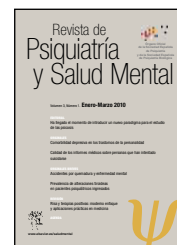


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ORIGINAL ARTICLE

Longitudinal study comparing depressive female patients with and without premenstrual exacerbation

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KEYWORDS

Depression;
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Abstract

Introduction: The aim of this study was to evaluate whether there are any differences in the clinical features of depression, personality and the G factor among women with and without premenstrual exacerbation (PE) of depression.

Material and methods: Ninety-nine outpatients diagnosed with major depression (DSM-IV) were interviewed twice. At baseline, the patients were not taking medication. The 74 patients who achieved remission (Hamilton rating scale for depression ≤ 7) after 16 weeks were evaluated again through the 16-personality factor (16-PF) questionnaire (5th edition) and the D48 (or Dominos) test.

Results: No differences in clinical characteristics or prognosis were found between the two groups of women, except for the greater presence of seasonal features among women with PE. Women with PE also scored higher for self-control on the 16-PF and scored lower on the D48 (Domino) test. The logistic analysis showed that higher self-control scores increased the risk for PE in 51.3% of the sample, while higher scores on the D48 test decreased the risk in 8.6%.

Conclusions: There were no differences between the two groups in the clinical features or prognosis of depression, except for the higher rates of seasonal features in the PE group. In contrast, differences were found in personality traits and the D48 between the two groups.

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PALABRAS CLAVE

Depresión;
Exacerbación
premenstrual;
Personalidad;
Inteligencia general

Estudio longitudinal comparativo entre pacientes con y sin exacerbación premenstrual de la depresión

Resumen

Introducción: El objetivo del estudio fue determinar si existían diferencias respecto a las características de la depresión, la personalidad y el factor G entre mujeres con y sin exacerbación premenstrual (EP) de la depresión.

Material y métodos: Se estudiaron, en dos entrevistas, a 99 pacientes ambulatorias diagnosticadas de depresión mayor unipolar (DSM-IV). La primera entrevista se realizó previamente al inicio del tratamiento antidepresivo. A las 74 pacientes en las que remitió la depresión ($HRDS \leq 7$) durante las siguientes 16 semanas se aplicó el 16 PF-5.a edición y el test de Dominós.

Resultados: No se encontraron diferencias en las características clínicas y evolutivas de la depresión entre ambos grupos, excepto por la mayor presencia de patrón estacional en las mujeres con EP. También éstas pacientes obtuvieron puntuaciones más altas en el factor autocontrol del 16 PF-5, e inferiores en el test de Dominós. En el análisis logístico se observó que una mayor puntuación en autocontrol aumentaba el riesgo de presentar EP (51,3%), y el test de Dominós lo disminuía (8,6%).

Conclusiones: Según el estudio, no hay diferencias en las características clínicas y evolutivas de la depresión entre mujeres con y sin EP, excepto por la mayor frecuencia de patrón estacional en las primeras. Sí había diferencias entre ambos grupos en el perfil de personalidad y en el test de Dominós.

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Introduction

Premenstrual tension syndrome was first described by Frank¹ in 1931, as a state of indescribable tension in the days prior to menstruation; its symptoms are irritability, depression, headaches, and swelling of the breasts and abdomen. In 1989, Spitzer et al² defined premenstrual syndrome (PMS) as a series of physical and mood disorders occurring regularly and repeatedly before menstruation that abate when this arrives, and which are severe enough to cause medical care to be sought. PMS has also been associated with both hereditary³ and cultural factors.^{4,5}

It has been considered a mild or subclinical manifestation of affective disorders. In fact, PMS has been shown to be closely associated with depression. In this respect, between 70% and 78% of women with PMS had a depressive phase,⁶ and 37% of women diagnosed with PMS developed depression during the following 3 years.⁷

Meanwhile, several authors have raised the need to differentiate PMS from cases that were merely premenstrual exacerbations (PE), specifically, premenstrual exacerbations of depression, as both are often included in the same group.^{2,8-10} Harrison et al¹¹ found that 38.6% of the women who requested treatment for PMS really had a PE. Other studies showed that between 27% and 64% of women with depression said that their premenstrual symptoms became worse.^{12,13} Compared with PMS, studies into PE are scarce.

