Female Reproductive Cycle and Obsessive-Compulsive Disorder

Javier Labad, M.D.; José Manuel Menchón, M.D., Ph.D.; Pino Alonso, M.D.; Cinto Segalàs, M.D.; Susana Jiménez, Ph.D.; and Julio Vallejo, M.D., Ph.D.

Background: The aim of our study was to assess whether there is a relationship between reproductive cycle events and the initiation or changes in symptoms of obsessive-compulsive disorder (OCD).

Method: Forty-six female outpatients meeting DSM-IV criteria for OCD completed a semistructured interview at our OCD unit to assess the relationship between reproductive cycle events and OCD. Dates of data collection were from January 2001 to December 2003.

Results: In our sample, OCD onset occurred in the same year as menarche in 22% (N = 10), at pregnancy in 2% (N = 1), at postpartum in 7% (N = 3), and at menopause in 2% (N = 1). Worsening of preexisting OCD was reported by 20% of patients (9/45) at premenstruum, 8% (1/12) at pregnancy, 50% (6/12) at postpartum, and 8% (1/12) at menopause. The number of premenstrual mood symptoms, which included anxiety, irritability, mood lability and depressed mood, was associated with both premenstrual worsening of OCD (OR = 5.1, $p < .01$) and onset or worsening of OCD at postpartum (OR = 2.7, $p < .05$). Patients with an onset or worsening of OCD at postpartum also more frequently reported premenstrual worsening of OCD and previous history of major depressive disorder, including postpartum depression ($p \leq .05$ for all).

Conclusion: In a substantial number of patients, the onset or worsening of OCD was related to reproductive cycle events, especially at menarche and postpartum. Certain women with OCD seem to be vulnerable to worsening of OCD at different reproductive periods that imply hormonal fluctuations, and premenstruum and postpartum were the 2 reproductive events with a greater vulnerability. Those patients whose OCD symptoms appeared to be related to reproductive events also exhibited a greater history of mood symptoms (premenstrual depression and major depressive episodes).

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Corresponding author and reprints: Julio Vallejo, Department of Psychiatry, Hospital Príncipes de España, Hospital Universitari de Bellvitge, c/ Feixa Llarga s/n 08907 L'Hospitalet de Llobregat, Barcelona, Spain (e-mail: jvallejo@csub.scs.es).

Gonadal hormones play important roles in brain functioning.[1] Estrogen has multiple neuromodulating actions, including direct intracellular actions[1,2] and those mediated by its effects on several neurotransmitter systems in the central nervous system (CNS), with well-documented actions on serotonergic, adrenergic, and cholinergic neurons, pathways, and receptors.[1,3] Less is known about actions of progesterone upon monoamine neurotransmitter systems in the CNS, although one well-known action is a sort of alprazolam-like effect of progesterone on γ-aminobutyric acid (GABA) receptors.[3]

Fluctuations of gonadal steroids during premenstruum, pregnancy, postpartum, and the perimenopausal years seem to increase the risk of emotional disturbances in certain women.[4] Although most studies are focused on mood disorders,[5–11] some authors have also described worsening of panic disorder,[12–14] trichotillomania,[15] obsessive-compulsive disorder,[16–21] and schizophrenia[22] during these reproductive phases.

In obsessive-compulsive disorder (OCD), the reproductive events most studied have been pregnancy and postpartum. Onset of OCD related to the birth of a child had been classically estimated at around 3% to 17% for all patients and at 13% to 27% for female patients.[23–25] More recent studies have found that onset of OCD related to gestation occurred in up to 44% of women.[16,17] However, in none of these studies was a clear differentiation between pregnancy and postpartum as 2 distinct reproductive periods considered. In the only 2 studies that analyzed more

clearly the role of both pregnancy and postpartum as 2 independent events,[19,20] reported results were quite different: while Williams and Koran[19] described the onset of OCD related to pregnancy in 13% of women with children, with no onsets at postpartum, Maina et al.[20] reported the onset of OCD at postpartum in 50% of women who had been pregnant without onsets at pregnancy. Even though the influence of puberty on the onset of OCD has been already described,[23,26] to our knowledge, no previous studies have tried to analyze OCD onset related to the menarche in female patients. The onset of OCD at menopause has been described in classical studies[23,25] as 4% to 8%.

