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CASE REPORT

Long-Acting Injectable Aripiprazole in High-Risk Pregnancy: A Case Report on Relapse Prevention, Obstetric Outcomes, and Infant Development

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ABSTRACT

Pregnancy in women with bipolar disorder is high risk, with significant relapse rates. Medication nonadherence and teratogenicity concerns complicate treatment. Long-acting injectable antipsychotics offer improved adherence but are underutilized in pregnancy due to limited safety data. A 30-year-old woman with bipolar disorder and attention-deficit hyperactivity disorder, stable atomoxetine, and discontinued lithium pre-conception, resulting in mania requiring hospitalization. She was stabilized on oral aripiprazole, then transitioned to monthly LAI aripiprazole. She got pregnant two months later and chose to continue LAI throughout. The patient maintained mood stability throughout pregnancy with no manic, psychotic, or depressive episodes. Regular monitoring revealed no teratogenic effects. At 39 weeks, she delivered a healthy infant (APGAR 9, no malformations). Postpartum, she had paranoia (Young mania rating scale score increased to 14 from 8 during pregnancy), leading to increased LAI aripiprazole to 720 mg every 4 weeks. The infant continued normal development at 18 months and had no symptoms of autism or neuroatypicality. This case demonstrates the successful use of LAI aripiprazole throughout prepartum, antepartum, and postpartum periods in a high-risk pregnant woman with bipolar disorder. It maintained euthymia in the mother, prevented relapse-related hospitalization, and resulted in a healthy infant. Despite the development of gestational diabetes and postpartum exacerbation requiring dose adjustment, the case supports considering LAI antipsychotics in pregnant bipolar disorder patients with adherence difficulty, but it still warrants further research.

Abbreviations:

BD: Bipolar Disorder

ADHD: Attention Deficit Hyperactivity Disorder

LAI Antipsychotics: Long-Acting Injectable Antipsychotics

YMRS: Young Mania Rating Scale

HAM-D scale: The Hamilton Depression Rating Scale

Introduction

Pregnancy in women with bipolar disorder (BD) is considered high-risk due to various clinical and pharmacotherapeutic factors.[1] The administration of pharmacological treatment during pregnancy requires a thorough evaluation of the exposure to psychotropic drugs and the risk of BD relapse. According to a recent systematic review published in the American Journal of Psychiatry, 37% of patients with a history of bipolar disorder relapsed during pregnancy.[2] Failure to address bipolar disorder can have adverse effects on both the mother's health and the unborn child during a relapse.[3]

Maintaining antipsychotic therapy during pregnancy is crucial for preventing treatment failures, yet concerns about teratogenicity and fetotoxicity often lead to discontinuation of medication.[4] Long-acting injectable (LAI) antipsychotics improve medication adherence compared to oral formulations.[5,6] A systematic review of second-generation antipsychotics conducted by Terrana et al. concluded that there were no detrimental associations or malformations between the use of LAIs and the health of the infant.[7] According to a survey published in the National Library of Medicine, patients with BD who began receiving LAIs (with no previous LAI therapy) had a 5% better medication adherence and were 19% less likely to discontinue their medication than those taking oral formulations.[8] Their use has been pivotal in preventing relapse, reducing hospitalizations, and improving overall outcomes in patients with conditions such as bipolar disorder.[9,10] In a study conducted by Rashmi Patel et. al., it was concluded that patients discharged from inpatient settings who were prescribed only an LAI had a lower frequency of rehospitalization, lower risk of longer hospital stays, lower risk of becoming rehospitalized, and lower risk of outpatient visits compared to patients who were co-prescribed an oral formulation.[11]

This case report aims to explore the utilization of LAI antipsychotics in a pregnant woman, to address non-compliance and maintain a steady dose of antipsychotics during prepartum, antepartum, and postpartum, decreasing hospitalization due to relapse. This investigation is crucial for informing clinical decisions and guiding future research efforts in this underexplored domain.

Case Report

This case study presents a 30-year-old woman diagnosed with bipolar disorder in her late teens and attention-deficit hyperactivity disorder (ADHD) at 7 years old. Her treatment with atomoxetine has been stable over the past years. Despite a prior prescription of lithium for bipolar disorder, she stopped the medication upon deciding to become pregnant, resulting in a manic hospitalization episode before conception. In response, she received treatment with oral aripiprazole 20 mg at a crisis stabilization unit, yielding clinical improvement within a week.

The patient exhibited reluctance to initiate new medications during pregnancy due to concerns about relapse and teratogenicity. Because of her inconsistent medication adherence, the treatment plan transitioned to (LAI) aripiprazole 400 mg administered intramuscularly monthly. Subsequently, she reported occasional anxiety but denied manic or psychotic symptoms. Two months later, she became pregnant and opted to persist with her existing monthly injection regimen of intramuscular aripiprazole, warranted by its low-risk profile and the intention to minimize relapse risk.