The aim of this study was to compare women that suffer from premenstrual exacerbations of depressive symptoms

with those that do not, and understand the differences between them with regard to the clinical and evolutive characteristics of the depression, personality features, and the g factor.

Material and methods

A study was conducted on 99 outpatients between 18 and 50 years of age, referred by their health centre to different mental health units of the Vigo area. All had been diagnosed with major depression according to the DSM-IV criteria.¹⁴ Patients excluded were those who: 1) fulfilled any other diagnostic criteria on Axis I of the DSM-IV; 2) had taken any type of psychiatric drug in the previous 3 months (except benzodiazepines); 3) had been diagnosed with any other medical illness or had undergone any non-psychiatric treatment (including oral contraceptives) that could modify the symptoms of depression; 4) had been diagnosed with a personality disorder. The patients were questioned during a depressive phase about the exacerbation of depressive symptoms in the 5 days prior to menstruation during at least 2 menstrual cycles. Once diagnosed by a psychiatrist, the scales and questionnaires were collected by the interviewer.

In the first interview, before the onset of treatment with the antidepressant, demographic data was collected together with the highest educational level reached by the patient, and their socioeconomic level. This last variable depended

on the occupation of the head of the family,¹⁵ and the sample was classified into 6 groups, in accordance with the Spanish Classification of Occupations.¹⁶ Furthermore, an assessment was carried out of Axes III, IV and V, the longitudinal course, and seasonal pattern specifiers of the DSM-IV; the Hamilton Depression Rating Scale (HDRS)¹⁷ was applied, and clinical and evolutive variables were collected.

To avoid depressive symptoms affecting the assessment of personality and the g factor, only the 74 women whose depression abated (HDRS \leq 7) in the 16 weeks following the first interview, completed the second interview. The patients were treated with selective serotonin reuptake inhibitors and dual antidepressants (venlafaxine and mirtazapine) and the mean time between the 2 interviews was 10 weeks (SD=3.2). The second interview was performed in the follicular phase.¹⁸ The 5th edition of the 16-PF^{19,20} was used to study personality as it gives a full description of personality features. The Dominoes IQ test,²¹ which measures general intelligence (g factor), or crystallized intelligence according to Horn and Catell,²² is made up of 4 examples and 44 graphic problems, in increasing order of difficulty. The score obtained in the test depends on the number of correct answers in 25min.

The student's t-test was used to analyse the quantitative variables, and the Chi-square test to analyse qualitative variables (contingency tables) using the SPSS14.0 statistical software.²³ Then, a binary logistic regression model was performed including the variables associated with the presence of PE in the bivariate analysis. The model

included a goodness-of-fit test, and statistical significance was considered at $P<.05$.

Results

The mean age of the sample was 35 years (SD=8.4), 48.5% were married, most lived in urban areas (93.9%), and 73.7% did not have a university education. No significant differences were found in the distribution of socio-demographic variables (age, marital status, educational level, and socioeconomic level) when considering if the subject experienced from PE or not.

In accordance with the DSM-IV criteria, 49.5% of the patients were diagnosed with single episode major depression, and 59.6% met the criteria for the melancholic depression, 71.7% for moderate depression (Global Evaluation Scale), and 39.4% for seasonal depression. The mean age at which depression was first treated was 30.1 years (SD=9.8), the mean duration of the current phase was 7.6 months (SD=9), and the mean HDRS score in the first interview was 24.6 (SD=7). The only significant difference found in the clinical variables collected was the history of seasonal depression, which was more common in the women with PE than in those without (49.2% vs 22.2%; $\chi^2=6.99$; $P=.008$). Lastly, the only significant difference in the HDRS between the groups was that it was more common for women with PE to have worse symptoms of depression in the morning (58.3% vs 30.8%; t -test=-2.35; $P=.02$).