Changes in OCD symptoms at reproductive events in preexisting OCD have been also reported. Worsening of OCD has been set as 17% at pregnancy, 29% at postpartum, and 42% at premenstruum.[19] Pregnancy is the only reproductive event in which improvement of OCD symptoms has been reported,[17,19,20] by up to 14% of patients with pregnancies. As far as we know, no recent studies have assessed changes of preexisting OCD at menopause.

In contrast with the results obtained in female patients, male patients with OCD report a much lower proportion of onset and worsening related to the birth of a child, with percentages of about 5%.[16,20] These findings suggest that hormonal changes related to reproductive events in women may contribute to the high rates of onset or worsening of OCD.

Previous studies suggest that some female patients may be especially vulnerable to OCD symptoms at postpartum and premenstruum, even though results focused on the former period have been quite heterogeneous. On the other hand, premenstrual dysphoria and high rates of postpartum depression have been described in female patients with OCD.[18,19] It has been suggested that a common dysregulation of serotonergic neurotransmission may be involved in the pathophysiology of OCD,[27] postpartum depression,[4] and premenstrual syndrome.[6,28] The efficacy of serotonergic agents in the treatment of these disorders[6,8,28–31] lends support to the previous statement. However, although presence of mood symptoms and worsening of OCD at reproductive events have been described, a specific association between mood symptoms and OCD worsening at these periods has not been addressed.

Limitations of previous studies assessing OCD changes at reproductive events include the use of mailed questionnaires,[16] chart reviews,[18] and telephone interviews[19] to collect the data. In spite of these studies, we wanted to obtain our results by means of a specific clinical interview conducted in person. The study by Maina et al.[20] also obtained data with a semistructured interview conducted in person, but they focused their work only on the onset of OCD at pregnancy or postpartum.

The principal aim of our study was to assess whether there is a relationship between reproductive cycle events and the initiation or exacerbation of OCD. Moreover, we wanted to try to identify factors that could be related to an exacerbation of OCD at reproductive events. Three specific questions were raised: (1) Are patients who report more premenstrual mood symptoms more likely to report premenstrual worsening of OCD? (2) Are patients who report either more premenstrual mood symptoms or premenstrual worsening of OCD more likely to report onset or worsening of OCD at postpartum? and (3) Are there differences in pregnancy characteristics between those patients with an exacerbation of OCD at pregnancy or postpartum and those without?

METHOD

The sample of our study was formed by 49 consecutive female outpatients meeting DSM-IV[32] criteria for OCD who were assessed at our OCD unit from January 2001 to December 2003. Our OCD unit is an outpatient unit of a university hospital. Three patients were excluded from the study for refusing to participate (N = 1), comorbid diagnosis of psychotic disorder (N = 1), and cognitive deficit that made completion of interviews difficult (N = 1).

After written informed consent was obtained, all 46 patients were interviewed. OCD diagnosis was confirmed by 2 psychiatrists (J.M.M., P.A.) using the Structured Clinical Interview for DSM-IV (SCID-I/P).[33] Current or previous depressive episodes fulfilling DSM-IV criteria for major depressive disorder were assessed using the SCID-I/P. None of the patients had a comorbid diagnosis of schizophrenia or any other psychotic disorder or had a past history of psychoactive substance abuse. The Yale-Brown Obsessive Compulsive Scale (YBOCS)[34] was administered (P.A.) to all patients to assess OCD symptom severity.

A semistructured clinical interview was designed by the researchers to assess the relationship between reproductive cycle events and onset of OCD or changes in OCD symptoms (the interview is available from the authors upon request). All interviews were conducted in person by the same clinician (J.L.).

