

The Relationship Between Hormonal Profile and Depressive Symptoms in Menopausal Women

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ABSTRACT

The relationship between hormonal profile and depressive symptoms in menopausal women

Objective: As the average life expectancy gets longer and the menopausal women population increases, the notion of curing menopausal complaints becomes increasingly more important. The aim of this study is to evaluate the relationship between hormonal parameters and the severity of depressive symptoms.

Methods: In this study, 171 voluntary women referred to Bakırköy Dr. Sadi Konuk Training and Research Hospital, Gynecology and Obstetrics Department, Menopausal Clinic, from January 2009 to August 2009 and who had not had menstrual periods for at least 12 months were enrolled and questionnaires for sociodemographic data and menopausal symptoms, Hamilton Depression Rating Scale and Hamilton Anxiety Rating Scale were applied. Since surgical menopausal cases were considered as a different category, they were not included. The data were analyzed using NCSS.

Results: Mild depression was found in 49.7% of the cases. 18.7% of the cases had moderate depression, 65.5% had minor anxiety and 23% had major anxiety. We found no significant relation between Follicle Stimulating Hormone (FSH) levels and depression rate whereas there was a significant relation between FSH levels and the anxiety rate. There was also significant relation between estradiol (E2) levels and depression along with anxiety. Mild depression was found higher in our cases who had atrophic vulvovaginitis.

Conclusion: Levels of blood FSH and E2 are significantly related with the existence of depression and anxiety. Results suggest that although menopause itself cannot be accepted as the only reason for depressive symptoms, a multidisciplinary approach, including gynecologists, family doctors and psychiatrists, should be adopted to evaluate psychosocial and psychosomatic factors as a whole in premenopausal, perimenopausal and postmenopausal stages.

Key words: Menopause, depression, anxiety



ÖZET

Menopoz dönemindeki kadınlarda hormon profilinin depresif belirtiler ile ilişkisi

Amaç: Ortalama ömrün uzaması ve menopoz dönemi yaşayan kadın popülasyonunun artmasıyla menopoza bağlı yakınmaların tedavisi önem kazanmıştır. Çalışmamızda, menopozda hormonal parametrelerle depresif belirtilerin şiddeti arasındaki ilişkinin değerlendirilmesini amaçladık.

Yöntem: Çalışmaya, Ocak-Ağustos 2009 tarihleri arasında Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum Kliniği Menopoz Polikliniğine başvuran, en az 12 aydır adet göremeyen ve hormonal olarak menopozun doğrulandığı 171 gönüllü hasta dahil edilmiş ve kendilerine sosyodemografik bilgileri içeren ve menopoz belirtilerini sorgulayan anketler, Hamilton Depresyon Ölçeği ve Hamilton Anksiyete Ölçeği uygulanmıştır. Cerrahi menopoz olguları, farklı bir kategori olduğu düşünülerek, çalışma dışı bırakılmıştır. Veriler NCSS programı ile analiz edilmiştir.

Bulgular: Olguların %49.7'sinde hafif derecede depresyon, %18.7'sinde orta derecede depresyon görülmüş; %65.5'inde minör anksiyete, %23'ünde majör anksiyete saptanmıştır. Folikül Stimulan Hormon (FSH) düzeyine göre depresyon oranları arasında anlamlı bir ilişki bulunmazken, FSH ile anksiyete görülme oranı arasında anlamlı bir ilişki bulunmuştur. Östradiol (E2) düzeyine göre değerlendirildiğinde, depresyon ve anksiyetenin görülme oranları arasında istatistiksel olarak anlamlı bir ilişki bulunmuştur. Vajinal atrofi görülen olgularda depresyon oranı hafif derecede yüksek bulunmuştur.

Sonuç: Menopozal olgularda, serum FSH ve E2 seviyeleri ile anksiyete ve depresyon mevcudiyeti arasında anlamlı bir birliktelik olduğu görülmüştür. Bu bulgular, menopoz tek başına depresif semptomların majör sebebi olarak kabul edilmese de jinekolog, aile hekimi ve psikiyatristlerin premenopozal, perimenopozal ve postmenopozal evrelerde psikosomatik ve psikososyal faktörleri bir bütün halinde değerlendirerek, multidisipliner biçimde yaklaşımları gerektiğini göstermektedir.

