Mastalgia Assesment and Hormonal Correlations in Patients with Polycystic Ovary Syndrome

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ABSTRACT

OBJECTIVE: The aim of this study is the assesment of relationship between mastalgia and hormonal parameters and frequency of mastalgia in polycystic ovary syndrome (PCOS).

STUDY DESIGN: 141 patients who are admitted to our clinic were included in this study after taking their informed consent. 78 patients who were diagnosed as PCOS according to the Rotterdam Criteria constitute the patient group. 63 patients who are admitted for routine control and had no hormonal pathology constitute the control group. Age of the patients were noted, complaints of mastalgia were questioned and hormonal parameters (Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), Estradiol (E2), Testosterone, Dehydroepiandrosterone Sulphate (DHEAS), Thyroid-Stimulating Hormone (TSH), Body Mass Index (BMI)) were recorded.

RESULTS: Frequency of mastalgia was found as 24.4% in PCOS group and 33.3% in control group and there is no statistical difference ($p>0.05$). It is apparent that the PCOS group, when compared with the control group, is characterized by higher LH levels and higher Testosterone, DHEAS and TSH levels ($p<0.001$, $p<0.001$, $p=0.019$, $p=0.04$)

CONCLUSION: Although there were different LH and Testosterone levels, we couldn't find statistical difference for the frequency of mastalgia between PCOS and the control group. There were no relationship between age, BMI and hormonal parameters in patients with mastalgia, so PCOS couldn't be a factor that effects the frequency of mastalgia. It seems that in mastalgia positive PCOS group, age and BMI effects the frequency of mastalgia but we can't say the same for hormones.

Keywords: Polycystic ovary syndrome, Mastalgia, Hormone levels
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Introduction

Polycystic ovary syndrome (PCOS) is seen about 1,6-10 % frequency in reproductive ages. It's a complex and heterogeneous disease which occurs with interrelations between environmental, endocrine and genetic factors.[1] Diagnosis of the disease is established by the presence of two of these three criterias: excess androgen levels oligo or an ovulation and polycystic ovarian appearance by ultrasound.[2] Biochemically androgen excess, high LH levels, normal or low FSH, increased LH/FSH ratio and hyperinsulinemia can be found.[3,4] Hyperinsulinemia is related with chronic anovulation and hyperandrogenism and causes unopposed estrogen excess.[5,6]

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Mastalgia is a common symptom during reproductive period.[7] This effects about 70% of the patients.[8-9] Two-thirds of these has cyclical mastalgia and one-third has non-cyclical mastalgia. Less than 0.5% of patients with breast cancer will present with pain exclusively. In about 15% of patients, the pain is adequately severe to affect their lifestyle and warrant drug therapy.[10] Etiology of cyclic mastalgia has not been established but some evidence has implicated the elevated estrogen levels, the low progesterone levels, or an abnormal estrogen/progesterone ratio.[11]

Etiology is uncertain. Although estrogen, progesteron and prolactin hormones are related with menstrual cycle straight relationship between mastalgia and these hormones couldn't be proven. However, during hormone replacement therapy, menopause, use of oral contraceptives, pregnancy and lactation; mastalgia could be seen. It was claimed in some studies that hypersensitivity to prolactin was increased and promoted by thyrotropin releasing hormone. In another study lipid metabolism anomalies were supposed to be responsible.[7,12] Psychiatric factors were also taken into considerations in some studies.[13]

As mastalgia is seen more frequently in luteal phase of menstruel cycle, the higher estrogen and progesterone levels in breasts were claimed as related factors.[12] It was thought that high levels of estrogen are more pertain to mastalgia than low levels of progesteron.[14]

Our aim in this study is to find if there is a significant relation between high levels of gonadotropins and mastalgia in PCOS patients.

Material and Method

Among obstetric and gynecologic patients, 141 volunteers were included in the study. The study was reviewed and approved by local ethical committee. This was a prospective study. Seventy eight patients who had PCOS diagnosis according to Rotterdam criterias were selected, other patients were included in to the clinically diagnosed group. The latter group was control group and they haven't had any hormonal pathology. Sixty three patients were included in healthy controls. Age, BMI, presence of cyclic or noncyclic mastalgia were determined. Routine breast examination was carried out by department of general surgery. We applied ultrasonography for patients less than 35 years old and ultrasonography and mammography for those older than 35 years. Exclusion criteria were history of breast cancer, previous breast surgery with a diagnosis of known breast pathology diagnosed by ultrasound or mammography, hyperprolactinemia, thyroid disease, Cushing syndrome, congenital adrenal hyperplasia, adrenal tumor, virilizing ovarian tumor, autoimmune diseases, central nervous system diseases, existence of pregnancy or a history of pregnancy in the last year, administration of any pharmaceutical or oral contraceptive in the last 6 months, and smoking habit.