Patients were asked about their current or previous history of premenstrual mood symptoms (we included the 4 mood symptoms of the DSM-IV research criteria for premenstrual dysphoric disorder: anxiety, irritability, mood lability, and depressed mood) and onset of OCD or changes in OCD symptoms (worsening, improvement, or no changes) at menarche, premenstruum (defined as 7 days before menses), pregnancy, postpartum (defined as 6 months following childbearing), abortions or miscarriages, perimenopause, and/or menopause. We also inquired about any use of oral contraceptive pills or hormone replacement therapy.

If a woman had more than 1 child, each pregnancy and postpartum period was individually assessed, obtaining the following information: age at pregnancy; type of

delivery (cesarean or vaginal); pregnancy, delivery, and postpartum complications; OCD onset or changes in OCD symptoms; changes in antiobsessive treatment; and depressive episodes during pregnancy or postpartum.

Presence of specific obsessions or compulsions related to the fetus or the child at any pregnancy or postpartum was also questioned. Ages at onset of OCD, menarche, and menopause were obtained. We requested information on somatic climacteric complaints (e.g., hot flashes).

The following events close to the onset of OCD were also assessed: death or serious illness of a family member or a close friend, school or employment changes, geographic changes in living, economic or legal problems, physical illness, and any other stressful event that was considered important by the patient. Psychosocial factors that may have been associated with reproductive events were not assessed.

In order not to induce patients to relate the onset of OCD to reproductive events, the age at onset of OCD and the role of major events were assessed at the first part of the interview, before the specific questions about reproductive cycle events were made. Patients were asked about major events (but not reproductive cycle events) related to the onset. OCD onset was considered to be related to a reproductive cycle event if the patient reported spontaneously that her OCD began just after the event (which happened especially for pregnancy, postpartum, and menopause). For patients with an onset related to pregnancy and postpartum, it was asked in which month the onset of OCD occurred. Onset at menarche was determined by the difference in years between age at menarche and age at onset of OCD. If the difference was 0 or 1, then it was asked if the patient remembered whether the onset of OCD occurred within the 12 months following menarche.

Regularity of menses was assessed. All cycles within 21 to 35 days with 7 or fewer days of variation from cycle to cycle were considered regular. In those patients who were reproductively active, menstrual regularity was studied in the last year. Perimenopausal or menopausal patients were asked about the regularity of their cycles when they were between 20 and 35 years old.

Data were analyzed with SPSS v.11.0 (SPSS Inc., Chicago, Ill.). Two-tailed Fisher exact test was performed for 2×2 categorical comparisons, setting the statistical significance at $p < .05$. The analyses were powered using the program Sample Power v.1.20 (SPSS Inc., Chicago, Ill., 1997), with an alpha of 0.05 and a beta of 0.80. To test the association between experiencing some degree of premenstrual mood symptoms (1 or more symptoms) and premenstrual worsening of OCD, a power of 91% was obtained. For this calculation, we used the proportion of premenstrual mood symptoms found in our sample.

As logistic regression can be used to estimate odds ratios,[35] we applied this multivariate analysis to study vulnerability to OCD and mood symptoms at premenstruum and the potential relationship with postpartum exacerbation of OCD. Two regression models were constructed to answer the first 2 questions posed at the end of the introduction section. In the first model, premenstrual worsening of OCD was the dependent variable, and the number of premenstrual mood symptoms (which ranged from 0 to 4) was the independent variable. This model estimates the odds ratio for premenstrual worsening of OCD as the number of mood symptoms increases by 1. In the second model, postpartum onset or worsening of OCD was the dependent variable, and 2 independent variables were introduced: number of premenstrual mood symptoms and premenstrual worsening of OCD. For all models, stepwise logistic regression by likelihood ratio was used. The probability of F entering the regression equations was set at 0.05 and of F being removed from the regression equations was set at 0.10.

In the analysis of data exploring factors related to OCD exacerbation at reproductive events, we assigned the only woman who reported that onset of her OCD was in menopause to the group of women who did not perceive changes in OCD during the menstrual cycle and did not observe the onset or worsening of OCD at pregnancy or puerperium.

