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Original Article

Investigation of premenstrular dysphoric disorder comorbidity and related factors in patients with anxiety disorder

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Abstract

Aim: Because of the fact that the frequency of both anxiety disorders and premenstrual dysphoric disorder (PMDD) are high in women and that studies investigating PMDD comorbidity in patients diagnosed with anxiety disorder are limited, this study was aimed to investigate PMDD comorbidity and related factors in patients with anxiety disorders.

Materials and Methods: 183 subjects who were followed up with a diagnosis of anxiety disorder in Necmettin Erbakan University Meram Medical Faculty Psychiatry Outpatient Clinic were included in the study and were evaluated with Sociodemographic Data Form, Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI). PMDD comorbidity was investigated according to The Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV-TR) criteria by making psychiatric interviews.

Results: 57 (31.2%) of 183 subjects diagnosed with PMDD constituted the PMDD group and the remaining 126 patients constituted the non-PMDD group. The mean BAI scores of the PMDD group were significantly higher than those of the non PMDD group, whereas the mean age of the PMDD group was significantly lower than that of the non PMDD group. The BMI of the PMDD group was significantly higher than that of the non PMDD group.

Conclusion: PMDD is common in patients followed up with a diagnosis of anxiety disorder and what is associated with PMDD is be young age as well as excessive chocolate consumption.

Keywords: Anxiety disorders; premenstrual dysphoric disorder; premenstrual syndrome

INTRODUCTION

Premenstrual dysphoric disorder (PMDD) is a chronic and cyclic disorder in women, manifested by mental and physical symptoms in the late luteal phase of the menstrual cycle with a prevalence of % 3-8. (1,2).

PMDD was defined as late luteal phase dysphoric disorder in The Diagnostic and Statistical Manual of Mental Disorders third edition (DSM-III-R); later this term was changed to a premenstrual dysphoric disorder in DSM-IV (3,4) and located in the depressive disorders section in DSM-V (5).

More than 100 symptoms have been described in PMDD. Anxiety, depression, tension, unstable mood, restlessness and irritability are some of the most common affective symptoms seen in both PMDD and anxiety disorders, whereas the most important cognitive symptoms are concentration impairment, imbalance and forgetfulness. Growth and tenderness in breasts, weakness, headache, muscle and joint pain, abdominal bloating and edema, constipation or diarrhea are physical symptoms. In addition, some women describe increased libido, insomnia or hypersomnia, appetite changes (eating cravings, especially against carbohydrate foods and chocolate) and suicidal thoughts. These symptoms decrease with the onset of menstruation and disappear in the first week of menstruation (6).

Even though the etiology of PMDD is not entirely clear today, it is likely to have multiple biological, psychological and sociocultural factors (7). In recent years, research has focused largely on the role of serotonin in the pathophysiology of PMDD, and the effect of neuromodulation on PMDD symptoms (8). Findings showing rapid symptom relief using SSRIs support the role of serotonin in the etiology of PMDD, and is currently the recommended first line treatment for the disorder (9).

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In addition, there are studies reporting that obesity and caffeine consumption are associated with the development of PMDD and symptom severity (10,11).

It is often found in such additional psychiatric disorders as anxiety disorder, major depression, post-traumatic stress disorder and bipolar disorder in PMDD patients. In addition, exacerbation of psychiatric disorders like obsessive compulsive disorder, alcoholism, schizophrenia, bipolar disorder, panic disorder and general anxiety disorder are reported in the premenstrual period (12-14).

Although the frequency of both anxiety disorders and PMDD is quite high in women, studies investigating PMDD comorbidity in patients diagnosed with anxiety disorder are quite limited. What was aimed in this study is to investigate PMDD comorbidity and related factors in patients with anxiety disorders.

MATERIALS and METHODS

This study was conducted at Necmettin Erbakan University Meram Medical Faculty. The study was approved by the Ethical Committee of University and written informed consent was obtained from all the participants.

Participants

238 patients who were admitted to Necmettin Erbakan University Meram Medical Faculty Psychiatry Outpatient Clinic and diagnosed with anxiety disorder were included in the study. The patients with such comorbid psychiatric diseases as depression, bipolar disorder and schizophrenia, those using oral contraceptives for the past three months, those who were pregnant or breastfeeding, those with a history of hysterectomy or oophorectomy were excluded from the study. 183 patients were included in the study. 40 patients had obsessive compulsive disorder (OCD), 55 patients had panic disorder (PD), 47 patients had generalized anxiety disorder (GAD), 20 patients had post-traumatic stress disorder (PTSD), 13 patients had social anxiety disorder (SAD) and 8 patients had specific phobia (SP). Diagnoses were confirmed by applying SCID to the patients. Sociodemographic characteristics of the patients were recorded. PMDD comorbidity was investigated according to DSM-IV-TR criteria by making psychiatric interviews.

