Treatment of Depression in a Patient With Intractable Hyperemesis Gravidarum

Verinder Sharma, MBBS[a,b,*]

Hyperemesis gravidarum (HG) affects 0.3%–3% of pregnant women and is characterized by severe nausea and vomiting, dehydration, electrolyte imbalance, nutritional deficiencies, ketonuria, and weight loss.[1] Some studies[2] have reported an association between HG and poor neonate outcomes. Women with HG have a significantly increased frequency of depression compared to controls, but rates of diagnosis and referral for psychiatric care are low.[3,4] Due to its association with low birth weight, preterm birth, and fetuses or newborns being small for gestational age, depression may worsen pregnancy outcomes in women with HG.[5] Data from a population-based cohort study of all deliveries in Nova Scotia, Canada, found that psychiatric illness was an independent risk factor for hospitalization for HG.[6] This case describes a woman who had sustained remission of HG following treatment with olanzapine.

Case Report

A 26-year-old woman was referred to our perinatal clinic for management of depression in pregnancy. In her late teens, she was treated for depression with citalopram 20 mg daily. She found the medication effective and well-tolerated. Upon its discontinuation, she remained well until recurrence of depression in early pregnancy. At the time of initial consultation at the clinic, she was taking sertraline 50 mg daily. She denied any side effects of the medication.

Due to symptoms of HG including severe nausea and vomiting, dehydration, and weight loss (over 20 lb), she was hospitalized at 14 weeks gestation. Despite treatment with pyridoxine-doxylamine, metoclopramide, and ondansetron, she had continued to struggle with severe nausea and vomiting. As per the *DSM-5*, she was diagnosed with major depressive disorder-recurrent. Since there was minimal improvement following the initiation of sertraline, it was decided to add olanzapine 5 mg for augmentation of the antidepressant. Olanzapine was chosen in part due to its antiemetic effect. Within 5 days of its initiation, she experienced improvement in her mood, sleep, and appetite. There was a marked reduction in the frequency of nausea and vomiting. Compared to an average of 6 episodes of emesis a day prior to her initial consultation at the clinic, she was having only 3 episodes of vomiting a week in late pregnancy. With sustained improvement in symptoms of depression and HG, she gained 33 lb during pregnancy, prompting her regular antiemetic drugs to be tapered off. Olanzapine was well-tolerated, and her blood glucose level was in the normal range throughout the pregnancy. She delivered a healthy full-term child weighing 3,300 g and had no recurrence of depression postpartum. Olanzapine was stopped shortly after delivery, but she continued to take sertraline 50 mg daily. She was discharged to her family physician's care following her 6-month postpartum visit.

Discussion

Commonly recommended drugs for treatment of HG include pyridoxine-doxylamine, ondansetron, or dopamine antagonists such as promethazine or metoclopramide.[7] Treatment options for women with HG and comorbid depression are limited. Due to its antidepressant, antiemetic, sedative, and appetite-stimulating effects, mirtazapine is recommended for patients with depression who have HG.[8] Olanzapine is approved for treatment of schizophrenia and bipolar I disorder, and it is also indicated in combination with fluoxetine for treatment-resistant depression. Olanzapine has an affinity for multiple neurotransmitter receptors including dopaminergic, serotonergic, adrenergic, histaminergic, and muscarinic. Olanzapine shares the 5-HT_3 receptor blockade properties with other antiemetics such as mirtazapine and ondansetron. Although commonly used as an antiemetic in patients with advanced cancer and conditions such as cannabinoid hyperemesis syndrome, there are no reports of olanzapine use in women with HG. Olanzapine is generally considered safe in pregnancy.[9,10] A review of data from global safety surveillance outcomes found that most women treated with olanzapine had normal births.[9] The most reported adverse events in infants were somnolence (3.9%), irritability (2%), tremor (2%), and insomnia (2%). There are reports that olanzapine may increase the risk of gestational diabetes in some women.[11]

In summary, depression is a common comorbidity in women with HG and may contribute to poor neonate outcomes. The addition of olanzapine should be considered in women with depression and comorbid HG who fail to

[a]Department of Psychiatry and Department of Obstetrics and Gynecology, University of Western Ontario, London, Ontario, Canada

[b]Parkwood Institute Mental Health Care Building, London, Ontario, Canada

*Corresponding author: Verinder Sharma, MBBS, Parkwood Institute Mental Health Care Building, PO Box 5777, Stn B, London, ON N6A 4V2 (vsharma@uwo.ca).

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respond to antidepressant monotherapy and standard antiemetic therapy for control of HG symptoms. In addition to its antiemetic effect, olanzapine may stimulate appetite, improve sleep, and cause weight gain in women with HG. Olanzapine may also obviate the need for the antiemetic therapy and reduce the overall side effect burden.

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