Anahtar kelimeler: Menopoz, depresyon, anksiyete

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INTRODUCTION

Depression and depressive symptoms are frequently seen in menopause and in transition period to menopause. Menopausal changes in transition leads to critical influence on the woman's biological, social and psychological status (1-3). Many reports emphasize sudden hot flashes and sweating due to dramatic decrease in estrogen, sleep disturbances as a result of hormonal changes may induce depression, panic and generalized anxiety disorders. Changes in the perception of body image and alterations in sexual life which is a major source of satisfaction may play a role in the development of depression (4).

Many women experience mood disorders associated with low estrogen levels during the menstruation, postpartum and menopause periods. Even though studies strongly emphasize the risk of depression in perimenopausal period, serum hormone levels was not found to be directly correlated with the severity of the mood disorder symptoms (5). Endogenous and exogenous estrogen fluctuations are reported to be related with cognitive functions, memory, sleep, stress response and mood control (1,2,6,7), but a distinct effect of hormone levels on depression is still not clear (8).

In this study, we aimed to investigate the effect of hormonal fluctuations and physical changes on symptoms of depression and anxiety in patients with hormonally confirmed menopause.

MATERIALS AND METHODS

Participants

This study was conducted in Bakirkoy Dr. Sadi Konuk Education and Research Hospital, Department of Obstetrics and Gynecology, Menopause outpatient Clinic between January and August 2009. A total of 171 female volunteers in spontaneous menopause who had amenorrhea in previous 12 consecutive months and whose hormonal levels indicate menopause included in the study. Local ethics committee approval and informed consent from all patients were taken. Patients

with surgical menopause are regarded as a different category and excluded from the study. Before proceeding with the registration process, subjects were informed about the study and their personal information (name, age, date of admittance) were recorded. During the interview, patients were informed about the routine menopausal laboratory tests FSH and E2 (AIA-1800ST, Tosoh) and TSH measurements.

Scales

1. Socio-demographic data form: A questionnaire regarding the patients' medical history of chronic diseases, any hormone replacement therapy and its route if it has done, premenstrual syndrome disorders, existence of previously diagnosed psychiatric disorders in patients or in their first degree relatives. The marital status, profession, education, economical level, siblings, living alone or in a family were recorded. Also vaginal atrophy diagnosis was sought by questioning vaginal burning, stinging, dryness and dyspareunia.

2. Hamilton Depression Rating Scale (HAM-D): This is a scale developed to rate the level of depression in patients with depression (9). Seventeen-item version was used in this study. The reliability and validation studies of Turkish version were done by Akdemir et al. (10). Scores between "0-7" indicate no depression, while "8-15" as mild depression, "16-28" as moderate depression and 29 or more indicate severe depression.

3. Hamilton Anxiety Rating Scale (HAM-A): A scale containing 14 questions was developed by Hamilton (11) scores the mental and physical symptoms. It predicts the level of anxiety, symptom distribution and measures the severity. Turkish validity and reliability studies were done by Yazici et al. (12). The scores obtained from the scale were classified as: "0-5" points no anxiety, "6-14" points minor anxiety, "15" points and above as major anxiety.

The local ethical committee of Bakirkoy Dr. Sadi Konuk Research and Training Hospital approved the study (03 June 2008/34).

Statistical Analysis

The findings of the study were assessed for statistical analysis, NCSS (Number Cruncher Statistical System) 2007 and PASS 2008 Statistical Software (Utah, USA) were used. Evaluations of the data were done by descriptive statistical methods (mean, standard deviation, frequency) and chi-square test was used for qualitative data. The significance level of p was accepted as over 0.05.

RESULTS

Analysis of the demographic characteristics revealed that the majority of patients were: between 45-55 years old (n=140, 81.9%), married (n=148, 86.5%), graduated from primary school (n=138, 80.7%) and housewives (n=116, 67.8%) (Table 1).

Of all patients 119 (69.6%) had history of premenstrual syndrome. 26 (15.2%) of the patients perceived the menopause as aging, 8 (4.7%) of them as end of femininity and sexuality, 17 (9.9%) of them as maturation, 91 (53.2%) of them as a normal stage of human life and 29 (17%) of them had no knowledge or idea about it. 94 (55%) of women had symptoms of vaginal atrophy and 36 (21.1%) had urinary incontinence.

