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Treatment of postpartum psychosis in breastfeeding females

Lauren Chaney, PharmD, BCPP[1]

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[1] (Corresponding author) Clinical Pharmacy Practitioner, VA Augusta Health Care System, Augusta, Georgia, Lauren.Chaney@va.gov, ORCID: https://orcid.org/0009-0009-2327-231

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Case

Mrs. M is a 36-year-old female, 2 weeks postpartum, with a past medical history of depression and migraines. She presented to the emergency room with her husband, and upon examination, she was found to have tangential speech, psychomotor agitation, and delusions that her neighbor was planning to kill her child. Her husband states that this started about a week ago. All labs were within normal limits (ie, thyroid stimulating hormone [TSH], vitamin D, vitamin B12, folate, comprehensive metabolic panel, complete blood count, lipid panel, hemoglobin A1c) except the following: blood glucose 76 mg/dL (normal: 80-120 mg/dL) and serum creatinine 1.7 mg/dL (normal: 0.6-1.2 mg/dL). The urine drug screen was negative. Given physical presentation, Mrs. M is diagnosed with postpartum psychosis (PPP). After Mrs. M is admitted, her husband states that she has been breastfeeding and would like to continue to breastfeed as they are unable to afford formula.

Background

Currently, there is no universally accepted definition of PPP; however, it is considered a severe, potentially life-threatening psychiatric emergency that affects approximately 1 to 2 cases per 1000 deliveries.[1,2] The peak time of occurrence is typically 1 to 14 days postpartum and can last months.[1] It presents as acute mania or depression with psychosis.[2] The most common types of psychosis are persecutory delusions and delusions of reference.[2] Approximately 40% of women diagnosed with PPP have no history of severe psychiatric illness; however, studies show an increased risk of PPP (260 in 1000) in women previously diagnosed with bipolar disorder.[1-3] There is an even higher risk of PPP (570 in 1000) for those previously diagnosed with bipolar disorder with a family history of PPP.[1-3] Ergo, there is evidence to suggest a strong, specific relationship with bipolar disorder and PPP.[1,2] Overall, research on PPP is limited, which is likely related to the rare nature of the condition, small sample sizes, and cross-sectional study designs.[3]

Treatment of Postpartum Psychosis

The first priority of treatment should be ensuring the mother and child are safe; although not ideal, hospitalization of the mother suffering from PPP is pertinent. Additionally, it is important to avoid leaving the mother alone with the child as the infanticide rate of PPP ranges from 1% to 4.5%.[1] For the treatment of PPP, the impacts of benzodiazepines, antipsychotics, lithium, and electroconvulsive therapy (ECT) have been studied.[1-4]

There is no specific clinical treatment guideline for PPP; however, the American College of Obstetricians and Gynecologists (ACOG) provides a few recommendations in their (2023) guideline.[5] Specifically, it is recommended that a psychiatrist provide assessment and treatment for the patient with PPP.[5] Additionally, the ACOG discourages the use of antidepressants for acute depression with psychosis, especially without the presence of appropriate mood stabilization.[5] Further, initiation of a sedative antipsychotic medication, such as olanzapine or haloperidol, with short-acting benzodiazepines, such as lorazepam, is the first-line recommended treatment for PPP during the acute stabilization period while awaiting assessment by a psychiatrist.[5] No specific dosing is recommended by the ACOG for these medications; however, it is suggested that if intramuscular haloperidol doses greater than 5 mg are used, benztropine or diphenhydramine should be administered to prevent extrapyramidal symptoms and dystonia.[5] Lithium is another therapeutic option for PPP.[1,5,6] The ACOG does not provide specific dosing recommendations for lithium treatment; one source recommends a target level of 0.8-1.2 mmol/L for acute stabilization and a target level 0.6-0.8 mmol/L for relapse prevention.[4] Currently brexanolone and zuranolone are recommended treatments for postpartum

Practice Points:

1. PPP should be considered a clinical and public health concern.
2. The first priority of treatment is to ensure the safety of the mother and infant.
3. ACOG recommends the use of a sedative antipsychotic with a short-acting benzodiazepine for first-line treatment in the acute stabilization period.
4. Lithium monotherapy has shown efficacy in relapse prevention of PPP.
5. ECT may be safe and effective in patients with catatonia and/or severe depression.

depression; however, there are no studies that examine the efficacy of these medications for treatment of PPP.[6] From a nonpharmacological standpoint, ECT has also shown benefits in refractory cases and for patients with catatonia or severe depression symptoms.[4-6] Additionally, foregoing breastfeeding overnight as part of sleep preservation can also be helpful in the early phase of treatment and stabilization.[5] If treated appropriately and quickly, the ACOG guidelines suggest full remission of PPP can be achieved when the mother is approximately 2 months postpartum.[5]

As previously mentioned, evidence supporting the treatment of PPP is limited. One of the few studies, Bergink et al,[4] applied a 4-step approach to treatment of psychosis and mania in 64 women during the postpartum period (Table). Results showed that 4 of 64 patients remitted after step 1, suggesting that sleep restoration may have been the etiological factor for PPP.[4] Twelve patients (18.8%) remitted during step 2. The majority of patients (47/64; 73.4%) remitted during step 3 of treatment.[4] No patients completed the last step (ie, ECT). Overall, sustained remission at 9 months was observed in 51 of 64 patients (79.7%).[4] This study also showed that lithium monotherapy (target level for relapse prevention: 0.6-0.8 mmol/L; target level for acute stabilization: 0.8-1.2 mmol/L) was protective against relapse of mania, psychosis, and depression in the first year postpartum; however, antipsychotic monotherapy was not.[4]

