and insulin resistance. In this study due to the absence of insulin resistance in PCOS patients, levels of Nesfatin -1 were similar with control group. Nesfatin levels were associated with glucose metabolism, but further studies are needed in this regard.

Key words: Nesfatin-1, insulin resistance, polycystic Ovary Syndrome.

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Introduction

Polycystic ovary syndrome (PCOS) is an important disorder in women of reproductive age which is characterised with menstrual dysfunction, anovulation and hyperandrogenism. 5-10% of the female population affected by this syndrome (1,2). Obesity causes to infertility and increased the risk of amenorrhea (3). Insulin resistance is frequently found in obese PCOS women. Hyperglycemia is caused by increased insulin resistance, and increased androgen levels as a result of hyperinsulinemia enhances the action of luteinizing hormone (LH) on theca cell (6,7,8).

LH induce androgen secretion in the ovary, thereafter follicle growth and maturation are suppressed (9,10). Nesfatin-1/nucleobindin 2 (NCUB2) is composed of 82 amino acids and the half-life of 6 hours with low molecular weight11. This biomarker secretion is affected by hunger and satiety (12). Nesfatin-1 is a new anorexigenic hormone which is expressed from several regions of hypothalamus and peripheral tissues, including the adipose tissue, gastric mucosa, pancreatic beta-cells.

Recent studies demonstrated that Nesfatin-1 is related with obesity, insulin resistance and appetite. In this study we aimed to evaluated the Nesfatin-1 levels in patients with PCOS who have frequently seen with obesity and insulin resistance.
Material and method

Sixty-five patients (37 patients with PCOS and 28 healthy control subjects) were enrolled in the study. Each participant signed an informed consent form in accordance with the Declaration of Helsinki, and this study was approved by the local ethical committee of Canakkale Onsekiz Mart University.

We included newly diagnosed patients with PCOS in our study. Diagnosis of PCOS was based on the 2003 ESHRE/ASRM diagnostic criteria; oligo or anovulation, clinical and/or biochemical hyperandrogenism including elevated serum concentrations of testosterone (>2.8nmol/l) and/or a hirsutism score of more than 8 (according to Ferriman-Gallwey score) or positive ultrasound presentation of polycystic ovaries by transvaginal scan and/or abdominal scan defined as the presence of 12 or more follicles in each ovary measuring 2-9 mm in diameter and/or ovarian volume of > 10ml. We excluded patients who had a history of cardiovascular disease, cancer, systemic infection, diabetes mellitus, liver disease, renal disease, haematological disease, thyroid dysfunction, congenital adrenal hyperplasia, hyperprolactinemia or those who have received medical treatment and those who smoked or used alcohol. The control group was composed of healthy female volunteers who were tested negative for pregnancy at the Obstetrics and Reproductive Medicine Clinics. Demographic, anthropometric, and clinical variables, including age, gender, body mass index (BMI), were also recorded.

Collection and storage of blood samples

Venous blood samples of 5 mL were drawn simultaneously from the cases after one night fasting on 3-5 days of the follicular phase between 09:00 and 10:00 a.m. These samples were stored at -80 C until the time of analysis.

Hormonal and biochemical measurements

Levels of estradiol (E2), follicle-stimulating hormone (FSH), luteinizing hormone (LH), progesterone, prolactin (PRL), thyroid-stimulating hormone (TSH), total testosterone (TT), androstenedione (AD), dehydroepiandrosterone sulphate (DHEA-S), 17alpha hydroxyprogesterone (17-OHP), fasting serum insulin (FSI) and fasting blood glucose (FBG), cholesterol, triglyceride, high-density lipoprotein (HDL), low density lipoprotein (LDL) and very LDL (VLDL) were determined in the fasting venous blood samples. These laboratory parameters were measured in a Roche Cobas e 601 (Roche Diagnostics, Indianapolis,IN) autoanalyzer, using the kits recommended by manufacturers. Nesfatin-1 was measured in blood samples using a Human Nesfatin-1 ELISA kit (EIAab Science, Co, Ltd., Wuhan, China), with a measurement interval of 0.312-20 ng/mL. Homeostasis model of assessment-insulin resistance index (HOMA-IR) was calculated for each patient using the formula [fasting glucose (mg/dL) x fasting insulin (IU/mL)/405].