Table 1 Personal factors (16 PF-5) of the whole sample, and student t-test depending on whether the patient experienced premenstrual exacerbations or not

	Total (N=74)	Premenstrual Exacerbation		<i>t</i>	<i>P</i>
	Mean (SD)	Presence (N=48)	Absence (N=26)		
		Mean (SD)	Mean (SD)		
Warmth	4.7 (1.8)	4.9 (1.8)	4.5 (1.8)	-0.98	N.A.
Reasoning	4.7 (2.4)	4.3 (2.4)	5.6 (2)	2.31	.024
Emotional stability	3.6 (1.5)	3.3 (1.4)	4 (1.5)	2.04	.045
Dominance	4.6 (2.2)	4.4 (2.2)	5 (2.1)	1.11	N.A.
Liveliness	3.7 (1.8)	3.3 (1.8)	4.4 (1.8)	2.37	.021
Rule-consciousness	5.9 (1.9)	6.2 (1.9)	5.4 (1.9)	-1.74	N.A.
Social boldness	4.7 (1.8)	4.4 (1.8)	5.3 (1.6)	2.25	.028
Sensitivity	5.7 (1.9)	5.9 (1.7)	5.4 (2.3)	-1.13	N.A.
Vigilance	5.9 (1.9)	5.9 (2)	5.9 (1.9)	0.06	N.A.
Abstractedness	6.2 (1.8)	6.0 (1.6)	6.6 (2)	1.25	N.A.
Privateness	6 (2)	5.7 (1.9)	6.5 (2.2)	1.57	N.A.
Apprehension	7 (1.6)	7.2 (1.6)	6.5 (1.4)	-1.99	N.A.
Openness to change	4.6 (1.8)	4.4 (1.9)	4.9 (1.7)	1.25	N.A.
Self-reliance	6.7 (2.1)	6.9 (1.9)	6.4 (2.4)	-0.98	N.A.
Perfectionism	5.3 (1.8)	5.6 (1.6)	4.8 (2.1)	-1.78	N.A.
Tension	6.5 (1.8)	6.7 (1.8)	6.3 (1.9)	0.81	N.A.
Extraversion	4.6 (2.2)	4.9 (2.1)	4.4 (2.5)	-0.47	N.A.
Apprehension	7.1 (2)	7.5 (2)	6.5 (1.7)	-2.21	.03
Agreeableness	6.4 (1.9)	6.5 (1.9)	6.1 (1.8)	-0.81	N.A.
Openness	4.2 (2.2)	3.7 (2)	5.1 (2.3)	2.61	.011
Conscientiousness	6.4 (2.2)	7 (2)	5.3 (2.1)	-3.50	.001

Table 2 Results of the logistic regression analysis

Variables	N	Odds ratio	95%CI	P
Conscientiousness	74	1.513	(1.152-1.986)	.003
Dominoes Test	74	0.914	(0.845-0.989)	.026

Among the 74 patients who underwent the 5th edition 16-PF test, Emotional Stability, Liveliness, and Apprehension showed the greatest deviation in relation to the mean values. Table 1 shows that the women with PE obtained higher scores than those without for Conscientiousness and Neuroticism, and lower scores for Self-Reliance, Liveliness, Reasoning, Social Boldness, and Emotional Stability. The mean score of the sample in the Dominoes test was 23.1 (SD=8), the women with PE obtaining lower scores than those without (21.5 [SD=9] vs 26.1 [SD=5.2]; t-test=2.9; $P=.006$).

Lastly, a logistic regression analysis was performed in which the dependent variable was the presence of PE. The explanatory variables were the factors of the 5th ed. of 16 PF in which differences were observed between both groups (Conscientiousness, Self-Reliance, Liveliness, Reasoning, Social Boldness, Apprehension and Emotional Stability) and the score obtained in the Dominoes test. The bivariate analysis established that the other variables did not correlate with the dependent variable. The Homer-Lemeshow test showed a good-fitting model ($P=.084$). From the results of the analysis we can conclude that each additional point in the Conscientiousness score increases the relative risk of having PE by 51.3% whereas in the Dominoes test each additional point reduces this risk by 8.6% (table 2).

