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# Combined Oral Contraceptive Pill Initiation in a Patient With Major Depressive Disorder, Premenstrual Dysphoric Disorder, Social Anxiety, Panic Disorder, and Histrionic Personality Disorder

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**Background:** Comorbid psychiatric conditions present an added layer of challenge in managing patients, as each condition and associated set of symptoms exacerbate the complexity of the overall presentation. Premenopausal women may be at particular risk for inadequate care, as their comorbid conditions may present overlapping symptoms and mask independent premenstrual symptoms. The prevalence of premenstrual dysphoric disorder and associated conditions can be as high as 8% in women of reproductive age. Recognizing and assessing premenstrual symptoms that are comorbid with other psychiatric conditions can help contribute to a comprehensive treatment strategy and potentially improve the treatment response for the comorbid conditions. Combined oral contraceptive pills (COCPs) have been approved for premenstrual conditions and should be considered by the psychiatrist as an available treatment option.

**Case Report:** A 34-year-old Caucasian female patient with comorbid major depressive disorder, premenstrual dysphoric disorder, social anxiety, panic disorder, and histrionic personality disorder, with persistent suicidal ideation and distress intolerance, was treated with norgestimate-ethinyl estradiol with improvement in mood, anxiety, and menstrual cramping and with associated diminished suicidal ideation and improved distress tolerance.

**Conclusion:** In this case, Beck Depression Inventory and Beck Anxiety Inventory scores, as well as self- and peer-reported functionality, all suggested improvement in symptoms following the introduction of COCPs. The neurohormonal contribution to psychiatric conditions continues to be studied and is becoming increasingly important. An understanding of the presence and etiology of premenstrual symptoms should be part of a comprehensive psychiatric assessment of female patients, and consideration of COCPs in the treatment plan adds a potentially potent option for symptom mitigation and remission.

***Keywords:*** *Contraceptives–oral–combined, depressive disorder, panic disorder, premenstrual dysphoric disorder, stress–psychological*

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## INTRODUCTION

Comorbid psychiatric conditions present an added layer of challenge in managing patients, as each condition and associated set of symptoms exacerbate the complexity of the overall presentation. Premenopausal women may be at particular risk for inadequate care, as their comorbid conditions may present overlapping symptoms and mask independent premenstrual symptoms. The prevalence of premenstrual dysphoric disorder (PMDD) and associated conditions can be as high as 8% in women of reproductive age.[1] Recognizing and assessing premenstrual symptoms that are comorbid with psychiatric conditions can help contribute to a comprehensive treatment strategy and potentially improve the treatment response for the comorbid conditions. Combined oral contraceptive pills (COCPs) have been approved for premenstrual conditions and should be considered by the psychiatrist as an available treatment option.

We present the case of a patient with comorbid major depressive disorder, PMDD, social anxiety, panic disorder, and histrionic personality disorder, with persistent suicidal ideation and distress intolerance, who was treated with norgestimate-ethinyl estradiol.

## CASE REPORT

A 34-year-old Caucasian female presented to psychiatry for treatment of mood and anxiety symptoms. The patient was unemployed owing to debilitating social anxiety and panic attacks. She lived at home with her boyfriend and husband and

practiced a polyamorous lifestyle that included cyber relationships. She was heavily involved with the online gaming community for recreation and admitted that she had left the house only sparingly in the past 3 years owing to her refractory depression and poorly managed anxiety. Her medication treatments during the past 5 years had produced only mild improvement in mood and anxiety symptoms and included various medications from the selective serotonin reuptake inhibitor (SSRI), selective norepinephrine reuptake inhibitor, benzodiazepine, and atypical neuroleptic classes, as well as lithium. At the time of her presentation, however, she was only taking risperidone and sertraline. Throughout the course of her management, psychotherapy had been recommended on various occasions, as she had struggled with significant interpersonal issues in her romantic relationships. While she was open to considering therapy, cost was a considerable limitation. In addition to the associated mood symptoms of depression, anhedonia, fatigue, insomnia, and chronic feelings of worthlessness, she experienced frequent crying episodes and chronic suicidal ideation. Upon a more detailed assessment, the patient reported that her symptoms were qualitatively worse for the 8-10 days preceding her menstrual cycle, and that for a number of years her mood and anxiety symptoms had been less tolerable owing to severe menstrual cramping. She had been diagnosed with PMDD the previous year. A previous provider had attempted to ameliorate the patient's premenstrual symptoms by adding 10 mg of citalopram during the week preceding her menstrual cycle to the 40 mg she was taking daily. This approach did not improve symptoms.

COCP options were discussed with the patient who agreed to a trial. She was not currently using nor had she ever used any form of hormonal contraception. At the time of COCP initiation, the patient was taking 200 mg of sertraline daily and 1 mg of risperidone nightly. The medications were continued at these doses without any changes throughout the course of the COCP trial. The COCP norgestimate-ethinyl estradiol 0.25 mg/35 mcg was initiated and was chosen on the basis of formulation and concerns for cost. Two weeks preceding COCP initiation, the patient's Beck Depression Inventory (BDI-II) score was 35, and her Beck Anxiety Inventory (BAI) score was 19. At 1-month follow-up post-COCP initiation, her BDI-II and BAI scores were 11 and 21, respectively. She reported that she felt more capable of managing her emotions, was having reduced frequency and duration of crying spells, reduced insomnia, and no further suicidal ideation. She also reported only mild menstrual cramps that did not interfere with her functionality. Behaviorally, she began leaving the house to spend time with friends and began working independently through a cognitive behavior therapy workbook that had been provided to her. The patient's roommate who accompanied her for follow-up visits confirmed the patient's report of improved mood and functionality. At 13 weeks' follow-up from COCP initiation, her mood continued to remain improved, anxiety diminished, and gains in functionality were maintained. BDI-II and BAI scores were 17 and 9, respectively (Figure). At 28 weeks' follow-up, the patient continued to report diminished anxiety, improved mood, and controlled cramping.