Biochemical analysis

All blood samples were taken from the antecubital vein in the morning, after a 13-hours fasting, during the early follicular phase of spontaneous menses or of medroxyprogesterone acetate-induced withdrawal bleeding. Serum FSH, LH, Estriol, Testosterone, TSH and DHEAS levels were measured by electrochemicalluminescence immunoassay (ECLIA) on the Cobas e 411 analyser (Roche Diagnostic, Mannheim, Germany). We used mIU/ml for FSH, LH, TSH and pg/ml for E2, ng/ml for Testosterone, ug/dL for DHEAS.

All of the patients were examined under ultrasonography by the radiology specialist (7-12 MHz lineer prob, Alpha 6, Japan medical system).

Statistical analysis

Statistics were run with Software package STATA 11.0 (College station, Texas, USA). Continuous variables were expressed as mean±standard deviation (SD) and categorical variables were expressed as percentage. Chi-square test was used to compare proportions. Continuous variables were compared using an independent-groups Student's t test if normality assumptions were met; otherwise, groups were compared using the Wilcoxon rank sum test. An analysis of normality of the continuous variables was performed with the Kolmogorov-Smirnov test. A p-value of <0.05 was considered as statistically significant.

Results

One hundred and forty one convenient patients were included in the study. The clinical characteristics and biochemical variables for the two groups (78 PCOS and 63 controls) are summarized in Table 1. There were no significant differences between the age, BMI, FSH, and Estradiol levels (p values were 0.07, 0.5, 0.55 and 0.36 respectively) and Mastalgia symptoms were higher in the PCOS group than the controls but not significant statistically (p=0.26). It is apparent that the PCOS group, when compared with the control group, is characterized by higher LH levels and higher Testosterone, DHEAS and TSH levels (p values were 0.001, 0.001 and 0.0019 respectively)

Table 1: Comparison of the demographics and hormonal values of the patients. Mean values defined as ± S.D

Variable	PCOS (n:78)	Controls (n:63)	P value
Mastalgia (+)	19 (24.4%)	21 (33.3%)	0.264
Age	25±5.8	23.8±5.9	0.074
BMI	26.1±4.7	26.5±5.4	0.502
FSH	6.6±7.3	5.8±2.2	0.556
LH	10.5±6.9	8.4±7.2	<0.001
E2	71.1±57.5	78.6±61	0.364
Testosterone	0.8±1.6	0.3±0.2	<0.001
TSH	2.5±1.3	2.3±1.7	0.040
DHEA	259.8±158.5	209.7±92.1	0.019

Table 2 presents mastalgia positive patients in comparison to the mastalgia negative patients in PCOS group. Age and BMI were significantly higher in patients with mastalgia positive PCOS patients (p=0.025, p=0.053). There were no statistically significant differences between PCOS patients with mastalgia and the PCOS patients without mastalgia in respect to FSH, LH, E2, Testosterone, TSH and DHEAS levels (p values were 0.162, 0.385, 0.195 and 0.723 respectively).

Table 2: Comparison of the features of the PCOS patients. Mean values defined as ± S.D

Variable	Mastalgia (+) n:19	Mastalgia (-) n:59	P value
Age	25.4±6.2	23±5.6	p=0.025
BMI	27.2±4.9	25.6±4.5	p=0.053
FSH	6.1±1.7	6.9±8.8	p=0.162
LH	10.9±6.9	10.3±6.8	p=0.385
E2	83.6±69.2	65.5±51.1	p=0.195
Testosterone	0.7±0.3	0.9±1.9	p=0.723
TSH	2.2±1.1	2.6±1.3	0.151
DHEAS	246.6±127.5	265.8±170.9	0.981

The control groups included mastalgia positive and mastalgia negative patients and were shown in Table 3. BMI, E2, Testosterone and TSH levels were significantly higher in control group patients with mastalgia (p=0.049, p=0.015), whereas age, FSH, LH, DHEAS levels do not significantly differ than mastalgia negative control patients (p values were 0.757, 0.989 and 0.365 respectively).