RESULTS

Onset of OCD at Reproductive Events

Demographic and clinical data of the sample are represented in Table 1. Table 2 summarizes the onset of OCD at different reproductive events. The peak onset of OCD at menarche is represented in Figure 1. It is interesting that most of the onset is seen between 1 year before menarche to 9 years after this reproductive event.

All onsets of OCD at pregnancy or postpartum happened at the first gestation. The patient whose OCD was initiated at pregnancy reported her onset during the third trimester. All 3 postpartum onsets were reported as having occurred within the first month after delivery. There were no onsets of OCD related to an abortion or a miscarriage.

Changes in Existing OCD at Reproductive Events

Improvement in preexisting OCD symptoms was only reported at pregnancy by 1 patient. None of the patients reported improvement of OCD at other reproductive events. Worsening of OCD at reproductive events is represented in Table 3, with postpartum and premenstruum being the 2 periods with greatest risk.

Factors Related to Exacerbation of OCD at Reproductive Events

Premenstrual mood symptoms and worsening of OCD at premenstruum. A greater proportion of premenstrual mood symptoms (1 or more) was reported by those patients whose OCD worsened at premenstruum (100% vs.

Table 1. Demographic and Clinical Information on Female Outpatients With DSM-IV Obsessive-Compulsive Disorder (OCD) Interviewed for a Relationship Between Reproductive Cycle Events and OCD

Variable	All Patients (N = 46)
Age at study, mean ± SD, y	35.2 ± 13.2
Age at study, y, N (%)	
18–30	19 (41)
31–40	11 (24)
41–50	8 (17)
51–60	6 (13)
≥ 61	2 (4)
Age at onset of OCD, mean ± SD, y	19.0 ± 9.4
Major events (not reproductive) at onset of OCD, N (%)	9 (20)
YBOCS scores, mean ± SD	
Obsessions	14.4 ± 2.9
Compulsions	13.5 ± 4.3
Total	27.9 ± 6.3
Reproductive status at study, N (%)	
During the reproductive years, before perimenopause	34 (74)
At perimenopause/menopause[a]	1 (2)
Postmenopausal	11 (24)
Hormonal treatments at assessment, N (%)	
Contraceptive pills[b]	3 (7)
Hormone replacement therapy	0 (0)
Age at menarche, mean ± SD, y	12.6 ± 1.6
Age at menopause, mean ± SD, y	46.9 ± 5.3
Age at natural menopause, mean ± SD, y[c]	47.8 ± 5.5
History of regular menstrual cycles, N (%)	34 (74)
Patients with at least 1 abortion or miscarriage, N (%)	6 (13)
Patients who delivered at least 1 live-born child, N (%)	17 (37)
Delivered only 1 child	8 (17)
Delivered 2 children	8 (17)
Delivered 3 children	1 (2)
History of somatic climacteric complaints, N (%)[d]	7/11 (64)
History of mood disorders, N (%)	
Premenstrual affective symptoms (1 or more)	27 (59)
Anxiety	12 (26)
Irritability	22 (48)
Mood lability	16 (35)
Depressed mood	21 (46)
Current or previous history of major depressive episodes	11 (24)
Postpartum depression in women who had been pregnant	4/17 (24)

[a]A 46-year-old perimenopausal patient referred to an amenorrhea of 3 months and reported hot flashes.
[b]All 3 patients were reproductively active.
[c]Excluding 2 women with surgical menopause after a hysterectomy with removal of both ovaries.
[d]Calculated only in those patients who had arrived at menopause.
Abbreviation: YBOCS = Yale-Brown Obsessive Compulsive Scale.

Table 2. Onset of Obsessive-Compulsive Disorder at Reproductive Events

Reproductive Event	N/N	%
Menarche (within the following 12 months)	10/46	22
Pregnancy		
All patients	1/46	2
Patients with children[a]	1/17	6
Postpartum		
All patients	3/46	7
Patients with children[a]	3/17	18
Menopause		
All patients	1/46	2
Postmenopausal patients[b]	1/11	9

[a]Patients who delivered at least 1 live-born child.
[b]Patients with natural menopause (N = 9) or surgical menopause (N = 2) following a hysterectomy with removal of both ovaries.