Table 2 shows the mean values of the patients' hormonal levels. There was no statistically significant difference in the incidence of depression between two groups with high and low levels of FSH formed by cut-off point of 40 mIU/ml ($p > 0.05$). The measurement of E2 inversely correlated with severity of depression ($p < 0.01$). Mild depression rates were higher in patients with E2 level below 50 mIU/ml, while moderate depression rates were higher in patients with E2 level higher than 50 mIU/mL ($p < 0.001$) (Table 3).

The difference of depression incidences in patients with and without the presence of vaginal atrophy were statistically significant ($p < 0.05$). The group with vaginal atrophy had higher rate of mild depression, while patients with no vaginal atrophy had low rate of depression (Table 3).

The incidence of anxiety according to the levels of FSH vs E2 were significantly different ($p < 0.01$). In

Table 1: Sociodemographic and clinical features of cases

| | n | % |
|--|-----|------|
| Age | | |
| 35-45 | 17 | 9.9 |
| 46-55 | 140 | 81.9 |
| 56-65 | 14 | 8.2 |
| Education | | |
| Illegible | 7 | 4.1 |
| Primary School | 138 | 80.7 |
| High School | 19 | 11.1 |
| University | 7 | 4.1 |
| Occupation | | |
| Working | 14 | 8.2 |
| Left the job | 13 | 7.6 |
| Retired | 28 | 16.4 |
| Housewife | 116 | 67.8 |
| Marital status | | |
| Married | 148 | 86.5 |
| Single | 3 | 1.8 |
| Divorced | 7 | 4.1 |
| Widow | 13 | 7.6 |
| Previous hormonal replacement therapy | | |
| Yes | 21 | 12.3 |
| FSH (mIU/ml) | | |
| <40 | 60 | 35.1 |
| ≥40 | 111 | 64.9 |
| E2 (mIU/ml) | | |
| <50 | 102 | 59.6 |
| ≥50 | 69 | 40.4 |
| Hamilton Depression Scale | | |
| No depression | 54 | 31.6 |
| Mild depression | 85 | 49.7 |
| Moderate depression | 32 | 18.7 |
| Hamilton Anxiety Scale | | |
| No anxiety | 36 | 21.1 |
| Minor anxiety | 112 | 65.5 |
| Major anxiety | 23 | 13.5 |

FSH: Follicle Stimulating Hormone, E2: Estradiol

Table 2: Levels of hormonal profiles

| | Minimum-Maximum | Mean±SD | Median |
|---------------------|-----------------|-------------|--------|
| FSH (mIU/ml) | 11-218 | 54.94±33.98 | 51.3 |
| E2 (mIU/ml) | 10-333 | 57.96±62.56 | 28.0 |
| TSH | 0.01-20.2 | 2.41±3.42 | 1.6 |

FSH: Follicle Stimulating Hormone, E2: Estradiol, TSH: Thyroid Stimulating Hormone, SD: Standard Deviation

patients with FSH level <40 mIU/ml the incidence of minor anxiety was higher, while FSH levels above this value was related with higher incidence of major anxiety. In patients with E2 level below 50 mIU/ml,

Table 3: The comparison of Hamilton Depression Scale in subgroups

| | Hamilton Depression Scale | | | p |
|------------------------|---------------------------|--------------------------|------------------------------|--------|
| | No depression n (%) | Mild depression n (%) | Moderate depression n (%) | |
| Age | | | | |
| 35-45 | 8 (47.1) | 8 (47.1) | 1 (5.9) | 0.42 |
| 46-55 | 42 (30.0) | 71 (50.7) | 27 (19.3) | |
| 56-65 | 4 (28.6) | 6 (42.9) | 4 (28.6) | |
| FSH (mIU/ml) | | | | |
| <40 | 17 (28.3) | 36 (60.0) | 7 (11.7) | 0.09 |
| >=40 | 37 (33.3) | 49 (44.1) | 25 (22.5) | |
| E2 (mIU/ml) | | | | |
| <50 | 34 (33.3) | 39 (38.2) | 29 (28.4) | 0.001* |
| >=50 | 20 (29.0) | 46 (66.7) | 3 (4.3) | |
| Vaginal Atrophy | | | | |
| Present | 24 (25.5) | 56 (59.6) | 14 (14.9) | 0.017* |
| Not present | 30 (39.0) | 29 (37.7) | 18 (23.4) | |

