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Original Article

Status of serum selenium and zinc in patients with the polycystic ovary syndrome with and without insulin resistance

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ABSTRACT

Objectives: Insulin resistance (IR) is one of the important factors associated with the clinical signs in patients with the polycystic ovary syndrome (PCOS). There are some studies which report a correlation between insulin resistance and trace elements. The present study primarily focuses on the investigation of serum selenium (Se) and zinc (Zn) levels as well as their relationship with insulin resistance in PCOS patients.
Design: This is a case control study.
Setting: The study was conducted at Fatemeh Zahra Infertility and Reproductive Health Research Center of Babol University of Medical Sciences, Babol, Iran.
Methods: This study includes 60 women with PCOS (20–40 years old) and 90 healthy women. The PCOS group was divided into two sub-groups including insulin-resistant (n = 36) and non-insulin-resistant (n = 24) groups. Fasting blood sugar, fasting insulin, insulin resistance indexes and the serum levels of Se and Zn were measured in both groups.
Results: Serum selenium levels were significantly lower in the patient group as compared with the control group (40.42 ± 21.12 VS 51.79 ± 15.65; p = .001). The mean zinc levels were also significantly lower in the PCOS women than in the controls (81.33 ± 24.28 VS 108.31 ± 63.29; p = .022). In addition, Zn levels in PCOS-IR were negatively correlated with the homeostatic model assessment for insulin resistance (r = −0.332, p = .048) and positively correlated with the glucose/insulin ratio (r = 0.354, p = .040) and insulin (r = 0.429, p = .009).
Conclusion: The findings show decreased serum Se and Zn levels in the PCOS patients as compared to the controls. Additionally, the results confirm the correlation between zinc and insulin resistance.

1. Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine metabolic disorders which affects approximately 7–10% of women during their reproductive age worldwide [1]. PCOS is associated with different complications including reproductive features (e.g. hyperandrogenism, hirsutism, anovulation, infertility, and menstrual disturbance), metabolic features (e.g. obesity, insulin resistance, and cardiovascular risk), and psychological features (e.g. mood disorders and decreased quality of life) [2]. In PCOS patients, risk of developing insulin resistance, hyperinsulinemia and decreased glucose tolerance is increased [3]. Insulin resistance is one of the main biochemical signs of this syndrome, and about 70% of patients with PCOS are insulin-resistant [1,4]. Abnormal ovarian androgen metabolism, defective follicle growth and alteration of gonadotropin response are some outcomes of chronic hyperinsulinemia [5].

In our last study on PCOS, we indicated that PCOS women have a significantly high level of insulin resistance and oxidative stress in comparison to healthy women [6]. In the present study, we selected two trace elements, i.e. selenium and zinc, that have

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important roles in regulation of glucose homeostasis as well as insulin metabolism and serve as the cofactors of antioxidant enzymes [5,7,8].

Selenium is a basic component of selenoproteins which plays a crucial role in human health [9]. It activates anti-carcinogenic factors, prevents cardiovascular diseases, and performs anti-proliferative and anti-inflammatory activities [8]. It also affects several reproductive and obstetric complications including female infertility [8,10]. Additionally, selenium has essential enzymatic functions including thyroid hormone metabolism, insulin-like action, protection from oxidative stress and redox homeostasis [11].

Zinc is a cofactor of antioxidant enzymes like as catalase and superoxide dismutase [5]. It is involved in a multitude of processes within the pancreas. Different roles of zinc in insulin synthesis, secretion, and signaling as well as the consequent actions of insulin on metabolism have been reported in the literature [12,13]. Several systemic disorders like dyslipidemia, insulin resistance, cardiovascular disease, hyperhomocysteinemia and arrest of the follicular development, which are prevalent in PCOS, may be related to zinc deficiency [5].

As a matter of fact, although some studies have examined the concentrations of serum trace elements in relation to insulin resistance and PCOS, their results are partly or completely contradictory [14,15,16].

It seems that Se and Zn have effects on insulin resistance, so their alteration in association with PCOS can be evaluated. The present investigation primarily aims to measure serum Se and Zn levels in patients with PCOS and in control individuals. Moreover, the relationship between the levels of these elements and insulin resistance is analyzed.

2. Materials and methods

2.1. Subjects

This case control study was conducted at Fatemeh Zahra Infertility and Reproductive Health Research Center of Babol University of Medical Sciences, Babol, Iran, from March to December 2015. The Ethics Committee of Babol University of Medical Sciences approved the study (MUBABOL.REC.1394.65). Informed consents were taken from all the individual participants included in the study.