49%, Fisher exact test [2-tailed], $p < .01$). A significant association was found between each premenstrual mood symptom (anxiety, irritability, mood lability, and depressive mood) and premenstrual worsening of OCD (Fisher exact test [2-tailed], all $p < .01$).

As can be seen in the first regression model in Table 4, there is a significant increase in the odds ratio for premenstrual worsening of OCD as the number of premenstrual mood symptoms increases.

Characteristics of pregnancies and postpartum exacerbation of OCD. The 13 patients with onset of OCD prior to pregnancy or at first pregnancy completed 20 full pregnancies. Several characteristics of the pregnancies have been analyzed. Of these 20 pregnancies, only 1 case (5%) referred to depression during pregnancy, and 5 cases (25%) reported postpartum depression. Only the existence of postpartum depression seemed to be associated with the onset or worsening of OCD at this period (Fisher exact test [2-tailed], $p < .01$). Being primiparous; type of delivery; presenting complications during pregnancy, delivery, or postpartum; and changes in antiobsessive treatment during pregnancy were not associated with onset or postpartum worsening of OCD. Two patients mentioned obstetric complications, all in the third trimester of pregnancy: 1 reported preeclampsia, and the other reported metrorrhagia. Neither patient reported a worsening of OCD during the pregnancy in which the obstetric complication occurred. No delivery or postpartum complications were described. Antiobsessive treatment was withdrawn in all OCD patients during pregnancy.

The proportion of postpartum worsening of OCD was similar for first pregnancies (6 of 13, 46%) and second pregnancies (3 of 6, 50%). Only 1 patient had a third pregnancy without worsening at the postpartum. Of the 13 patients with known OCD at pregnancy or postpartum, 7 patients (54%) had specific obsessions or compulsions related to the fetus or the newborn during these reproductive periods. These symptoms were especially frequent at the postpartum, and included obsessive thoughts of fearing to harm the child and contamination obsessions with compulsions related to the newborn.

Mood and OCD premenstrual symptoms and postpartum exacerbation of OCD. Premenstrual depressive mood was significantly associated with postpartum onset or worsening of OCD (Fisher exact test [2-tailed], $p < .05$). Irritability at premenstruum and premenstrual worsening of OCD were also more frequent in those patients with postpartum onset or worsening of their disorder, with a statistical significance in Fisher test equal to .05.

The second regression model in Table 4 describes the association of premenstrual mood symptoms with postpartum exacerbation of OCD. As the number of premen-

Figure 1. Age at Onset of Obsessive-Compulsive Disorder (OCD) and Menarche (N = 46)

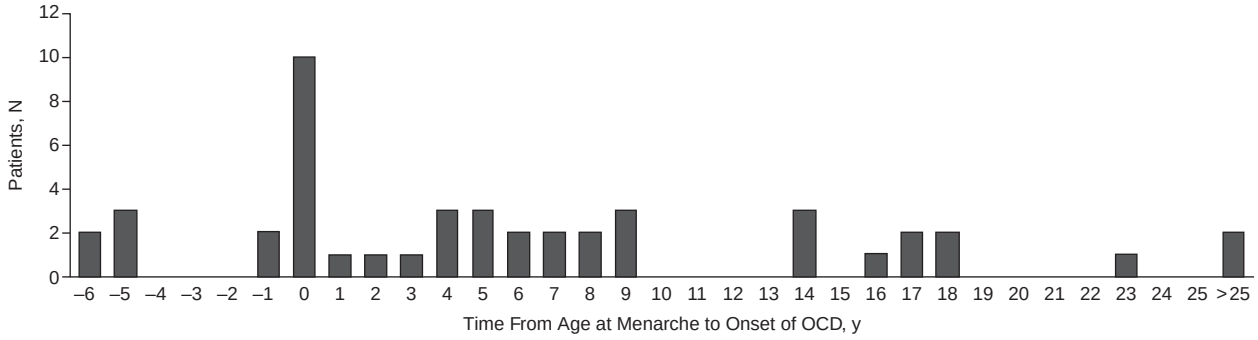

Table 3. Worsening of Preexisting Obsessive-Compulsive Disorder (OCD) at Reproductive Events

Reproductive Event	N/N[a]	%
Premenstruum	9/45	20
Abortion or miscarriage	0/6	0
Pregnancy	1/12	8
Postpartum	6/12	50
Perimenopause/menopause	1/12	8

[a]Sample sizes are compounded by the number of patients with preexisting OCD at each reproductive event.

strual symptoms increases, so does the odds ratio for onset or worsening of OCD at postpartum. It can be seen that the covariate premenstrual worsening of OCD was not significant and consequently did not enter the model.