Discussion

The association between seasonal affective disorder and PMS has been observed in several studies.^{24,25} Some authors have explained that genetic factors are behind this, both disorders appearing on the clinical records of family members.²⁶ On the other hand, other authors prefer to emphasise the clinical similarities between the two.^{27,28}

This study found no significant differences in the severity, duration and clinical manifestations of depression in the patients with and without PE. However, Bancroft et al²⁹ found that women with PE had longer and more severe depressive phases, while Kornstein et al¹³ also found that women with PE had longer depressive episodes, but that they were less severe. Of all the studies reviewed, only Kornstein et al reports differences in the clinical manifestations of depression.¹³ In the patients with PE, somatic complaints, psychomotor retardation, and paralysis were more common, while blunted affect was less frequent.

Reviewing the studies analysing the personality of patients with PMS or premenstrual dysphoric disorder, we can conclude that the following features are more common in these women: anxiety, psychasthenia, anankastic personality disorder, neuroticism, perfectionism, low-assertiveness, and harm avoidance.³⁰⁻³⁴ In our study, only

the second order factor Conscientiousness remained in the logistic regression model analysis; this factor is obtained by getting a high score in Rule-Conscientiousness and Perfectionism and a low score in Liveliness and Abstractedness. According to these results, it can be said that women with a greater sense of responsibility and increased self-control are more susceptible to PE.

In 1927, Spearman formulated the Two-factor Intelligence Theory, which can be broken down into a general factor (g factor) and another specific one (s factor).³⁵ Among the most reliable tests for assessing the g factor are the WAIS,³⁶ Raven's matrices,³⁷ and the Dominoes test.²¹ Keenan et al³⁸ found that women with PMS had more difficulty performing learning tests than those without, and showed that these differences were independent of depression or the phase of the menstrual cycle in which the tests were performed. In a later study³⁹ they discovered that women with PMS had impaired retrieval of coded information. In our study, the patients with PE also obtained lower scores in the Dominoes test than those without; however, studies with more specific neuropsychological tests are necessary to confirm and explain these findings.

Several limitations of this study must be highlighted, such as the retrospective assessment of PE. Different authors have pointed out that assessments of PMS should be performed prospectively, objectively, daily, and with specific questionnaires, in order, among other things, to confirm the absence of symptoms during the rest of the cycle.^{2,13,40} However, a retrospective analysis was used in several studies of PE^{13,41} as, unlike PMS, the symptoms of PE are present during the whole cycle. Furthermore, only studying the personality and g factor of the women who improved during the period before the 2nd interview could also have led to bias.

Several studies have found serotonergic impairment in patients with PMS, in particular low levels of plasma serotonin during the luteinic phase.^{10,42-45} Supporting the relationship between serotonergic dysfunction and the presence of PMS is evidence that selective serotonin reuptake inhibitors are effective at treating PMS,⁴⁶ and that symptoms worsen with acute dietary tryptophan depletion.⁴⁷ Furthermore, a recent study has found that women with premenstrual dysphoric disorder who were carriers of the short-allele of the serotonin transporter gene (5-HTTLPR) scored higher in scales of neuroticism.⁴⁸

In conclusion, the results of the study show no significant differences in the clinical and evolutive characteristics of depression between women with and without PE, except for the higher frequency of the seasonal pattern in those with PE. However, once depression abated, differences were found between the groups, both in their personality profiles and their performance in the Dominoes test.

References

1. Frank RT. The hormonal cause of premenstrual tension. *Arch Neurol Psychiatry*. 1931;26:1053-7.
2. Spitzer RL, Severino SK, Williams JB, Parry BL. Late luteal phase dysphoric disorder and DSM-III-R. *Am J Psychiatry*. 1989;146:892-7.