Data Collection Instruments

Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)

It is a clinical interview scale developed and structured to investigate DSM-VI Axis I diagnoses (15). Validity and reliability tests of the Turkish version were performed by Corapioglu et al (16).

Beck Anxiety Inventory (BAI)

It is self-rated inventory used to determine the frequency of anxiety symptoms. It is composed of 21 items and is a Likert-type inventory rated from 0 to 3. Higher total scores indicate higher severity of anxiety. Developed by Beck et al (17). Validity and reliability tests of the Turkish version were performed by Ulusoy et al (18). The Cronbach's alpha coefficient of the Turkish version of BAI was 0.930. In this study, Cronbach's alpha coefficient was 0.929.

Beck Depression Inventory (BDI)

The inventory was developed by Beck et al. and measures physical, emotional, and mental symptoms in depression (19). It is self-rated inventory with 21-symptom category. Higher total scores indicate higher severity of depression. Validity and reliability tests of the Turkish version were performed by Hisli (20). The Cronbach's alpha coefficient of the Turkish version of BDI was 0.80. In this study, Cronbach's alpha coefficient was 0.893.

Statistical Analysis

Data analysis was evaluated with R 3.0.0 software. The compliance of the data to normal distribution was evaluated using the Shapiro-Wilk test. Levene test was used for variance homogeneity. Comparisons between groups were evaluated with chi-square analysis for qualitative variables, two independent samples t test for quantitative variables and Mann-Whitney U tests. Data were expressed as frequency, percentage, average and standard deviation, and median and minimum-maximum values. $P < 0.05$ was accepted statistically to be significant.

RESULTS

57 (31.2%) of 183 women were diagnosed with PMDD and these patients constituted the PMDD group and the remaining 126 patients constituted the non-PMDD group. Sociodemographic characteristics such as age, body mass index (BMI), educational status, marital status, employment status, number of children and age of marriage belonging to PMDD and non-PMDD groups are shown in Table 1. The mean age of the PMDD group was significantly lower than the non PMDD group ($P = 0.026$). There was no significant difference between the two groups in terms of other socio-demographic features. The BMI of the PMDD group was significantly higher than that of the non PMDD group ($P = 0.001$) (Table 1).

Diagnostic distrubutions of PMDD group were 14 (%24.6) OCD, 23 (%40.4) PD, 9 (%15.7) GAD, 6 (% 10.5) PTSD, 4 (% 7) SAD, 1 (%1.8) SP.

Nutritional Characteristics of the two groups are shown in Table 2. Both of the groups were compared for nutritional characteristics and chocolate consumption in PMDD group was significantly higher than that in non PMDD group ($P = 0.005$) (Table 2).

The menstrual period characteristics of the two groups are shown in Table 3. Pain in menstrual period ($P < 0.001$), frequency and severity of pain ($P < 0.001$) in PMDD group were found to be significantly higher than that in non PMDD group. The number of patients feeling worse in the week before menstruation was significantly higher in the PMDD group ($P < 0,001$). There was no significant difference between the two groups in terms of other menstrual features (Table 3).

Table 1. Sociodemographic characteristics of PMDD and non PMDD group

	PMDD Group (n=57)	Non-PMDD Group (n=126)	P
Age (mean±SD)	27.56±5.26	29.66±6.95	0.026
BMI (mean±SD)	24.23±3.65	22.22±2.74	<0.001
Educational status n (%)			0.379
Primary	5(8.8)	17(13.5)	
Secondary	34(59.6)	74(58.7)	
University	18(31.6)	35(27.8)	
Marital status n (%)			0.685
Single	23(40.4)	46(36.5)	
Married	28(49.1)	70(55.6)	
Divorced	6(10.5)	10(7.9)	
Profession n (%)			0.786
Housewife	28(49.1)	64(50.8)	
Working	29(50.9)	62(49.2)	
Number of child (median)	1(0-3)	1(0-4)	
Marriage Age (mean±SD)	21.14±2.26	20.79±4.57	0.661

Values are expressed as n (%) and mean ± SD, PMDD: Premenstrual dysphoric disorder

Table 2. Nutritional characteristics of PMDD and non PMDD group

	PMDD Group (n=57)	Non-PMDD Group (n=126)	P
Tea Consumption (cups/day)			0.658
0-5	15(26.3)	28(22.2)	
6-10	31(54.4)	64(50.8)	
11 and more	11(19.3)	34(27.0)	
Coffee Consumption (cups/day)			0.051
0-1	7(12.3)	32(25.4)	
1-4	36 (63.1)	79(62.7)	
5 and more	14(24.6)	15(11.9)	
Cola Consumption (cups/day)			0.432
0-1	1(1.8)	9(7.1)	
1-4	35(61.4)	79(62.7)	
5 and more	21(36.8)	38(30.2)	
Chocolate Consumption (daily)			0.005
0-1	1(1.8)	7(5.5)	
1-3	34(59.6)	99(78.6)	
3 and more	22(38.6)	20(15.9)	
Dairy Consumption (cups/day)			0.261
0-1	2(3.5)	4(3.2)	
1-3	52(91.2)	111(88.1)	
3 and more	3(5.3)	11(8.7)	
Smoking			0.065
Yes	20(35.1)	26(20.6)	
No	37(64.9)	100(79.4)	