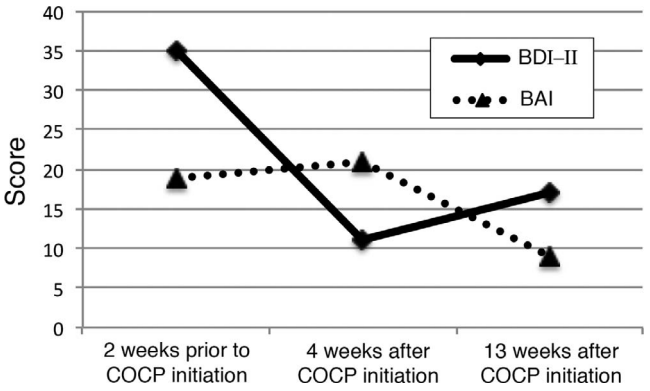


**Figure. Changes in the Beck Depression Inventory (BDI-II) and Beck Anxiety Inventory (BAI) scores over time after combined oral contraceptive pill (COCP) initiation.** The BDI-II is rated on a 4-point scale ranging from 0 to 3 based on the severity of each item. The maximum total score is 63. The higher the score, the higher the depression severity. The BAI is also rated on a 4-point scale ranging from 0 to 3 based on the severity of each item. The maximum total score is 63. The higher the score, the higher the anxiety severity.

## DISCUSSION

Premenstrual conditions refer to symptoms surrounding the luteal phase of menstruation and include premenstrual syndrome and PMDD. Symptoms can be both psychological (tearfulness, irritability, anxiety, depressed mood, and lability) and physiological (bloating, breast tenderness, insomnia, fatigue, weight gain, and skin changes). PMDD is a more severe condition in which these symptoms interfere with the quality of life and may affect occupational functionality and interpersonal relationships. PMDD has been associated with an increased risk of nonfatal suicidal ideation, plans, and attempts.[2] PMDD is estimated to affect 3%-8% of premenopausal women.[1] The major feature that distinguishes PMDD from other depressive disorders is the presence of symptoms or marked exacerbation of symptoms only during the luteal phase of the menstrual cycle.

The pathophysiology of PMDD is not well understood; social, genetic, biologic, environmental, and psychologic factors are all thought to contribute to the development.[3] Various mechanisms have been proposed. Studies of hormonal mechanisms suggest that women with PMDD have a higher vulnerability to fluctuations in gonadal hormones associated with the menstrual cycle; in particular, susceptibility to changing levels of the centrally acting progesterone metabolite allopregnanolone may have a role in PMDD.[4,5] Estrogen receptors have interactions with serotonin pathways that may affect mood and anxiety.[6] Symptomatic women have been reported to have a lower density of serotonin transporter receptors compared to controls[7] and higher levels of serotonin responsiveness during the follicular phase compared to the luteal phase.[8]

Other possible mechanisms include alterations in responsiveness to vitamin D [1,25 (OH)2D] metabolism as a trigger for PMDD,[9] and alterations in intercellular magnesium levels have also been reported.[10] Magnetic resonance imaging studies of the anterior cingulate cortex suggest low gamma-aminobutyric acid (GABA) receptor density in women with PMDD compared to controls,[11] and allopregnanolone may influence mood symptoms by positive modulation of $GABA_A$ receptors.[4] Genetic vulnerabilities associated with the 5-HT1A and estrogen receptor alpha gene (ESR1), as well as

high body mass index, stress, and trauma exposure, have been suggested as risk factors.[1]

Treatment options for PMDD continue to be developed as the pathophysiology becomes better understood. Lifestyle factors, including regular exercise and healthy diet, as well as supplementation with calcium and vitamin B6 (pyridoxine), may be of benefit.[12] Pharmacologic agents that have shown some benefit include SSRIs,[13] COCPs (particularly those containing ethinyl estradiol and drospirenone[3,14,15]), and gonadotropin-releasing hormone (GnRH) agonists.

In this case, our patient reported improvements in mood, anxiety, social function, and the physical symptoms of bloating and cramping associated with PMDD. Consequently, further interventions were not required.

In this case, BDI-II and BAI scores, as well as self- and peer-reported functionality, all suggested improvement in symptoms following introduction of COCPs. BDI-II and BAI scores trended generally downward over a 13-week period. Other authors have suggested that the greatest gains with COCPs might be seen during the first cycle with less improvement over subsequent cycles.[15]

The treatment of PMDD is primarily based on expert opinion. Many authors recommend beginning with an SSRI as first-line treatment for severe PMDD.[3] Various SSRIs have been studied and may be prescribed either daily or during the luteal phase only beginning on day 14. When SSRI management fails to produce a resolution of symptoms, as in this patient's case, a trial of COCPs has been recommended. Drospirenone/ethinyl estradiol contraceptive formulations are approved for management of PMDD. GnRH agonists such as leuprolide have been used and may be efficacious by inducing anovulation and amenorrhea.[3] Others have suggested beginning with an integrated approach to symptom mitigation that includes lifestyle modifications, psychoeducation, and dietary supplements in addition to psychopharmacology.[12] The efficacy of COCPs for PMDD has had mixed results, with some studies showing benefits, while others have not.[16]

## CONCLUSION

The neurohormonal contribution to psychiatric conditions continues to be studied and is becoming increasingly important. An understanding of the presence and etiology of premenstrual symptoms should be part of a comprehensive psychiatric assessment of female patients, and consideration of COCPs in the treatment plan adds a potentially potent option for symptom mitigation and remission.

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