3. Kendler KS, Karkowski LM, Corey LA, Neale MC. Longitudinal Population-Based Twin Study of Retrospectively Reported Premenstrual Symptoms and Lifetime Major Depression. *Am J Psychiatry*. 1998;155:1234-40.
4. Janiger O, Riffenburgh R, Kersh R. Cross Cultural Study of Premenstrual Symptoms. *Psychosomatics*. 1972;13:226-35.
5. Johnson TM. Premenstrual syndrome as a western culture-specific disorder. *Cult Med Psychiatry*. 1987;11:337-56.
6. Warner P, Brancroft J, Dixon A, Hampson M. The relationship between perimenstrual depressive mood and depressive illness. *J Affect Disord*. 1991;23:9-23.
7. Graze KK, Nee J, Endicott J. Premenstrual depression predicts future major depressive disorder. *Acta Psychiatr Scand*. 1990;81:201-5.
8. Chisholm G, Jung SO, Cumming CE, Fox EE, Cumming DC. Premenstrual anxiety and depression: comparison of objective psychological tests with a retrospective questionnaire. *Acta Psychiatr Scand*. 1990;81:52-7.
9. Dell DL. Premenstrual Syndrome, Premenstrual Dysphoric Disorder, and Premenstrual Exacerbation of Another Disorder. *Clin Obstet Gynecol*. 2004;47:568-75.
10. Yonkers KA, O'Brien PM, Eriksson E. Premenstrual syndrome. *Lancet*. 2008;371:1200-10.
11. Harrison WM, Endicott J, Nee J, Glick H, Rabkin JG. Characteristics of Women Seeking Treatment for Premenstrual Syndrome. *Psychosomatics*. 1989;30:405-11.
12. Halbreich U, Endicott J. Relationship of dysphoric premenstrual changes to depressive disorders. *Acta Psychiatr Scand*. 1985;71:331-8.
13. Kornstein SG, Harvey AT, Rush AJ, Wisniewski SR, Trivedi MH, Svikis DS, et al. Self-reported premenstrual exacerbation of depressive symptoms in patients seeking treatment for major depression. *Psychol Med*. 2005;35:683-92.
14. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)*. 4th ed. Washington DC: American Psychiatric Association; 1994.
15. Domingo A, Marcos J. Propuesta de un indicador de «clase social» basado en la ocupación. *Gac Sanit*. 1989;3:320-6.
16. Instituto Nacional de Estadística. *Clasificación Nacional de Ocupaciones*. Madrid: INE; 1979.
17. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960;23:56-62.
18. Berlin RE, Raju JD, Schmidt PJ, Adams LF, Rubinow DR. Effects of the Menstrual Cycle on Measures of Personality in Women With Premenstrual Syndrome: A Preliminary Study. *J Clin Psychiatry*. 2001;62:337-42.
19. Cattell RB, Cattell AK, Cattell HEP. *Sixteen Personality Factor Questionnaire*. Fifth Ed. Illinois: Institute for Personality and Ability Testing, Inc. Champaign IL; 1993.
20. Russell MT, Karol DL. 16 PF-5.a Ed. Madrid: TEA Ediciones, 2000.
21. Anstey E. D-48. *Tests de Dominós*. Madrid: TEA Ediciones; 1999.
22. Horn JL, Cattell RB. Refinement and test of the theory of fluid and crystallized intelligence. *J Educ Psychol*. 1966;57:253-70.
23. SPSS 2006. Version 14.0 [computer program]. Chicago, Illinois: SPSS Inc.
24. Praschak-Rieder N, Willeit M, Neumeister A, Hilger E, Stastny J, Thierry N, et al. Prevalence of premenstrual dysphoric disorder in female patients with seasonal affective disorder. *J Affect Disord*. 2001;63:239-42.
25. Portella AT, Haaga DA, Rohan KJ. The association between seasonal and premenstrual symptoms is continuous and is not fully accounted for by depressive symptoms. *J Nerv Ment Dis*. 2006;194:833-7.
26. Praschak-Rieder N, Willeit M, Winkler D, Neumeister A, Hilger E, Zill P, et al. Role of family history and 5-HTTLPR polymorphism in female seasonal affective disorder patients with and without premenstrual dysphoric disorder. *Eur Neuropsychopharmacol*. 2002;12:129-34.
