



Aripiprazole and lactation failure: The importance of shared decision making. A case report

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ABSTRACT

Bipolar disorder is a chronic and severe psychiatric illness affecting many patients during their childbearing years. Bipolar disorder is often managed with aripiprazole, a generally well tolerated second-generation antipsychotic medication. Published data regarding its safety profile are reassuring and aripiprazole is prescribed during pregnancy, postpartum and during lactation. Pregnancy and the postpartum period represent times of increased vulnerability for patients with bipolar disorder, especially those who are untreated, highlighting the need for medical management. However, aripiprazole may interfere with human milk production. Currently, there is limited evidence to understand lactation failure in patients who take aripiprazole. This case reinforces the need for shared decision making regarding the potential impact on lactation when aripiprazole is being considered for the pregnant patient with bipolar disorder.

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1. Introduction

Bipolar disorder (BD) is a chronic illness affecting 2–4% of the world's population and is the fourth leading cause of disability among young people [1]. It is characterized by a combination of manic, hypomanic, and depressive episodes [2]. Of all psychiatric disorders, BD is associated with the highest risk of psychiatric hospitalization in the postpartum period. There is a 23-fold greater risk of psychiatric admission within the first 30 days after delivery compared to non-postpartum women with BD [3]. While BD has been successfully treated with antipsychotic medication, the safety and tolerability of medication is important to consider for treatment selection and compliance.

Aripiprazole is a second-generation antipsychotic used to treat severe mental illness, including BD. Aripiprazole, a partial agonist of specific dopamine and serotonin receptors, has been embraced as first-line treatment for psychotic disorders. As compared with other second-generation antipsychotics, it has a more favorable tolerability profile, including less sedating effect and lower risk of weight gain without an increased risk of metabolic complications such as dyslipidemia and diabetes [4,5].

Aripiprazole is used for treatment of BD during pregnancy and in the postpartum setting and while there is no definitive research about the risks and benefits of aripiprazole and its safety, the published data

are reassuring and do not contraindicate its use during pregnancy or lactation [6].

This case discusses a new mother with BD, maintained on aripiprazole during her pregnancy, who experienced lactation failure after the birth of her first child.

2. Case Presentation

A 30-year-old G1 (1 total pregnancies) P1001 (1 term pregnancy, 0 pre-term pregnancies, 0 miscarriages, and 1 living child) woman with a history of bipolar depression and anxiety presented to the outpatient pediatric primary care setting with her nine-day-old full-term (41 weeks) female infant born via Cesarean section due to non-reassuring tracing and nuchal cord with a complaint of not producing human milk since birth.

The patient had latched infant to the breast within 4 h of delivery but was not able to exclusively breastfeed during the hospital stay. The infant experienced an 11.3% weight loss from birth weight, requiring formula supplementation. The patient initiated hand expression and the use of an electric pump starting on day three postpartum to stimulate milk production. She continued to attempt latching the infant directly onto the breast every 2–3 h but continued to supplement with formula.

The patient denied breast enlargement during pregnancy or engorgement of the breasts at any time in the days immediately postpartum. There was no history of breast surgery, specifically breast reduction, augmentation or biopsy. There was no history of inverted or flat nipples. She reported breast development at age 11–12 with first menses at age 13. She denied difficulty getting pregnant.

Abbreviations: BD, bipolar disorder; PPD, postpartum depression; EPDS, Edinburgh Postnatal Depression Scale; G, total # of pregnancies; P, # of full-term pregnancies; # of pre-term pregnancies; # of miscarriages and/or abortion # of living children.

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She reported a remote history of hypothyroidism as a child, requiring thyroid replacement until age 8, but she was not able to provide additional details regarding this history.

She was taking sodium valproate and clonazepam prior to pregnancy and her psychiatrist changed her to aripiprazole 10 mg tablet daily and sertraline 50 mg daily, in the first few weeks of pregnancy. She continued these medications through pregnancy and postpartum with no medication dose adjustments and no psychosis.

Upon physical examination the patient had round-appearing breasts, soft to palpation without engorgement, no breast fullness or venous prominence. Her nipples were everted without nipple damage, cracking, scabbing or active bleeding. No colostrum or transition milk was expressed from nipple.

The patient was administered the Edinburgh Postnatal Depression Scale (EPDS) and obtained an abnormal score of 12. She admitted to feeling guilty regarding formula supplementation as her intention was exclusively to provide human milk to the infant.

A baseline prolactin level was checked with a TSH (reflex to Free T4) followed by 10 min of bilateral breast stimulation with electric pumping, 5 min hand expression on each breast followed by a repeat prolactin level approximately 25 min after initial blood draw.