Babu et al,[7] performed a naturalistic prospective study in India, which included 78 women with PPP. Of 78 women, 34 (43.6%) received ECT.[7] The most common indications for ECT use in this study were catatonia and suicidality.[7] Overall, the duration of hospital admission was lower among those who received ECT (19 vs 23 days); however, this was not statistically significant.[7]

Psychotropic Use in Breastfeeding Women

While breastfeeding is not required, it is important to some patients. In such cases, the benefits of the medication used for treatment may supersede concerns regarding its use in breastfeeding. With that being said, the severity of illness should also be considered, as some mothers may be too disorganized to safely breastfeed their child. The relative infant dose (RID) can be calculated for medications to assess safety. It is the dosage received via breast milk (mg/kg/d) relative to the mother's dose (mg/kg/d). A RID of 10% is frequently used as an empiric cutoff for assuming safety during breastfeeding.[8]

Information regarding antipsychotic use while breastfeeding is limited for newer, second-generation antipsychotics, such as cariprazine, brexpiprazole, and asenapine. Some sources suggest olanzapine, risperidone, and quetiapine have lower excretion in breast milk and minimal side effects.[8] There is also evidence for the use of first-generation antipsychotics, specifically medium or high-potency agents (eg, haloperidol), as side effects appear to be rare.[8]

Olanzapine may be a preferred medication while breastfeeding as the RID is estimated to be less than 2%.[9] In 1 study, 102 breastfed infants whose mothers were taking olanzapine were followed.[9] Sixty-two mothers reported taking olanzapine at an average dose of 7.5 mg/d. Infant exposure was averaged at 74 days.[9] Of the exposed infants, 15.6% reportedly experienced adverse effects, such as somnolence, irritability, tremor, and insomnia.[9] Overall, there is limited, conflicting evidence surrounding the use of haloperidol in breastfed infants.[9] Some information suggests that up to 10 mg/d of haloperidol produced low levels of the drug in milk and may not affect the breastfed infant.[9] One study suggested that haloperidol RID was up to 12%, and the authors discouraged its use while breastfeeding.[10]

TABLE: Four-step approach to treatment of psychosis and mania in postpartum women

Steps	Treatment[a]
Step 1 (days 1-3)	Treat with benzodiazepine (eg, lorazepam) for 3 d
Step 2 (days 4-18 [2 wk])	Combination treatment with a benzodiazepine and antipsychotic (eg, haloperidol, olanzapine, quetiapine)
Step 3 (days 19-103 [12 wk])	Combination treatment with benzodiazepine, antipsychotic, and lithium. Lithium dosing was achieved based on plasma level (target, 0.8-1.2 mmol/L)
Step 4 (days 104-270)	Electroconvulsive therapy

[a]If symptoms do not improve after treatment period, proceed to next step.

A few case reports assessed infants' exposure to benzodiazepines. The authors found that infants may experience sedation, poor feeding, and respiratory distress.[7] However, when amalgamated, the risk of adverse events with benzodiazepines was low.[8] Evidence from breastfeeding mothers suggests that lorazepam does not cause adverse effects.[9] This is supported by low levels of lorazepam in breast milk and the medication's short half-life.[9]

Lithium is excreted at relatively high levels in breast milk; RID is estimated to be 12% to 30%.[10] Infant serum levels appear to be approximately one-third to one-half of the mother's serum levels. Signs of lithium toxicity in infants may include cyanosis, hypotonia, and hypothermia.[8] If breastfeeding occurs with lithium therapy, it is recommended to use the lowest possible effective dose of the medication; it is also recommended to check infant serum lithium levels, TSH, blood urea nitrogen, and serum creatinine every 6 to 8 weeks while the child is nursing.[8]

Babu et al,[7] noted side effects of anterograde amnesia in a few women who received ECT. Of note, no adverse effects were noted in infants who were breastfed while the mother received ECT.[7] Raberu suggests that breastfeeding does not need to be ceased during a course of ECT, and anesthetic medications may have minimal risk of adverse events if infants are exposed.[11] Additionally, exposure to medications can be reduced if breastfeeding is delayed for a few hours posttreatment or by collecting and storing breast milk the day before ECT.[11]

Conclusion

PPP is a rare, life-threatening psychiatric emergency that typically occurs within the first 2 weeks of postpartum. Literature remains scarce, and more research is needed to make evidence-based recommendations for treatment. The ACOG guidelines recommend a sedative antipsychotic and short-acting benzodiazepine as the preferred treatment for PPP in acute stabilization. Some studies support the use of lithium for relapse prevention. Although antipsychotic monotherapy has not proven as effective as lithium for relapse prevention, it may be a preferred treatment option in breastfeeding patients, given safety concerns. Specific benzodiazepines and antipsychotics (ie, lorazepam and olanzapine, respectively) have evidence supporting safety in breastfeeding. While lithium is not contraindicated, there are still necessary monitoring parameters that need to be implemented for a breastfeeding mother and infant. ECT is considered a nonpharmacological treatment that can also be used, especially for cases that include catatonia or severe depression. Overall, to ensure patient-inclusive care, clinicians should conduct a risk versus benefit discussion regarding the treatment of PPP while breastfeeding.

Case Continued

After 3 days of treatment with lorazepam 2 mg every 8 hours as needed and haloperidol 5 mg every 6 hours as needed, Mrs. M continues to experience delusions and tangential speech. The psychiatry team completes an assessment and decides to initiate olanzapine 5 mg/d with a plan to titrate to efficacy. After 4 days of treatment, Mrs. M's delusions have decreased and are less severe. Additionally, her speech is goal-directed and logical; at this time, she continued to express interest in breastfeeding. Therefore, the care team provided in-depth counseling and discharged Mrs. M on olanzapine 10 mg/d with a plan to monitor the infant for adverse events, such as somnolence, irritability, tremor, and insomnia.

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