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Evening not morning plasma cortisol level is higher in women with polycystic ovary syndrome

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Dodatkowe słowa kluczowe:
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Introduction: The aim of our study was to assess the morning and evening cortisol plasma levels in women with polycystic ovary syndrome (PCOS).

Material and method: 95 patients gave their informed consent to participate in the study and were divided into 2 groups. Group A consisted of 40 PCOS patients and group B consisted of 55 women without features of PCOS. Between day 5 and 8 of the menstrual cycle, morning (7 am), fasting blood samples were taken for the assessment of luteinizng hormone (LH), follicle stimulating hormone (FSH), estradiol, cortisol, prolactin, thyreotropin (TSH), testosterone and dehydroepeiandrosterone (DHEAS). Evening (5 pm) blood samples were also taken for the evaluation of plasma cortisol level

Results: There were no differences in mean age, body mass index (BMI), FSH, SHBG, PRL, estradiol and TSH levels between group A and group B. Mean plasma LH level was higher in group A compared to group B (10.7±6.8 IU/l vs 6.6±4.5 IU/l, p<0.02). Mean plasma testosterone and DHEAS levels were also higher in PCOS patients (3.8±0.6 nmol/l vs 1.63±0.6 nmol/l; 427.7±162.9 vs 236.6±97.8 respectively, p<0.001). Mean evening plasma cortisol level was higher in PCOS patients (11.8±4.1 ug/dl vs 4.7±1.3 ug/dl, p <0.02). Mean morning plasma cortisol levels did not differ between groups.

Conclusion: PCOS women showed the increased evening plasma cortisol level with impacted diurnal secretion rate.

Wstęp: Celem badania była ocena porannego i popołudniowego poziomu kortyzolu w surowicy krwi u kobiet z zespołem policystycznych jajników (PCOS).

Materiał i metodyka: 95 pacjentek, które wyraziły zgodę na udział w badaniu zostało podzielone na dwie grupy. Grupa A składała się z 40 pacjentek z PCOS, a grupa B z 55 pacjentek bez tego schorzenia. Pomiędzy 5 a 8 dniem cyklu pobierano na czczo, o godzinie 7 rano próbki krwi, w których oznaczano stężenia hormonu luteinizujacego (LH), hormonu folikulotorpowego (FSH), estradiolu, kortyzolu, prolaktyny, tyreortopiny (TSH), testosteronu, globuliny wiążącej hormony płciowe (SHBG) i dehydroepiandrosteronu (DHEAS). Popołudniu o godzinie 17 pobierano krew celem ponownej oceny stężenia kortyzolu.

Wyniki: Nie stwierdzono różnic w średnim wieku i wartościach wskaźnika masy ciała (BMI) pomiędzy grupami. Nie wykazano różnic w średnim poziomie FSH, SHBG, PRL, estradiolu i TSH pomiędzy grupami. Średnie stężenie LH było wyższe w grupie A w porównaniu z grupą B (10,7±6,8 IU/l vs 6,6±4,5 IU/l; p<0,02). Średni poziom testosteronu i DHEAS był wyższy u pacjentek z PCOS (3,8±0,6 nmol/l vs 1,63±0,6 nmol/l; 427,7±162,9 vs 236,6±97,8 odpowiednio, p<0,001). Średnie stężenie kortyzolu oznaczanego popołudniu było wyższe u kobiet z PCOS (11,8±4,1 ug/dl vs 4,7±1,3 ug/dl, p<0,02). Nie wykazano różnic w średnim poziomie kortyzolu o godzinie 7 rano pomiędzy grupami.

Wniosek: U kobiet z PCOS obserwuje się wyższe stężenie kortyzolu w godzinach popołudniowych, co świadczy o zmienionym dobowym rytmie wydzielania kortyzolu.

