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Biological correlates of major depression and generalized anxiety disorder in women with polycystic ovary syndrome

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ABSTRACT

Objective: We aimed to compare the levels of serum androgens in women with polycystic ovary syndrome (PCOS) who had a diagnosis of only major depressive disorder (MDD), only generalized anxiety disorder (GAD) or who had no psychiatric disorder, as determined by a structured clinical interview. Another objective of the study was to examine whether an association exists between these psychiatric diagnoses and insulin resistance or body mass index via a comparison among the study groups in terms of these parameters.
Method: This study was performed between March 2011 and February 2012. A total of 73 patients were included in the study. The study sample consisted of three groups: PCOS patients with only major depressive disorder (n = 23), PCOS patients with only generalized anxiety disorder (n = 20), and PCOS patients without any diagnosed psychiatric disorders (not diagnosed — ND group, n = 30).
Results: Significant difference was found among the three groups with regard to the serum levels of 17-OHP and DHEAS. When multiple comparisons were performed among the groups, 17-OHP levels were significantly higher in the MDD group than in the ND group. DHEAS levels were significantly higher in the MDD group and the GAD group than in the ND group.
Conclusion: The present study suggests that MDD and GAD appear to be associated with higher DHEAS levels.

Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder during a woman's reproductive period and it affects 12% to 18% of all women [1]. PCOS is characterized by androgen hypersecretion, insulin resistance, and chronic anovulation. Clinical manifestations include hirsutism, acne, alopecia, menstrual irregularities, obesity, and infertility [2]. It has been shown that physical symptoms such as weight gain, hirsutism, and acne cause a reduction in psychosocial well-being and may be associated with mood disturbance [3].

It is known that patient with endocrine disorders are at increased risk of developing psychiatric disorders. Fornaro et al. suggest an increased prevalence of major depressive disorder and other axis-I disorders among women with newly diagnosed endocrine disorder [4]. A number of studies evaluated the relationship between PCOS and psychiatric disorders in the literature. However, most of them evaluated psychiatric symptoms based on self-report measures and had more limitations. Several studies have established that women with PCOS are more likely to experience depressive symptoms than a comparison group of women without PCOS [5–8]. According to a few studies based on structured clinical interviews, 56.9% of women with PCOS have at least one psychiatric disorder [9–11]. These studies suggest that, in women with PCOS, the most common psychiatric diagnose is major depressive disorder (MDD). Rassi et al. suggest that, in women with PCOS, the most common psychiatric diagnoses are major depressive disorder (MDD) and Bipolar Disorders (BD). In this study, GAD has been reported as the most common anxiety disorder [9]. Fornaro et al. suggest that Panic Disorder (PD) is more common than GAD in women with PCOS [4].

Obesity and resistance to insulin play a significant role in the pathogenesis of PCOS. Obesity increases the risk of insulin resistance, although insulin resistance can also occur in the absence of obesity [2,12]. The resulting state of hyperinsulinemia stimulates the production of ovarian androgen and hypophyseal luteinizing hormone [13]. Approximately two thirds of women with PCOS are overweight or obese, and obesity has been implicated in depression in women in the general population [14–17]. In one of the largest studies of mental health correlates of PCOS to date, approximately 15% of women with

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PCOS indicated that they had psychological distress. Women in the high distress group differed from other women with PCOS only in regard to greater body mass, suggesting that obesity was a significant contributor to mental health difficulties in the aforementioned study [18].

Despite the most common psychiatric disorders observed in women with PCOS, in these subjects the pathogenesis of major depression, and especially generalized anxiety disorder, is unclear. Some authors suggest that women with hyperandrogenic syndromes may be at an increased risk for mood disorders due to an association between elevated androgen levels and depression [19,20]. Rasgon et al. [20] suggest that woman receiving oral contraceptives for the treatment of PCOS were less depressed than patients not receiving treatment. These results imply a relationship between depression and hormonal factors in women with PCOS, although studies that directly examined this relationship are inadequate. Additionally, the available studies on the topic have controversial results with respect to the association of mood disorder with levels of serum androgens [11,21]. Hollinrake et al. didn't observe any significant differences in the adrenal androgen DHEAS between depressed women with PCOS and non-depressed women with PCOS [11]. Although a few studies suggest a correlation between depressive symptoms and serum androgens [19,20] another study has failed to demonstrate this association [21]. Moran et al. and Weiner et al. both provide some preliminary research around androgens and anxiety [8,22]. These studies did not use structured clinical interviews, and more comprehensive investigation is required regarding the potential role of androgens in the pathogenesis of GAD. For these reasons, in the current study, we aimed to compare levels of serum androgens in women with PCOS who had a diagnosis of only MDD, only GAD, or who did not have any psychiatric disorder, as determined by a structured clinical interview. Another objective of the study was to examine whether an association exists between these psychiatric diagnoses and insulin resistance or body mass index via a comparison among the study groups in terms of these parameters.