The baseline prolactin level was 7.4 and the repeat prolactin level was 7.7. Thyroid stimulating hormone level was normal at 2.93 (no reflex performed). The low prolactin level supported agalactorrhea or lactation failure. Feeding options were reviewed with the mother, including the use of a supplemental nursing system at the breast. The mother refused this option. Psychiatric medication changes were briefly discussed, but without the prolactin signaling during pregnancy the breasts were likely not lactational and milk production would not occur despite antipsychotic medication adjustment.

Unfortunately, this patient did not meet her breastfeeding goals, which, according to the patient, caused a disruption in infant bonding. Given the mother's history of BD and concern for postpartum depression, the mother and infant were seen weekly for close follow-up over the postpartum period. Repeat EPDS screens were administered at day 13 postpartum with a score of 13, day 30 postpartum with a score of 11 and again at 2 months with a score of 7. The mother continued to see her psychiatrist, but admitted to feeling betrayed or misguided, degrading the trust she once had with this provider. With guidance she was able to find a new psychiatrist who practiced within a larger women's mental health consortium.

3. Discussion

There is emerging evidence concerning the safety and efficacy of pharmacologic management of BD in the perinatal period. Women with untreated BD are at higher risk of relapse during pregnancy and very high risk of relapse after delivery. Overall treatment recommendations during the perinatal period for women with BD include collaborative care between psychiatry, obstetrics or midwifery, and the pediatrician to provide pragmatic-personalized treatment for the patient and her infant [7]. It is important to differentiate BD from postpartum depression (PPD) as PPD is generally treated with SSRIs and does not require antipsychotics [8]. Manic or hypomanic symptoms accompany BD, requiring antipsychotic treatment.

Several case studies discuss drug concentrations or transfer of aripiprazole to breast milk in lactating women [9,10] with more recent studies reviewing antipsychotic use and safety during pregnancy, peripartum and lactation providing reassurance of a relatively low milk to plasma ratio of aripiprazole during lactation, but highlighting the need for more information on medication safety [6,11–13]. A new safety scoring system for the use of psychotropic drugs during lactation has been proposed and decisions concerning pharmacologic treatment in the lactation period should be made after careful clinical evaluation [14].

While there is emerging evidence regarding the safety of aripiprazole during lactation there is little available information

concerning its impact on lactation, specifically milk suppression. Mendhekar et al., 2006, presented a case study of a medically healthy pregnant woman with schizoaffective disorder treated with aripiprazole until 8 weeks of gestation and then 20 weeks of gestation until delivery, with the medication abruptly stopped by the patient for 12 weeks until relapse occurred, and the medication was restarted. The infant was healthy at birth but the mother experienced lactation failure. This was attributed to the partial agonistic effect of aripiprazole in the tuberoinfundibular dopaminergic system, interfering with prolactin secretion by pituitary lactotrophs [15].

Two additional case reports discuss a decrease in maternal milk supply associated with aripiprazole initiation in the postpartum period with milk supply improving after discontinuation of the medication, but these reports do not discuss the pregnant patient taking aripiprazole [16,17].

Many mothers set breastfeeding targets and goals during pregnancy and not meeting these targets may trigger PPD. Borra, et al., 2015, found that the effect of breastfeeding on maternal mood differed by both maternal mental health during pregnancy and whether mothers intended to breastfeed [18]. Breastfeeding decreased the risk of PPD among mothers who had intended to breastfeed. This patient experienced a depressed mood due to her inability to breastfeed, which raised concerns regarding infant bonding. The first few months after birth are a highly sensitive period for the development of the mother-child relationship [19] and therefore supporting mothers' intentions to breastfeed has a potential meaningful impact on her mental health.

This case highlights the importance of shared decision making with full explanations of treatment options and their benefit to harm ratio for all women of childbearing years who suffer from BD. Clinicians should provide anticipatory guidance for women with BD who desire pregnancy or who are early in pregnancy and taking aripiprazole, including a discussion regarding medication alternatives. In the event of lactation failure, clinicians should include all feeding options, including human donor milk.

Finally, studies with large sample sizes are needed to better understand the risk of lactation failure in pregnant women taking aripiprazole. Guiding patients to make informed decisions regarding their health and the health of their infant is the foundation of ethical care.

4. Conclusion

The patient had treatment success on aripiprazole for BD during pregnancy, but experienced lactation failure associated with the medication, which was an unknown risk to her. This case highlights the need for individualized treatment choices via risk-benefit analysis. The treatment choice cannot be based on clinical history, past or ongoing treatment or current symptoms alone. It must include a shared decision-making model to engage the patient, maximize her autonomy and outline her treatment goals as well.

Contributors

Ariana Komaroff is the sole author of this case report.

Conflict of Interest

The author declares there is no conflict of interest regarding the publication of this case report.

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Patient Consent

Obtained.

Provenance and Peer Review

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