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Introduction

Polycystic ovary syndrome (PCOS) affects 7% of reproductive –aged women [1]. Impaired adrenal function is common in patients with polycystic ovary syndrome (PCOS) [2]. Patients with PCOS demonstrate a generalized hypersecretion of adrenocortical products, basally and in response to adrenocorticotropic hormone (ACTH) stimulation [3]. The adrenal cortex accounts for about 25% of the circulating testosterone levels [3]. There is no difference both in basal morning plasma levels of ACTH and the circadian or diurnal variation of this hormone

between PCOS women and healthy ones [4]. Endogenous or exogenous corticotropin-releasing hormone (CRH) triggers normal ACTH response in PCOS women. That may suggest normal pituitary responsivity in PCOS women [5]. However Glintborg et al. found the adrenal hyperresponsiveness to ACTH in PCOS patients [6]. Invitti et al. and Lanzone et al. documented elevated nighttime plasma ACTH and cortisol levels as well as exaggerated ACTH and cortisol response to CRH and naloxone in women with PCOS [7, 8]. Roelfsema et al. showed equally increased cortisol production in PCOS women and obese healthy control women [9]. Cinar et al. found higher basal and stimulated adrenal androgen in PCOS patients and women with hyperandrogenemia only compared to controls [10]. All hyperandrogenic subphenotypes of PCOS exhibit similar and higher basal and stimulated adrenal androgen secretion patterns compared to non-hyperandrogenic subphenotype [10]. Insulin within physiologic levels appeared to increased dehydroepeiandrosterone (DHEAS) production, while alternatively decreasing the secretion of DHEAS [11].

The aim of the study was to assess the cortisol plasma levels in PCOS women.

Table I

Clinical characteristics of PCOS patients (group A) and controls (group B).

Charakterystyka kliniczna pacjentek z PCOS (grupa A) i z grupy kontrolnej (grupa B).

Parameter	Group A n=40	Group B n=55	P
Age (years) Range	27.3±3.6 (20-32)	29.8±6.8 (15-36)	NS
BMI (kg/m²) Range	24.1±6.5 (17.8-42.3)	25.7±7.2 (16.5-44.8)	NS

BMI- body mass index; data is presented as mean ± standard deviation (SD) and minimal and maximal value.

Patients and methods

95 patients gave their informed consent to participate in the study. These women were divided into 2 groups. Group A consisted of 40 women with PCOS and group B consisted of 55 women without PCOS. Blood samples were taken at 7 am and 5 p.m. between day 5 and 8 of the menstrual cycle. Fasting, basic 7 am samples were taken for the assessment of cortisol, luteinizing hormone (LH), follicle stimulating hormone (FSH), estradiol, cortisol, prolactin, thyreotropin (TSH), testosterone and DHEAS and 5 pm samples were taken for the assessment of cortisol concentration. Body mass and height of the patients were taken to calculate body mass index (BMI). FSH and estradiol levels were measured using ECLIA Roche kits (sensitivity: 1 ng/ml for estradiol, cross reaction with LH, TSH, human chorionic gonadotropin 0.039%; sensitity for FSH of 0.5 mIU/ml less than 5% interference with bilirubin and haemoglobin, cross-reaction with hCG 0.016%). PRL, TSH, testosterone, DHEAS, progesterone concentrations were measured by ECLIA Roche kits.

Descriptive statistics, including mean values, median and standard error (SE) were calculated for all the variables. For comparisons between the groups ANOVA was applied. Significance level was set at $p<0.05$. Statistical calculations were performed using Statistica 3.1 software.

Table II

Hormonal characteristics of PCOS patients (group A) and controls (group B).

Charakterystyka hormonalna pacjentek z PCOS (grupa A) i z grupy kontrolnej (grupa B).

Parameter	Group A n=40	Group B n=55	P
LH (IU/l) Range	10.7±6.8 (4.5-29.0)	6.6±4.5 (2.2-19)	<0.02
FSH (IU/l) Range	6.2±1.7 (1.6-8.8)	5.7±2.0 (2-9.9)	NS
Estradiol (ng/l) Range	76.5±14.0 (37.9-99.0)	86.9±103.7 30.8=537.0)	NS
Prolactin (µg/l) Range	13.3±6.4 (4.9-28.1)	14.2±11.3 (2.4-28.0)	NS
Testosterone (nmol/l) Range	3.8±0.6 (3.1-5.5)	1,6±0,6 (0.3-2.7)	<0.001
DHEAS (nmol/l) range	427.7±162.9 (148.1-647.8)	236.6±97.8 (95-436.0)	<0.001
SHBG (ng/ml) Range	65.4±36.6 (14.6-138.3)	63.8±36.4 (14.5-132.8)	NS
TSH (uIU/ml) Range	1.6±0.7 (0.5-3.0)	2.1±1.2 (1.0-3.9)	NS