27. Möller SE. Serotonin, carbohydrates, and atypical depression. *Pharmacol Toxicol*. 1992;71(Suppl 1):61-71.
28. Wurtman JJ. Carbohydrate craving. Relationship between carbohydrate intake and disorders of mood. *Drugs*. 1990;39 (Suppl 3):49-52.
29. Bancroft J, Pennie D, Warner P. Vulnerability to Perimenstrual Mood Change: The Relevance of a Past History of Depressive Disorder. *Psychosom Med*. 1994;56:225-31.
30. Parry BL, Ehlers CL, Mostofi N, Phillips E. Personality traits in LLPDD and normal controls during follicular and luteal menstrual-cycle phases. *Psychol Med*. 1996;26:197-202.
31. Coppen A, Kessel N. Menstruation and Personality. *Br J Psychiatry*. 1963;109:711-21.
32. Watts S, Dennerstein L, Horne DJ. The premenstrual syndrome. A psychological evaluation. *J Affect Disord*. 1980;2:257-66.
33. Taylor RJ, Fordyce ID, Alexander DA. Relationship between personality and premenstrual symptoms: a study in five general practices. *Br J Gen Pract*. 1991;41:55-7.
34. Hsu SC, Liu CY, Hsiao MC. A comparison of the Tridimensional Personality Questionnaire in premenstrual dysphoric disorder and major depressive disorder. *Compr Psychiatry*. 2007;48:366-70.
35. Spearman CE. *The abilities of man, their nature and measurement*. New York: Macmillan; 1927.
36. Wechsler D. *Escala de inteligencia de Wechsler para adultos*. Madrid: TEA Ediciones; 1970.
37. Raven JC, Court JH, Raven J. *Test de Matrices Progresivas. Escalas Coloreada, General y Avanzada*. Manual. Buenos Aires: Paidós; 1993.
38. Keenan PA, Stern RA, Janowsky DS, Pedersen CA. Psychological aspects of premenstrual syndrome. I: cognition and memory. *Psychoneuroendocrinology*. 1992;17:179-87.
39. Keenan PA, Lindamer LA, Jong SK. Menstrual Phase-Independent Retrieval Deficit in Women with PMS. *Biol Psychiatry*. 1995;38:369-77.
40. Rubinow DR, Roy-Byrne P. Premenstrual Syndromes: Overview From a Methodologic Perspective. *Am J Psychiatry*. 1984;141:163-72.
41. Hsiao MC, Hsiao CC, Liu CY. Premenstrual symptoms and premenstrual exacerbation in patients with psychiatric disorders. *Psychiatry Clin Neurosci*. 2004;58:186-90.
42. Halbreich U, Tworek H. Altered serotonergic activity in women with dysphoric premenstrual syndromes. *Int J Psychiatry Med*. 1993;23:1-27.
43. De Diego E, De la Gándara JJ. TDP: revisión general desde el punto de vista de la psiquiatría. En: De la Gándara JJ, editors. *Síndrome Premenstrual*. Madrid: Cauce Editorial; 1996. 37.
44. Gilbert J, Bundío L. Neurobiología y neuroendocrinología. En: Leal C, editors. *Trastornos depresivos en la mujer*. Barcelona: Masson; 1999. 21.
45. Kikuchi H, Nakatani Y, Seki Y, Yu X, Sekiyama T, Sato-Suzuki I, et al. Decreased blood serotonin in the premenstrual phase enhances negative mood in healthy women. *J Psychosom Obstet Gynaecol*. 2010;31:83-9.
46. Brown J, O'Brien PM, Marjoribanks J, Wyatt K. Selective serotonin reuptake inhibitors for premenstrual syndrome. *Cochrane Database Syst Rev*. 2009;5:CD001396.
47. Menkes DB, Coates DC, Fawcett JP. Acute tryptophan depletion aggravates premenstrual syndrome. *J Affect Disord*. 1994;32:37-44.
48. Gingnell M, Comasco E, Orelund L, Fredrikson M, Sundström-Poromaa I. Neuroticism-related personality traits are related to symptom severity in patients with premenstrual dysphoric disorder and to the serotonin transporter gene-linked polymorphisms 5-HTTLPR. *Arch Womens Ment Health*. 2010 [in press].