History of major depressive disorder and exacerbation of OCD at reproductive events. Patients with (N = 11) or without (N = 35) history of major depressive episodes did not differ in frequencies of premenstrual mood symptoms or premenstrual worsening of OCD.

Past or present history of major depressive episodes, including postpartum depression, was found in 9 (53%) of the 17 patients who had been pregnant. Patients with a postpartum onset or worsening of OCD had a greater history of major depressive disorder than those patients without postpartum exacerbation of OCD (86% vs. 30%, Fisher exact test [2-tailed], p = .05). These differences were not found for onset or worsening of OCD during pregnancy.

Six (50%) of the 12 postmenopausal or perimenopausal patients had a history of major depressive disorder. The patient with a menopausal onset of OCD had a history of major depressive disorder, while the patient with an OCD worsening after a hysterectomy did not.

DISCUSSION

In our sample, OCD onset occurred in the same year as menarche in 22%, at pregnancy in 2%, at postpartum in 7%, and at menopause in 2%. Worsening of preexisting OCD was reported by 20% of patients at premenstruum, 8% at pregnancy, 50% at postpartum, and 8% at menopause. Those patients whose OCD worsened premenstrually reported more premenstrual mood symptoms. Patients with an onset or worsening of OCD at postpartum more frequently reported premenstrual mood symptoms, premenstrual worsening of OCD, and previous history of major depressive disorder, including postpartum depression.

Onset at Reproductive Events

It seems that the reproductive cycle, and especially some events that imply changes in gonadal steroids, may play a role in the onset and course of OCD in certain women.[19] The peak onset of OCD in the same year as the menarche, observed in nearly a quarter of our patients, suggests that changes in steroid hormones close to the menarche could be related to this high incidence.

Some authors have pointed out that fluctuations of gonadal hormones and gonadotropins that mark the onset of menarche may be associated with changes in the reactivity stress system, resulting in a higher incidence of hypothalamic-pituitary-adrenal (HPA) axis dysregulation and mood instability.[4] It has also been suggested that the female preponderance of depression in adulthood could be associated with changes in androgen and estrogen levels rather than morphological changes at puberty.[36] Freeman et al.[5] described the onset of bipolar disorder within 1 year of menarche in 9 (18%) of 50 female patients. Dysregulation of the serotonergic neurotransmitter system brought on by changes in the hormonal milieu at menarche may increase vulnerability to mood disorders[4] and perhaps predispose some patients to initiation of OCD in this period.

Another interesting finding is that most of the onset of OCD occurred not only at menarche, but also in the years following this reproductive event (from 1 year before to 9 years after menarche; see Figure 1). Besides changes in gonadal hormones and their interaction with serotonin, which have been mentioned above, another hormone that

Table 4. Results of Stepwise Logistic Regression for Premenstrual and Postpartum Exacerbations of Obsessive-Compulsive Disorder (OCD) and Their Association With Premenstrual Symptoms

	Model 1 Premenstrual Worsening of OCD[a]			Model 2 Onset or Worsening of OCD at Postpartum[a]		
Covariate	OR	95% CI	p	OR	95% CI	p
Number of premenstrual mood symptoms[b]	5.1	1.6 to 16.1	.006	2.7	1.1 to 6.8	.039
Premenstrual worsening of OCD[b]	NA	NA	NA	NS	NS	NS

[a]The dependent variable in the model.
[b]Acts as independent variable.
Abbreviations: NA = not assessable, NS = not significant.

may explain this high incidence could be oxytocin. Previous animal studies[37] suggest that this neuropeptide is regulated by circulating ovarian steroids, with an increase of oxytocin mRNA in the female brain concomitant with puberty. Leckman et al.[38] found increased cerebrospinal fluid (CSF) levels of oxytocin in a subgroup of patients with non–tic-related OCD, which had an earlier age at onset. In this subgroup of patients, the CSF oxytocin level was correlated with severity of OCD. This discussion about the role of hormones in OCD is highly speculative, but we wonder if changes in gonadal hormones and oxytocin may contribute to the increased onset of OCD in the years following menarche.