LH-luteinising hormone; FSH- follicle-stimulating hormone; DHEAS-dehydroepeiandrosterone; SHBG-sex hormone-binding globulin; TSH- thyroid stimulating hormone; data is presented as mean ± standard deviation (SD) and minimal and maximal value.

Table III

Plasma cortisol levels in PCOS patients (group A) and in controls (group B).

Poziom kortyzolu w surowicy krwi pacjentek z PCOS (grupa A) i z grupy kontrolnej (grupa B).

Parameter	Group A n=40	Group B n=55	P
Cortisol 7 am (µg/dl) range	14.6±9.8 (2.5-28.1)	14.2±10.0 (2.0-25.3)	NS
Cortisol 5 pm (µg/dl) Range	11.8±4,1 (2.6-17.7)	4.7±1.3 (2.9-7.7)	<0.02

Data is presented as mean ± standard deviation (SD) and minimal and maximal value.

Results

There were no differences in mean age, BMI, FSH, SHBG, PRL, estradiol and TSH between group A (40 PCOS women) and group B (55 controls) (Tab. I, II).

Mean plasma LH level was higher in group A compared to group B (10.7±6.8 IU/l vs 6.6±4.5 IU/l, $p<0.02$). Mean plasma testosterone and DHEAS levels were also higher in PCOS patients (group A) (3.8±0.6 nmol/l vs 1.63±0.6 nmol/l; 427.7±162.9 vs 236.6±97.8 respectively, $p<0.001$) (Tab. II).

Mean evening plasma cortisol level was higher in PCOS patients (11.8±4.1 ug/dl vs 4.7±1.3 ug/dl, $p<0.02$). Mean morning plasma cortisol levels did not differ between groups (Tab. III).

Discussion

Our results showed the impacted diurnal rhytm of cortisol secretion in PCOS patients. Shabir et al. published similar to ours observation. They measured morning cortisol plasma levels in 197 lean and obese women with PCOS. Their patients were younger than ours and mean plasma morning cortisol was higher in lean PCOS whereas lower in obese PCOS compared to controls. Mean morning plasma cortisol was similar in both studies [12]. In our study no difference between mean morning plasma cortisol in lean PCOS and controls were found. Evening mean plasma cortisol was twice as high as the one found in controls. Adrenocortical dysfunction and excess of adrenal androgen levels have been also observed in PCOS patients [13]. Yildiz et al. showed the hypersecretion of cortisol in PCOS women [14]. 24 hour urine free cortisol concentration is increased in PCOS women [15]. There are suggestions of increased metabolism of cortisol in PCOS patients [3]. The principal pathways for metabolism of cortisol include irreversible hepatic inactivation by 5a reductase type 1 and 5b-reductase and reversible interconversion with cortisone catalysed by 11b-hydroxysteroid dehydrogenase [3]. Studies in PCOS observed increased peripheral (hepatic) 5a reductase type 1 activity whereas decreased 11b-hydroxysteroid dehydrogenase activity [16,17]. Benson et al. found the enhanced cortisol stress response in PCOS patients compared to healthy controls [18]. Luboshitzky et al. reported similar to ours observation of higher basal plasma cortisol level in PCOS

patients compared to healthy controls [2]. Kondoh et al. found in their earlier study higher basal plasma cortisol in 60 PCOS women compared to 19 healthy controls [19]. Putignano et al. found higher urinary free cortisol in 60 obese PCOS women compared to 57 obese controls [20]. The same group observed increased plasma cortisol level in obese PCOS women compared to obese subjects without PCOS [20]. They also found the lack of relation between both plasma and urinary cortisol concentrations to insulin, androgens and gonadotrophin levels in PCOS women [20].

Conclusion

PCOS women showed the increased evening plasma cortisol level with impacted diurnal secretion rate.

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