The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column gave informed consent for its publication.

Treating comorbid premenstrual dysphoric disorder in women with bipolar disorder

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A 34-year-old woman has a diagnosis of bipolar disorder type I (BDI) and is currently euthymic on 7 mg daily of aripiprazole. A comorbid diagnosis of premenstrual dysphoric disorder (PMDD) was confirmed with 2 months of prospective charting. She was initiated on an oral contraceptive (estradiol 30 mcg plus levonorgestrel 0.15 mg daily), and after 6 weeks of treatment she noted substantial improvement in her PMDD symptoms. The improvement was confirmed with prospective symptom charting.

Premenstrual dysphoric disorder affects 3%–9% of women during reproductive years and detrimentally influences work/school productivity, relationships and/or social activities. Bipolar disorder is a major mental illness that affects 2.2% of our population,[1] and recent Canadian data ranked BD the second leading cause of disability among mental health and addiction problems.[2] A large community-based epidemiological study found that women with PMDD were 8 times more likely to have a comorbid diagnosis of BD.[3] In addition, 2 independent studies found higher rates of PMDD among women with BD.[4,5] The DSM-5 now recognizes PMDD as a distinct mood disorder, and its diagnosis is based on the presence of emotional and physical symptoms in the final week before the onset of menses, with marked improvement in the week following menses. Importantly, PMDD diagnosis must be confirmed by prospective daily charting during at least 2 symptomatic menstrual cycles. Given the paucity of literature in this area, the treatment of women with BD and comorbid PMDD can prove daunting and challenging. For the clinician treating a woman with known BD who is suspected of having comorbid PMDD, the following are practical, stepwise recommendations for the diagnosis and management of these comorbid conditions.

1. First it is critical to optimize the dosages of mood stabilizers and to stabilize the bipolar symptoms in order to rule out the possibility that the symptoms endorsed during the premenstrual phase are not simply secondary to untreated BD.
2. Once the BD is stabilized, then a minimum of 2 months of prospective daily charting is required. Several validated tools are available to help the clinician prospectively monitor premenstrual symptoms.[6,7]
3. Once the diagnosis of comorbid PMDD is confirmed, psychoeducation and lifestyle changes, such as diet, exercise and sleep hygiene, have been shown to alleviate premenstrual symptoms in some cases.[8]
4. Vitamin supplementation with 600 mg of elemental calcium twice daily[9] and 100 mg/d of vitamin B6[10] have also been proven to alleviate premenstrual symptoms and should be recommended.
5. Cognitive behavioural therapies seem effective in alleviating mood and anxiety symptoms, but not physical symptoms,[11,12] which suggests that these modalities likely enhance coping strategies rather than change the biological root of PMDD.
6. Antidepressants are considered the first-line treatment of PMDD,[13] as there is robust evidence of efficacy of serotonin and serotonin–norepinephrine reuptake inhibitors in randomized controlled trials.[14] However, this is precisely one of the main challenges in the treatment of PMDD with comorbid BD because, considering the well-established risk for mood worsening associated with the use of antidepressants in patients with BD, experienced clinicians will be very reluctant to prescribe an antidepressant to a patient with BD who is currently euthymic/stable from the BD standpoint. Therefore, we argue that the use of antidepressants in this population should be restricted to patients in whom PMDD is disabling and is not responsive to hormonal agents.
7. Hormonal agents are considered the second-line treatment for PMDD,[13] and their efficacy has also been confirmed in randomized controlled trials.[15] Although the literature on safety and efficacy of hormonal agents in women with comorbid BD is scarce, we have recently published a case series discussing some of our experience with the use of oral or transdermal contraceptives in this population.[16] Risks and benefits should always be carefully considered before prescribing hormonal agents.

In conclusion, the elevated disease burden and the complexity of the treatment of comorbid BD and PMDD impose an urgent need for randomized clinical trials in this population.

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