Although the incidence of OCD onset close to menarche is remarkable, an increase in prevalence of OCD at puberty has also been described in male patients.[26] For this reason, our findings should be considered preliminary results, and it would be interesting to assess the age at onset of OCD in further studies including both male and female patients while controlling for the age at menarche in women.

In our patients, as in the study by Maina et al.,[20] postpartum seems to be a period of greater risk than pregnancy for initiation of OCD. The proportion of patients with children who had a postpartum onset of OCD was lower in our sample (18%) as compared with their study (50%). Onset at pregnancy, which was referred to by one of our patients (6% of patients with children), was slightly lower than in the study by Williams and Koran[19] (13%). Our results suggest that both pregnancy and postpartum may be periods of risk for the initiation of OCD, and the postpartum period may be the one with a greater risk. Changes in steroid hormones during these reproductive events and the potentially stressful situation of having a baby may contribute to the onset of OCD in some women.

A low proportion of onset of OCD was found at menopause. These results agree with the rates reported by some previous studies.[23,25]

Changes in Preexisting OCD Symptoms at Reproductive Events

As in the only previous study that addressed the relationship between OCD symptoms and the menstrual cycle,[19] we found that some women with OCD reported premenstrual worsening of their disorder. In our series, 20% of patients reported premenstrual worsening of OCD, a smaller proportion than reported by Williams and Koran[19] (42%). This difference may be accounted for by differences between the 2 samples, as the mean age of the patients in the study by Williams and Koran was greater than ours and many patients were postmenopausal. Most patients in our study were reproductively active, which could mean that some young patients who did not report premenstrual changes in OCD symptoms might be susceptible to feel worsening of OCD at premenstruum in the following years.

A substantial proportion of patients with OCD who had been pregnant reported worsening at postpartum (50%) at a higher rate than reported by Williams and Koran[19] (29%). Our results about changes in preexisting OCD at pregnancy are in agreement with previous studies, which reported both improvement and worsening in preexisting OCD symptoms at this reproductive event.

Vulnerability to Mood and OCD Symptoms at Reproductive Events

The proportion of premenstrual mood symptoms (59%) found in our sample fits estimations in previous studies[6] stating that 50% to 80% of menstruating women experience some degree of premenstrual symptoms. Another study of patients with OCD[19] reported premenstrual dysphoria in 24% of patients. Differences in the findings between studies could be explained by methodological issues: in contrast with the latter study, which only asked about premenstrual dysphoria, we asked about 4 different premenstrual mood symptoms (anxiety, irritability, depressed mood, and mood lability).

We found a slightly lower proportion of patients with postpartum depression than in the study of Williams and Koran[19] (24% vs. 35%). In the study by Sichel et al.,[18] it was underscored that a high proportion (60%) of patients with postpartum onset of OCD developed depression. Our results are in agreement with their findings, as we found a greater proportion of depression (history of both major depressive disorder and postpartum depression) in those patients who seemed to be more vulnerable to OCD at postpartum (with an onset or worsening of OCD at this reproductive event).

The clinically and statistically significant association between depressive symptoms and worsening of OCD at the premenstruum and the postpartum may indicate a predisposition of some women with OCD to show emotional disturbances at these reproductive phases, when rapid changes in gonadal steroid concentrations occur.[39] A special vulnerability to OCD and mood symptoms may be shared by patients at both premenstruum and postpartum, as we have found that those women who reported more premenstrual mood symptoms also more frequently reported an onset or worsening of OCD at postpartum. The association found between past or present history of major depressive episodes and the puerperal onset or worsening of OCD may indicate a greater susceptibility of depressive patients to worsening OCD at postpartum.