*Chi-square

Table 4: The comparison of Hamilton Anxiety Scale in subgroups

| | Hamilton Depression Rating Scale | | | p |
|------------------------|----------------------------------|------------------------|------------------------|--------|
| | No anxiety n (%) | Minor anxiety n (%) | Major anxiety n (%) | |
| Age | | | | |
| 35-45 | 5 (29.4) | 8 (47.1) | 4 (23.5) | 0.374 |
| 46-55 | 28 (20.0) | 96 (68.6) | 16 (11.4) | |
| 56-65 | 3 (21.4) | 8 (57.1) | 3 (21.4) | |
| FSH (mIU/ml) | | | | |
| <40 | 6 (10.0) | 49 (81.7) | 5 (8.3) | 0.004* |
| >=40 | 30 (27.0) | 63 (56.8) | 18 (16.2) | |
| E2 (mIU/ml) | | | | |
| <50 | 29 (28.4) | 52 (51.0) | 21 (20.6) | 0.001* |
| >=50 | 7 (10.1) | 60 (87.0) | 2 (2.9) | |
| Vaginal Atrophy | | | | |
| Present | 20 (21.3) | 62 (66.0) | 12 (12.8) | 0.959 |
| Not present | 16 (20.8) | 50 (64.9) | 11 (14.3) | |

*Chi-square

major anxiety was prominent while higher levels were related with less severe anxiety ($p < 0.05$) (Table 4). Presence or absence of vaginal atrophy didn't statistically differ by both incidence and severity of anxiety ($p > 0.05$).

DISCUSSION

In this study, the relationship between hormonal status with depression and anxiety were investigated in menopausal women. The higher severity of depression was related with E2 levels lower than 40mIU/ml, while anxiety scores were higher in patients with lower levels of FSH and E2 significantly. Additionally, vaginal

atrophy in women was related with higher rates of depression and anxiety.

The clinical studies reveal higher prevalence of depression in menopausal women compared with general population, since studies are generally done in cases admitted to hospitals by various complaints (2,13-16). Menopause may differ according to culture, individual differences, presence of an anxiety disorder or depression history and level of literacy about menopause. Depression and anxiety symptoms seen in this stage of women may be a result of biological, social and psychological factors (1-3). Some studies report that the changes in the level of estrogen during transition to menopause and while menopause

would increase susceptibility to psychiatric disorders such as depression and anxiety (1,2,6,7). Nevertheless, the effect of hormone levels on depression and anxiety is still not clear entirely (8).

In our study, low level of E2 was found to be significantly related to high rates of depression and anxiety. Freeman et al. (16) reported any increase in depressive symptoms parallel to hormonal changes in women at menopause transition. Some studies reported an association between menopause and depression (6,17-19), some had different conclusions (20-22). Hallstrom et al. (20) couldn't find an association between depression and menopause. In a study with follow-up of 2,565 women between the ages of 45 to 55 for five years, reported that the depression did not increase with menopause but the presence of previous history of depression was the indicator of developing depression in menopause (21).

There are some limitations that may be considered when analysing the data of this study. First, comorbidities as diabetes, hypertension and medications may interfere with psychological well-being of patients. Another limitation of the study is the attitude of spouse that may aggravate or deactivate the psychological reaction of patient to her menopausal

transition. We didn't homogenize the patients according to these parameters.

CONCLUSION

According to the results of our study, serum levels of FSH and E2 in menopausal patients had a significant relationship between anxiety and depression. Various differences are present between the clinical studies and population-based studies, that parameters may change with environmental and social factors.

The lack of standardized scales accepted by all investigators and difficulty of creating homogeneous patient groups interfere with the results of studies on this subject. In this study, even though the menopause wasn't accepted as the major cause of depression symptoms alone, it may be concluded that the gynecologists, family physicians and psychiatrists have to collaborate against the psychosomatic and psychosocial factors as a whole in evaluating patients with multidisciplinary approaches in premenopausal, perimenopausal and postmenopausal stages. Large scale studies taking the geographical region and culture comorbidities into account, and using standard criteria for depression are mandatory.

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