Values are expressed as n (%) and median, PMDD: Premenstrual dysphoric disorder

Table 3. Menstrual Period Features of PMDD and non PMDD group

	PMDD Group (n=57)	Non-PMDD Group (n=126)	P
First menstrual age (mean±SD)	12.84±1.29	12.80±1.31	0.846
Menstrual period (day)	26(22-30)	26(22-30)	0.798
Bleeding time (day)	5(4-7)	5(4-7)	0.909
Menstrual pain			<0.001
Each menstrual period	49(86.0)	16(12.7)	
Some menstrual periods	6(10.5)	65(51.6)	
No pain	2(3.5)	45(35.7)	
Pain severity			<0.001
Mild	5(8.7)	34(42.0)	
Moderate	15(26.3)	37(45.6)	
Severe	37(65.0)	10(12.4)	
Premenstrual condition			<0.001
Better	0(0.0)	0(0.0)	
Same	0(0.0)	34(27.0)	
Worse	57(100.0)	92(73.0)	

Values are expressed as n (%), mean ± SD and median (min-max), PMDD: Premenstrual dysphoric disorder

Table 4. BAI and BDI scores of PMDD and non PMDD group

	PMDD Group (n=57)	Non-PMDD Group (n=126)	P
BAI	26±2.42	21±2.19	0.003
BDI	9±3.27	9±4.01	0.965

Values are expressed as mean ± SD. BAI: Beck Anxiety Inventory, BDI: Beck Depression Inventory, PMDD: Premenstrual dysphoric disorder. BAI Cronbach Alpha coefficient = 0.929 BDI Cronbach Alpha coefficient = 0.893

Table 5. Characteristic of premenstrual complaints in PMDD group

	PMDD Group (n=57)
Recovery duration of complaints (day) (median)	2(1-5)
Duration of complaints (day) (median)	12(5-25)
Change of complaints after delivery	
Increased	3(10.1)
Decreased	8(26.6)
Unchanged	19(63.3)
Change of Complaints with Age	
Increased	3(5.3)
Decreased	8(14.0)
Unchanged	46(80.7)
Influence relationships with others	
Yes	51(89.5)
No	6(10.5)
Influence quality of life	
Yes	54(94.7)
No	3(5.3)
Doctor application before	
Yes	12(21.1)
No	45(78.9)
Premenstrual Complaints in Mother or Sister	
Yes	44(77.2)
No	2(3.5)
No idea	11(19.3)
Request to go to the doctor	
Yes	46(80.7)
No	11(19.3)

Values are expressed as median and n (%), PMDD: Premenstrual dysphoric disorder

The BAI and BDI scores of both groups are shown in Table 4. The mean BAI scores of the PMDD group were significantly higher than those of the non PMDD group (P = 0.003).

Characteristic of premenstrual complaints in PMDD group is shown in Table 5. The majority of patients reported that their premenstrual complaints affected their interpersonal relationships and quality of life (Table 5).

DISCUSSION

In this study, the comorbidity rate of PMDD was found 31.2% in patients with anxiety disorder. Most of the studies investigating the prevalence of PMDD have been conducted in the general population (21-25).

The prevalence rates found in these studies are lower than those in our study, which supports the conclusion that women with anxiety disorder have a higher PMDD comorbidity rate than the general population does. This is likely to be because of the fact that the etiology of anxiety disorders and PMDD are similar. The most important neurotransmitter involved in the formation of premenstrual symptoms in the central nervous system is serotonin. The fact that many symptoms of PMDD are similar to psychiatric disorders associated with serotonergic system supports this view. Studies have shown that there are many important differences in the serotonergic system in women diagnosed with PMDD. Gonadal hormones are known to affect the emotional process in the brain. It has been reported that progesterone with an anxiogenic effect increases MAO activity by down regulating estrogen receptors and serotonin reuptake in cells in the median raphe nucleus in the brain. Progesterone is thought to cause dysphoric mood in PMDD through both estrogen and serotonin (8,26).

In a study conducted in 2004, the prevalence of premenstrual syndrome (PMS) was investigated in 31 female patients with Bipolar Disorder (BD) and PMS prevalence was found to be 38.7%, PMDD prevalence was 9.7% (27). This rate is lower than PMDD comorbidity rate in our study. The most important reason for this may be that 25 of 31 patients use at least one mood stabilizer. Mood stabilizers drugs may suppress depressive and anxious symptoms in PMDD. The patients in our study had not been using any psychotropic medication for the past three months. Other studies in patients with BD have also been reported to have a high PMDD comorbidity (28-30). In a study with 93 female patients with epilepsy, PMDD comorbidity was reported as 25.8% (31). This rate was similar to our finding although this study was conducted in a group with a neurological diagnosis.