The predisposition to worsen at the premenstruum and the postpartum that certain women with OCD seem to have should be studied further, since the existence of mood symptoms or worsening of OCD during the premenstruum could act as predictors of puerperal worsening of obsessive-compulsive symptoms. It would be interesting to replicate our results in other studies and assess in a prospective manner the premenstruum and the puerperium in the same group of patients in order to verify if this association between both reproductive periods does exist. If our findings are confirmed in further studies, women with OCD and premenstrual mood symptoms or premenstrual exacerbation of OCD would benefit from careful postpartum attention in order to preserve the health of both mother and child.

Study Limitations

The main limitation of our study is the retrospective collection of the data. This limitation is especially relevant for data related to previous gestations and information about menstrual cycles in the menopausal group. The retrospective design may cause a recall bias, which could make those patients with worsening of their OCD at reproductive events more accurately remember whether they had mood symptoms related to these events when compared with the group of patients whose OCD did not worsen at reproductive cycle events. It is also possible that patients with more intense premenstrual mood symptoms could tend to report worsening in their obsessive-compulsive symptoms during the premenstruum. However, it is remarkable that many patients agreed about suffering mood symptoms during this period and not feeling changes in their OCD.

As the information was obtained retrospectively, we cannot know which patients would meet the diagnosis of premenstrual dysphoric disorder (PMDD); thus, we cannot verify if those patients with PMDD more frequently report worsening of their obsessive-compulsive symptoms at the premenstruum than other patients. Another issue is the overreporting of premenstrual dysphoric symptoms that has been found in retrospective assessment.[40]

Besides these limitations, the fact that 76% of our patients were reproductively active should be noted. In the only previous report that studied the effects of the menstrual cycle on OCD,[19] the mean age of the sample was greater than ours and many patients were postmenopausal. We think that this fact could make our results more reliable.

To our knowledge, there are no prospective studies analyzing the course of OCD during different reproductive events. It would be difficult to follow up a woman with OCD during her reproductive cycle and prospectively assess her obsessive-compulsive symptoms at different reproductive events from menarche (or from the onset of OCD) to menopause. It seems better to separately study different reproductive periods in a prospective way, and probably the premenstruum would be the easiest period to assess, as it is a repetitive and cycling phase present in all women. Several authors[41–43] have pointed out the prospective assessment as the best way of recalling data for research of menstrually related mood disorders. However, clinical decisions are often made on the basis of retrospective reports of premenstrual symptoms, and the retrospective assessment may on occasion form the basis of clinical decision making.[40]

Another limitation of our study is the relatively small sample size, which makes it impossible to obtain definitive conclusions about the relationship between menopause or abortions/miscarriages and the initiation or worsening of OCD. The number of patients with pregnancies was also small, but we think that our clinical findings about the effects of the postpartum on OCD, with many statistically significant results, are noteworthy. However, it is important to mention the lack of statistical power, especially when studying the subgroup of patients who had been pregnant. For instance, the power decreases to 66% when testing the association between premenstrual mood symptoms and postpartum onset/worsening of OCD and to 55% when testing the association between premenstrual worsening of OCD and postpartum onset/worsening of OCD. From these results it can be said that many negative results may have been influenced by the small sample size, and perhaps some could achieve significance if sample size is increased.

Conclusion

The findings of our study underscore the relationship between female reproductive cycle events and OCD changes. They suggest that some women with OCD are liable to present mood symptoms and worsening of OCD at reproductive periods that imply hormonal fluctuations, with premenstruum and postpartum being the 2 reproductive events with greatest vulnerability. Further prospective studies are needed to confirm whether premen-

strual worsening of OCD, premenstrual mood symptoms, and history of major depressive episodes could act as clinical predictors of postpartum worsening of OCD, as our results suggest.

Drug name: alprazolam (Xanax and others).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside U.S. Food and Drug Administration–approved labeling has been presented in this article.

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