European Psychiatry 25 (2010) 450–454

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Original article

The impact of premenstrual dysphoric disorder among 92 bipolar patients

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ARTICLE INFO

Article history:
Received 21 August 2009
Received in revised form 27 November 2009
Accepted 29 November 2009
Available online 7 July 2010

Keywords:
Premenstrual dysphoric disorder (PMDD)
Bipolar disorder
DSM-IV

ABSTRACT

Objectives: To evaluate the impact of Diagnostic and Statistical Manual for Mental Disorders-Fourth Edition (DSM-IV)-defined premenstrual dysphoric disorder (PMDD) lifetime co-morbidity among 92 bipolar patients.
Method: Ninety-two women with a lifetime diagnosis of DSM-IV-defined Bipolar Disorder (BD) either type I or type II were consecutively enrolled to determine co-morbidity rates with PMDD and associated clinical features. Measures included the Structured Clinical Interview for the DSM-IV Axis I Disorders (SCID-I) and the Clinical Global Impression (CGI) rating scale.
Results: In our sample, 25 (27.2%) patients reported a lifetime history of PMDD according to DSM-IV criteria (PMDD+). PMDD+ reported higher rates of Cyclothymia and BP-II than PMDD− (respectively 72% vs. 36% and 88% vs. 60%). On the contrary, the carbohydrate-craving feature was more represented among PMDD− than PMDD+ (25% vs. 4%). PMDD was also significantly associated with post-partum depression (36% vs. 15%), Obsessive-Compulsive (24% vs. 7.5%) and Body Dysmorphic Disorders (24% vs. 6%). Finally, PMDD+ reported higher total number of Axis I co-morbid disorders than PMDD−.
Conclusions: In our cohort of BD women, PMDD is a frequent co-morbid condition, in particular among patients with BD-II or Cyclothymia. Multiple co-morbidities also represent a clinical variable associated with PMDD. Further perspective studies are necessary to better define the relationships between PMDD and BD.

Premenstrual dysphoric disorder (PMDD) is a Premenstrual syndrome (PMS) presenting with physical and psychic symptoms, including feelings of tension, panic attacks, diarrhea, mood swings, crying, apathy or loss of interests, fatigue, mild transient amnesia, sweet craving or binge eating, sleep or sexual drive disturbances, headaches and somatic pain [32]. According to Diagnostic and Statistical Manual for Mental Disorders-Fourth Edition (DSM-IV) criteria, the PMDD diagnosis requires five or more of the above, occurring during the 2 weeks before the menstrual cycle and (substantially) disappearing within a few days after the onset of the bleeding [2]. The cardinal symptom is irritability, often accompanied by anxiety, anger and mood reactivity. Originally called "Late Luteal Phase Dysphoric Disorder", the disorder was renamed "PMDD" by the American Psychiatric Association in its May 1994 revision of the DSM-IV [2], being subsequently proposed to shift from a position in the "appendix" of the manual to a "disorder requiring further study" [17].

Stating the paucity of studies on PMDD occurrence in general population, most of current prevalence data refer to the broader diagnosis of PMS which, on turns, largely depends on the stringency of the used definition. Up to 80% of menstruating women have experienced at least one symptom that could be better attributed to PMS, with general population prevalence estimates ranging from as low as 3% [22] to as high as 30% [6]. Employing stringent DSM-IV criteria, 3–8% of general population women meet criteria for lifetime PMDD, with similar prevalence rates been replicated by several epidemiological studies and surveys [12,24,33].

Additionally, PMS symptoms could be found in course of other psychiatric conditions as sub-threshold manifestations [7,27]. A suggestive correlation of PMS hormonal changes and symptoms like depression, irritability, tension, anger and panic attacks has already proposed [5,18], further increasing the interest for the study of the relationships between PMDD and other mental disorders. Bipolar Disorders (BDs) spectrum [25], particularly "softer" forms and Cyclothymia, share symptoms such as depression, anxiety, irritability and mood reactivity with PMDD [14,31]. Differentiating between PMDD and other disturbances, which often worsen during the premenstrual phase, is a poorly understood challenge. Controversy also exists on the possible coexistence of PMDD and other affective disorders, which could further increase the burden of the clinical picture, possibly leading

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doi:10.1016/j.eurpsy.2009.11.010

affected women to seek for hospital admission during the overlapping, destabilizing episodes [21], as reported in course of co-morbid Major Depressive Disorder (MDD) and Panic Disorder (PD) [4]. PMDD could also indirectly interface with non-affective disorders such as bulimia and binge eating, which, on the other hand, may be related with mood disorders in general and Cyclothymia in particular [10,19].

Although several studies have already pointed out a correlation between mood disorders and PMS [20], the prevalence and clinical correlates of PMDD among those diagnosed with lifetime BDs type I, type II are still far away from an exhaustive acknowledgment. The aim of present study is to investigate the prevalence of PMDD in a large sample of BD women and to assess its clinical impact on symptomatological and course characteristics of the mood disorder.