Statistical analysis

SPSS software (Version 19.0; IBM, Chicago, IL, USA) was used for statistical analysis, and a P value of <0.05 was considered statistically significant. Continuous variables were expressed as mean ± standard deviation. T tests and Mann-Whitney U test were used for parametric and non-parametric variables, respectively. The correlation between the parameters was analysed by the Pearson and Spearman methods for parametric and non-parametric variables, respectively. Differences were considered significant at p < 0.05.

Results

Demographical characteristics and biochemical values of PCOS patients and healthy controls are shown in Table 1. The patients with PCOS and controls were similar in terms of mean age body mass index (BMI), waist/hip (W/H) ratio and homeostasis model of assessment-insulin resistance index (HOMA-IR) index. Follicle-stimulating hormone, LH and TT levels were significantly higher in patients with PCOS (p<0.05), but dehydroepiandrosterone sulfate (DHEAS) and estradiol (E2) were not significantly different. Fasting blood glucose and lipid profiles were similar between groups. Plasma Nesfatin-1 levels were similar between groups. There was no correlation between plasma Nesfatin-1 levels and other parameters.

Discussion

PCOS is a common disorder of reproductive women, but the etiology is still unknown. As a result of the studies, the authors considered that obesity and insulin resistance play an important role in the etiology.
There is only one study in the literature about PCOS and Nesfatin-1 relationship. Deniz et al. demonstrated that Nesfatin-1 levels were lower in PCOS patients than the healthy subjects. However, in our study, plasma Nesfatin-1 levels were not significantly different in patients with PCOS as compared to healthy subjects with similar BMI, age and HOMA-IR.

Deniz et al. explained this situation with increased insulin resistance, because in their study the patients with PCOS had higher insulin resistance than the control subjects. Hyperinsulinemia may be another reason of reduced Nesfatin-1 levels. But in our study insulin resistance levels were similar between the groups.

Qing-Chun Li et al. (18) demonstrated that Nesfatin-1 levels were lower in patients with type 2 diabetes mellitus (DM) compared to patients with type 1 DM. In animal studies, pro-nesfatin-1 and insulin secreting β cells were localized in the same region (19), and may play a role in the insulin secretion. As known, insulin increases the androgen levels by affecting ovarian theca cells (20,21). In patients with PCOS, insulin resistance can be expected. This is also related to obesity. But in our study our patients with PCOS were not obese and HOMA-IR levels were similar between the groups, for this reason plasma nesfatin-1 levels were not lower than the healthy subjects.

The studies with type 2 diabetic patients have controversial results. A study which involved type 2 diabetic patients demonstrated that they had lower Nesfatin-1 levels. Conversely, another study with newly diagnosed type 2 diabetic patients found that they had elevated plasma Nesfatin-1 levels (22). Yijing Su et al. (23) showed that plasma glucose levels were decreased after nesfatin-1 injection in rats. They demonstrated that nesfatin-1 had anti-hyperglycaemic effect through the insulin signal pathways but the mechanism is unknown.

Recent studies demonstrated that Nesfatin-1 is an anorexigenic peptide which is regulated by appetite and decreased food intake and body weight. Saldanha et al. (24) showed that Nesfatin-1 levels did not differ between hemodialysis patients and control subjects and negatively correlated with protein intake. Moreover they showed that Nesfatin-1 was positively correlated with BMI. In Zhang et al studies Nesfatin-1 levels were positively correlated with BMI, FBG and HOMA-IR. In the present study we did not found correlation with plasma Nesfatin-1 levels and BMI. In the literature there is no consensus in this regard. Some reports found no correlation (25) and some reports showed positive correlation with BMI in humans (26,27,28). On the other hand Günay et al. showed that Nesfatin-1 levels were lower in patients with generalized anxiety disorders than the healthy subjects (29). Nesfatin-1 is a satiety hormone that is affected by the emotional changes such as anxiety (12,30).

In conclusion nesfatin-1 may play an important role in glucose metabolism, insulin resistance and is affected by emotional status. In this study due to the absence of insulin resistance in PCOS patients and due to different emotional status, levels of Nesfatin-1 were similar with control group. The levels of Nesfatin-1 in the same diseases in different studies in confusing, so further studies are needed in this regard. The limitations of our study are; i- a small sample and, ii- Insulin resistance did not differ between the groups.

### Table 1: Demographical characteristics and biochemical values of controls and PCOS patients.

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<td><strong>Control (n=28)</strong></td>
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<td>Age (year)</td>
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<td>BMI (kg/m2)</td>
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<td>W/H ratio</td>
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<tr>
<td>Nesfatin-1 (pg/mL)</td>
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References