Table 3: Comparison of the features of the control patients. Mean values defined as ± S.D

Variable	Mastalgia (+) n=21	Mastalgia (-) n=42	P value
Age	25.9±6.3	24.5±5.5	p=0.187
BMI	27.7±6.1	25.9±4.9	p=0.049
FSH	5.7±2	5.8±2.3	p=0.757
LH	8.4±4.5	8.4±8.3	p=0.989
E2	97.8±70.7	68.7±53.1	p=0.015
Testosterone	0.2±0.1	0.3±0.2	p=0.009
TSH	1.9±1.4	2.5±1.8	0.011
DHEAS	197.3±76.1	216±99.2	0.365

Discussion

Mastalgia could seriously effect the quality of life.[15] Although the etiology isn't certain, the hormones could be a factor, for example estrogen excess.[12] PCOS is a heterogenus disease which has reproductive metabolic symptoms due to endocrin disturbances.[16] Mammary glands are highly susceptible to estrogen and testosterone.[17] Estrogens have positive effect on mammary growth while androgens inhibit it. Studies demonstrated that high levels of androgens could be protective against mammary cancer development.[18,19] In another study; ıt was showed that high levels of androgens in PCOS patients is protective against mammarian cancer. In our study, according to the frequency of mastalgia, we couldn't find any significant difference between the PCOS and the control group patients (p=0.26). We think that the pathophysiological increases in LH, testosterone and DHEAS levels in PCOS patients effect the androgen metabolism and do not effect the progression of mastalgia. High androgen levels in PCOS patients could also be protective against mastalgia besides mammary cancer. In a study, benign breast disease prevalance was given as 45-70% [20] Pollitt et al.[10] showed that 25% of patients admitted to department of radiology had mastalgia. In another study 14.3-15% of women admitted to radiology clinic had mastalgia.[10] In our study mastalgia frequency was found 24,4% in PCOS patients and 33,3% in control group and these results were smilar with the other studies.

Ecocharda et al.[21,22] couldn't find any relation between cyclic mastalgia and BMI and age. In contrary this, macromastia was reported approximately 35% of obese patients in literature.[22,23] Besides this, there are studies in literature which says obesity could be the reason of macromastia and mastalgia could be seen among these patients.[23] In our study we found mastalgia more frequent among patients with high BMI. To best of our knowledge, this could be related with macromastia of obese patients.

In Ecocharda's study,[21] higher LH and FSH levels were reported in patients with cyclic mastalgia. But we defined that the increased levels of LH did not increase the rate of mastalgia. In Ecocharda study patients were included the study at the different days of their menstrual cycle and this could be the reason of discordance.

We saw that in the control group with mastalgia, estrogen and testosterone levels were significantly higher than the levels in the control group without mastalgia. This may be related with the small number of patients and we couldn't determine its pathophysiological mechanism.

As a result, in our study, there is no significant difference for mastalgia frequency between control and PCOS group but LH, DHEAS, TSH and Testosterone levels were found higher in PCOS group. In PCOS patients mastalgia frequency may be related with age, BMI and hormonal parameters. Hence PCOS isn't a determinant factor for mastalgia frequency. Hormones don't effect mastalgia but increasing age and BMI increases mastalgia frequency. The small number of patients limits our study, we need different studies including larger series of patients.

Polikistik Over Sendromlu Hastalarda Mastalji Sıklığının Değerlendirilmesi

ÖZET

AMAÇ: Kadınlar arasından yaygın görülen bir durum olan mastaljinin polikistik over (PCOS) hastalığında görülme sıklığı ve hormonal parametreler ile ilişkisini araştırmaktır.

GEREÇ VE YÖNTEM: Polikiniğimize başvuran hastalardan çalışmaya katılmayı gönüllü olarak kabul eden 141 kişi dahil edildi. Rotterdam kriterlerine göre PCOS tanısı alan 78 kişi, hasta grubunu oluşturmakta idi. Polikliniğimize genel muayene için başvuran ve ek bir hormonal patoloji saptanmayan 63 hasta kontrol grubunu oluşturmakta idi. Bu hastalarda yaş, vücut kitle indeksi, hormonal parametreler (FSH, LH, Estradiol, Testosteron, Dehidroepiandesteron sülfat (DHEASO4), Tiroid stimülan hormon (TSH)) değerlendirildi ve mastalji şikayetleri sorgulandı.

BULGULAR: Çalışmaya katılan PCOS grubunda ortalama mastalji görülme sıklığı %24.4. Kontrol grubunda bu oran %33.3 (p>0.05). Her iki grup arasında LH ve testosterone, $DHEASO_4$ ve TSH düzeyleri açısından anlamlı fark olduğu bulundu (p<0,001, p<0,001, p=0,01, p=0,04)).

SONUÇ: Çalışmamızda PCOS grubunda, kontrol grubundan farklı LH ve Tetosteron düzeyleri olmasına rağmen mastalji görülme sıklığı açısından anlamlı fark yoktur. Mastaljisi olanlarda yaş, BMI ve hormonal parametreler açısından ilişki yoktur yani PCOS, mastalji sıklığını etkileyen özel bir belirleyici değildir.

Mastaljiyi hormonlar etkilemiyor ancak ileri yaş ve BMI arttıkça mastalji görülme sıklığı artıyor gözükmektedir.

Anahtar Kelimeler: Polikistik over, Mastalji, Hormon düzeyleri

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