1. Methods

1.1. Participants

Ninety-two female outpatients and inpatients, aged ≥18 years (mean = 49, S.D. = 12.52), were consecutively enrolled at the San Martino University Hospital of Genoa and its facilities, the Galliera Hospital of Genoa and the Sarzana Psychiatric Mental Health Center "*Azienda ospedaliera locale* (ASL) 5". Inpatients and outpatients ratio was approximately 1:1. Patients with a lifetime PMDD diagnosis (group PMDD+) were 25; 67 were without (group PMDD−). After complete description of the study, participants signed written informed consent forms approved by the local Ethical Committee Review Boards.

1.2. Data collection

An intensive face-to-face interview consisting of structured and semi-structured components was used to collect clinical data. The interview lasted approximately 2 hours. Each interviewer underwent a training program in the use of the interview instruments that included direct observation of experienced interviewers, direct supervision of interviews and inter-rater reliability.

Since the data collection was largely dependent on patient recall of historical information, all clinical variables were reviewed by the senior author (G.P.) with the purpose of consensus agreement. When questions arose, patients were re-contacted for further clarification. In almost all cases, patients' medical records were reviewed and missing information were obtained from family members and/or previous physicians.

Patients provided demographic information and completed the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) [9] at entry into the protocol. The presence of DSM-IV-TR [3] criteria for PMDD was systematically investigated by means of a semi-structured interview:

A. in most menstrual cycles during the past year, five (or more) of the following symptoms were present for most of the time during the last week of the luteal phase, began to remit within a few days after the onset of the follicular phase, and were absent in the week postmenses, with at least one of the symptoms being either (1), (2), (3), or (4):
   1. markedly depressed mood, feelings of hopelessness, or self-depreciating thoughts,
   2. marked anxiety, tension, feeling of being 'keyed up' or 'on edge',
   3. marked affective lability (e.g. feeling suddenly sad or tearful or increased sensitivity to rejection),
   4. persistent and marked anger or irritability or increased interpersonal conflicts,
   5. subjective sense of difficulty in concentrating,
   6. lethargy, easy fatigability, or marked lack of energy,
   7. marked change in appetite, overeating, or specific food cravings,
   8. hypersomnia or insomnia,
   9. a subjective sense of being overwhelmed or out of control,
   10. other physical symptoms, such as breast tenderness or swelling, headaches, joint or muscle pain, a sensation of 'bloating', weight gain;

   B. the disturbance markedly interferes with work or school or with usual social activities and relationships with others (e.g. avoidance of social activities, decreased productivity and efficiency at work or school);

   C. the disturbance is not merely an exacerbation of the symptoms of another disorder, such as MDD, PD, dysthymic disorder, or a personality disorder (although it may be superimposed on any of these disorders). For this diagnosis the critical variable in this study, we attained excellent inter-rater reliability (Kappa = 0.89).

Severity of current (e.g., past week) depressive and manic/hypomanic symptoms was assessed using the Clinical Global Impression (CGI) [11] scale and the Young Mania Rating Scale (YMRS) [34].

1.3. Statistical analysis

Comparative analysis for familial, epidemiological, clinical and course characteristics of subgroups were conducted using the Student's *t*-test for the dimensional variables (Mann-Whitney's *U*-test, when appropriate) and the Chi^2 analysis for those categories (Fisher's exact-test, when appropriated). Owing to the multiple comparisons and the number of subjects, our results are prone both to type I and type II errors. Therefore, given the exploratory nature of the study, we set significance at 0.05 level, two-tailed, in order to detect potentially clinically meaningful associations. To examine which historical illness variables were associated with PMDD, a stepwise logistic regression backward procedure was performed. An alpha of 0.05 was selected as the cutoff for inclusion of the variables in the regression.

2. Results

Among the 92 BD women of our sample, 25 (27.2%) reported a lifetime history of PMDD according to DSM-IV criteria. Patients with (PMDD+) and without (PMDD−) PMDD did not differ in educational level and marital status: subjects with ≤8 years of scholarship were respectively 13 (52%) for PMDD+ and 25 (37.3%) for PMDD−; 10 (40%) vs. 27 (40.3%) patients reported a high school level; 2 (8%) vs. 15 (22.3%) the University level of education ($Chi^2 = 2.99$, df = 2, p = ns). PMDD+ and PMDD− were "never married" respectively in three (12%) vs. 18 (27.7%) cases, "married" in 13 (52%) vs. 23 (35.4%) cases and "widowed or divorced" in nine (36%) vs. 24 (37%) cases ($Chi^2 = 3.16$, df = 2, p = ns).

Both mean age at the moment of the evaluation and mean age at onset of mood disorder were similar among PMDD+ and PMDD− (Table 1). Concerning the bipolar diagnostic subtypes, the rates of BD-II and Cyclothymia were higher in PMDD+ than in PMDD− (respectively 88% vs. 60% and 72% vs. 36%). On the contrary, BD-I was more represented across PMDD− than in PMDD+ (40% vs. 12%). Interestingly, also post-partum depression was more frequently reported by PMDD+ than PMDD− (36% vs. 14.9%). Other clinical features such as age, age at onset, seasonal pattern, rapid cyclicity, psychotic features, melancholia, past hospitalization and suicidality were similar in the two groups; the only exceptions was carbohydrate craving that was more frequent