To begin with, 177 individuals at the age of 20–40 years were involved in this study. They were all from Mazandaran and Golestan provinces. A sample size of $\alpha = 0.05$, $\beta = 0.2$ and power = 80% was selected based on a previous study [5]. Subsequently, 27 women were excluded from the analysis due to hyperprolactinemia (n = 3), hypothyroidism (n = 5), consumption of fertility medicines (n = 6) or metformin (n = 6), and missing data in the records (n = 7). The remaining women (n = 150), who were included in the study, were divided into two separate groups of patients with PCOS (n = 60) and controls (n = 90) (Fig. 1).

Diagnosis of PCOS was based on Rotterdam Criteria (2003). Accordingly, it could be defined by two of the three following characteristics: (1) oligo- or anovulation, (2) clinical and/or biochemical symptoms of hyperandrogenism, and (3) polycystic ovaries on ultrasonographic examination [17].

The control group consisted of healthy women who referred to our research center with regular menstrual cycles and normal ovarian morphology identified by ultrasound. They were matched to the patients group for age, weight and BMI variables.

The exclusion criteria included endocrine disorders with similar presentations (e.g. Cushing's syndrome, congenital adrenal hyperplasia, androgen-secreting tumors and hyperprolactinemia), thyroid dysfunction, renal and liver disorders and diabetes mellitus. None of the participants had taken any drugs such as oral contraceptives, insulin sensitizers and mineral supplementation at least three months before participating in the study. Also, none of the subjects had a history of smoking or drug abuse.

In order to evaluate insulin resistance in the patients, this group was divided into two subgroups as PCOS patients with and without insulin resistance. Women who indicated IR with polycystic ovary morphology were 36 in number (PCOS-IR), and the second subgroup (PCOS-NIR) consisted of 24 women (Fig. 1).

The demographic data including the age, height and weight of all the subjects were recorded. The body mass index (BMI) was calculated using the following formula:

$$\mathrm{BMI} = [\mathit{weight}\ (\mathrm{kg})/\mathit{Height}\ (\mathrm{m})^2]$$

2.2. Laboratory analysis

From each subject, 5cc of venous blood was taken after an overnight fast. The serum was separated by centrifugation for 20 min at 3000 rpm and then stored at −80 °C until it was analyzed. The serum levels of Se (ppb) were measured by an atomic absorption spectrophotometer (PG-990, China). The wavelength (λ_{max}) of 196.0 nm was used to determine the Se levels. The serum concentration of Zn (μg/dl) was measured by 5-Br-PAPS method using commercial kits (Ziestchem Diagnostics, Tehran, Iran). The normal range of Zn was 70–140 μg/dl. The fasting blood glucose, FBG (mg/dl), was analyzed by the glucose-oxidase colorimetric method using commercial kits (Pars Azmoon Tehran, Iran). The normal range varied from 75 to110 mg/dl. The serum insulin levels (μIU/ml) were measured by ELISA using commercial kits (Demeditec Diagnostics GmbH, D-24145 Kiel-Wellsee, Germany). The normal range was between 2 and 25 μIU/ml.

2.3. Criteria for diagnosis of insulin resistance

Insulin resistance was assessed using the quantitative insulin sensitivity check index (QUICKI), the homeostasis model assessment (HOMA) and the glucose/ insulin ratio (GIR) [16]. The interactions between insulin and glucose were evaluated by HOMA, which is useful for prediction of insulin levels and fasting steady states for a wide spectrum of possible combinations of insulin resistance and β-cell function. The GIR decreased in the insulin-resistant patients, whereas the HOMA and insulin values increased [18,19]. The HOMA was assessed by [16]:

$$\mathrm{HOMA} = [\mathit{Fasting\ insulin}\ (\mu\mathrm{IU/ml})] * [\mathit{Fasting\ glucose}\ (\mathrm{mg/dl})]/405$$

The QUICKI, which is a mathematical model derived from fasting blood glucose and plasma insulin levels, supplies a reliable index of insulin sensitivity with a great positive anticipative power [19]. It was calculated by [16]:

$$\mathrm{QUICKI} = 1/[\log \mathit{fasting\ insulin}\ (\mu\mathrm{IU/ml}) + \log \mathit{fasting\ glucose}\ (\mathrm{mg/dl})]$$

Insulin resistance was considered as HOMA-IR ≥ 2.5 and QUICKI $\leq$ %0.333 [20].

2.4. Statistical analysis

Statistical analyses were done using the Statistical Package for the Social Sciences for windows software version 16.0 (SPSS, Inc, Chicago, IL, USA). The Kolmogorov-Smirnov test was used to test the distribution normality. The statistical analyses included the Student's *t*-test and the Pearson's test for normally distributed data

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