When the correlation between sociodemographic variables and PMDD is examined in our study, it is seen that PMDD is not related to education, marital status, employment status, monthly income, marriage age or number of children. These findings are consistent with the findings of some studies (22,27). In our study, it was observed that the mean age of the patients in the PMDD group was significantly lower than that of the ones in the non-PMDD group. This finding contrasts with the idea that PMDD is a disorder that mostly affects women over 30 years of age. The reason for this may be that our sample is relatively young. There are also studies in the literature that support this finding (22,23).

In our study, whether or not there was a relationship between nutrition and PMDD was investigated by asking the subjects how much food they consume as well as the amount of drinks such as tea, coffee, cola, chocolate and dairy products. There was no statistically significant relationship between the consumption of tea, coffee, cola and dairy products and PMDD. These findings are different from those found in the studies by Gunes et al. Premenstrual Syndrome (PMS) was found to be higher in those with high cola and tea consumption in the studies by Gunes et al. (21). This difference may be due to the fact that the study was conducted in a younger group with no psychiatric disease and only the diagnosis of PMS was investigated. There is an increase in appetite especially for carbohydrate foods in women with PMDD. Indeed, in our study, chocolate consumption was higher in the PMDD group. In addition, the BMI of the PMDD group was higher than that of the non PMDD group. Increase in BMI is a risk factor for PMDD (11).

In the literature, there are studies reporting that PMDD incidence is higher in women whose mothers or first-degree relatives have premenstrual symptoms (25,32,33). In our study, 77.2% of the patients in PMDD group had premenstrual symptoms in their mother or sister, which supports the idea that genetic factors may play a role in PMDD etiology (34).

In our study, no significant difference was found between the two groups in terms of first menstrual age, menstrual period and menstrual bleeding time. In PMDD group, menstrual pain (dysmenorrhea) and the severity of pain were significantly higher than THOSE IN THE non PMDD group. Dysmenorrhea is an important finding of PMDD. The correlation of PMDD with dysmenorrhoea has been shown in several studies (21,35,36). All patients in PMDD group stated that they felt bad the week before menstruation. This may be due to PMDD symptoms restricting patients' life activities and interpersonal relationships. PMDD negatively affects the interpersonal relationships and quality of life of the majority of patients. Previous studies support this finding (32,37).

78.9% of the patients stated that they did not have any previous medical applications due to premenstrual complaints. The primary reason for this is that women cannot distinguish their premenstrual complaints from their current psychiatric complaints and that premenstrual complaints are not considered as a disease. Another reason may be that women hesitate to express their premenstrual complaints for cultural reasons. Studies have also found that the rate of applying to a doctor due to PMDD is very low (38,39). After the patients were informed about the premenstrual period and PMDD, 80.4% reported that they would go to the doctor due to their premenstrual complaints in the future. This finding reveals the importance of informing patients in the treatment of PMDD.

There are different opinions about the change of PMDD with age in the literature (23,38,40). In our study, 80.7% of the patients in the PMDD group stated that their premenstrual complaints did not change with age, and 75.8% of the patients who gave birth did not change with delivery.

In our study, BAI scores were found to be significantly higher in PMDD group. It shows that PMDD exacerbates anxiety symptoms in patients.

LIMITATIONS

This study must be considered with its limitations. The major limitation of our study is that since our study was conducted in 2012, it is utilized among DSM-IV-TR criteria when investigating the comorbidity of PMDD in patients with anxiety disorders. Second limitation is that no scale was applied to determine the severity of premenstrual complaints in patients. In addition, the quality of life and interpersonal relationships of patients diagnosed with PMDD due to this disorder were evaluated with the self-report of the patients, and a scale for this purpose was not applied to the patients. One other limitation is that our sample is relatively small and does not represent all patients diagnosed with anxiety disorders in the community, since only the patients who applied to the university hospital psychiatry outpatient clinic were included in the study.

CONCLUSION

The findings of the study show that PMDD is relatively common in patients followed up with a diagnosis of anxiety disorder; young age and excessive chocolate consumption are associated with PMDD. PMDD symptoms are not frequently questioned in patients applying to the psychiatry outpatient clinic in daily practice and the diagnosis of PMDD is missed. A lack of PMDD diagnosis can lead to the exacerbation of existing problems. The diagnosis of PMDD should be investigated, especially in patients with cyclical increase in anxiety symptoms. We think that detecting PMDD in patients will increase the treatment success of the current psychiatric disorder.

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