Materials and methods

Setting and sample

This study was conducted among newly diagnosed with PCOS who were admitted to the Outpatient Clinic of Gynecology and Obstetrics at the Faculty of Medicine of Selçuk University between March 2011 and February 2012. The exclusion criteria for the study were as follows: a history or existence of bipolar disorder, schizophrenia or related disorders, a history of neurological disease and concomitant severe medical illnesses (e.g., cardiovascular or pulmonary diseases, severe renal or liver failure, any cancer, diabetes mellitus, thyroid, or surrenal gland disease), and those who had used psychotropic medications within the previous 4 weeks.

Initially, total 132 women with PCOS were screened. Four patients refused to participate in the study. Three participants had pre-existing psychiatric disorders; 1 patient had schizophrenia, and 2 other patients had Bipolar Disorder-I. A total of 125 consecutive women met the criteria of the present study were included in the study. According to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria [23], of these 125 patients, 23 had only MDD and 20 had only GAD. There was no Axis I diagnosis in 62 women and the first 30 of these women were included in the study. The remaining 20 women had some other psychiatric diagnoses such as obsessive compulsive disorder, panic disorder, social phobia, bulimia nervosa, and binge eating disorder (one or more psychiatric disorder). Only 3 women had both GAD and MDD. The sample size in this study was similar to previous studies. Thereby, the final study sample consisted of three groups: PCOS patients with only MDD (n = 23), PCOS patients with only GAD (n = 20), and PCOS patients without any diagnosed psychiatric disorders (not diagnosed — ND) (n = 30).

Procedures

The objectives and procedures of the study were explained, and written informed consent was obtained from all participants. Furthermore, the study was approved by the ethical committee of the Faculty of Medicine of Selçuk University. PCOS was defined according to criteria established by the Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group. Women with PCOS (n = 125) were included and they all met the Rotterdam criteria for PCOS [24]. After the socio-demographic characteristics of the participants were recorded in the outpatient clinic of gynecology and obstetrics, the women were referred to the psychiatry department. Psychiatric interviews were conducted by a psychiatrist and by means of the Structured Clinical Interview for DSM-IV (SCID-I) [23,25]. Major depressive disorder, GAD, and other Axis I psychiatric disorders were screened by means of SCID-I. Following the psychiatric evaluations, laboratory samples were obtained from the participants. The lab samples were not collected on the same day as the clinical interview. The laboratory assessments were performed blind to the participants' psychiatric status.

Laboratory measures

The clinical and biochemical characteristics collected from subjects included age, height, weight, and fasting a.m. serum levels of insulin and glucose. Body mass index (BMI) was calculated as kg/m^2. Insulin resistance was calculated by using the homeostasis model assessment insulin resistance index (HOMA-IR) (fasting insulin × fasting glucose/405) (μIU/mL) [26].

All venous blood samples were obtained in the morning between 08:00 and 09:00 h after an overnight fast during the early follicular phase (day 2–5) of a spontaneous menstrual cycle in PCOS women. All biochemical parameters were selected simply because they are standard endocrine tests. Levels of LH, FSH, SHBG, DHEAS, free testosterone, and 17-OH-P were assessed. Glucose concentrations were measured with the hexokinase method on Architect c16000 (Abbott, USA). Insulin, LH, FSH, SHBG, free testosterone, and DHEAS analysis were performed using the electrochemiluminescent method with original reagents on E170 Modular analytics (Roche Diagnostics, USA). 17-OH-P levels were measured with the ELISA technique using commercially available kits (Diametra, Italy).

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 13.0 for Windows. The data were checked with Kolmogorov–Simirnov test and normally distributed. Categorical variables among the study groups were compared using the chi-square test. For comparisons of continuous variables among the study groups, the one-way analysis of variance (ANOVA) was used. Tukey's honestly significant difference (HSD) test was used for post hoc multiple comparisons. All significant levels were two-tailed and set at the .05 level.

Results

The mean (±s.d.) age of the total sample (n = 73) was 21.97 ± 3.44 years. Most of the participants were still university students (76.7%), single (89.0%), and unemployed (87.7%). As shown in Table 1, the three study groups had similar sociodemographic characteristics. The mean (±s.d.) BMI of the total sample was 23.68 ± 5.12 kg/m^2 and the mean (±s.d.) insulin resistance index score was 2.37 ± 1.77 μIU/mL. We found no significant difference among three study groups in terms of BMI scores and insulin resistance index scores ($P > 0.05$ for both comparisons). This data is shown in Table 2.

Table 2 presents the mean serum hormone levels found in the study groups. We found no significant difference among groups in terms of levels of free testosterone,