Throughout her pregnancy, the patient was administered 400 mg intramuscular injections of aripiprazole, resulting in sustained mood stability

without manifestations of manic, psychotic, or depressive episodes. Her monthly Young Mania rating scales consistently fell within the range of 4-8. In addition to her primary treatment, the patient reported experiencing anxiety managed with propranolol as needed. Regular monitoring by a multidisciplinary team, comprising her psychiatrist and obstetrician, revealed no manic symptoms and no teratogenic effects on the growing fetus. Notably, the patient experienced a weight gain of 45 lbs within the initial 6-month period and subsequently developed gestational diabetes in the 8th month, necessitating insulin therapy. Despite this, she reported an overall sense of well-being and good mood. The patient delivered a healthy baby boy via cesarean section at 39 weeks, weighing 9 lbs and 7 oz, and exhibiting an APGAR score of 9, with no congenital malformations and a stable umbilical cord pH of 7.28 In the immediate postpartum phase, the patient exhibited symptoms of paranoia along with lack of insight and scored 14 on her young mania rating scale (YMRS), expressing concerns that the baby was not her own. Consequently, her medication dosage was adjusted to 400 mg monthly due to an elevated susceptibility to postpartum psychosis and depression. Subsequently, throughout the 6 months following delivery, her mental status remained stable, enabling a transition to a regimen of 720 mg aripiprazole i.m. administered every 4 weeks. Since then, the patient has consistently maintained stability on this medication regimen and has effectively reengaged in her daily activities.

Upon further consultation with the pediatrician, it has been observed that the patient's infant, now 18 months of age, has achieved all developmental milestones appropriate for their age and is exhibiting healthy growth and development without presenting any symptoms indicative of autism or neuroatypicality.

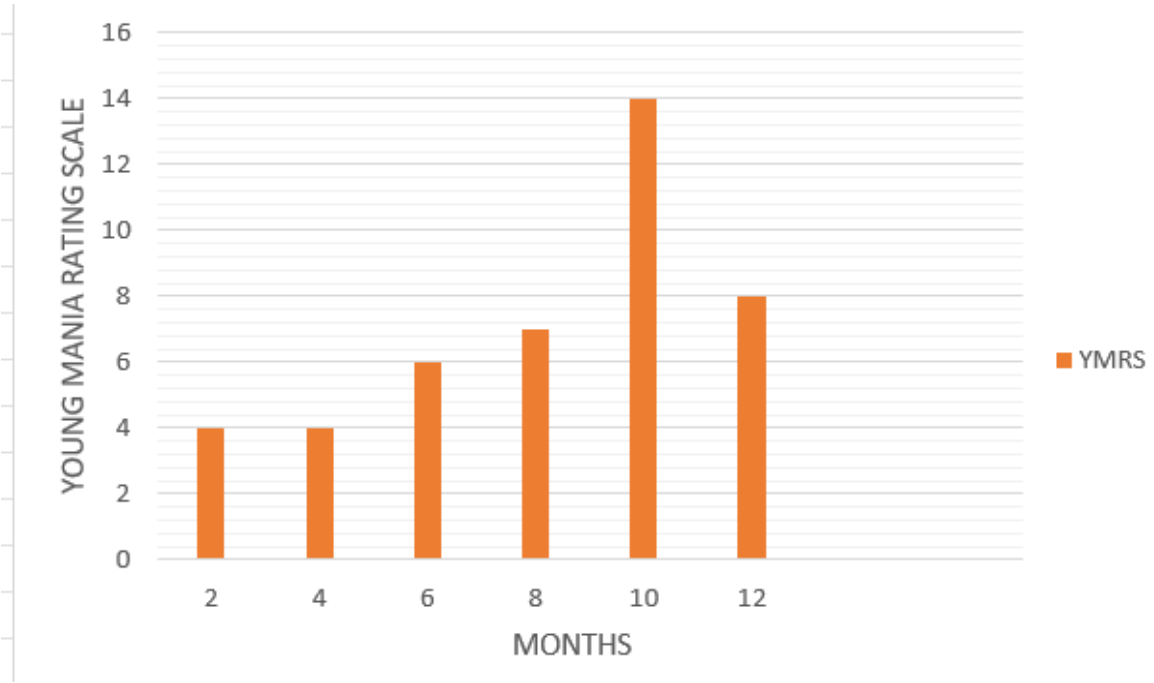

Figure 1. Young Mania Rating Scale over 12 months during pregnancy and the postpartum period.

Discussion

Long-acting injectable (LAI) antipsychotics play a crucial role in enhancing medication adherence and preventing the recurrence of psychiatric symptoms. In contrast to oral antipsychotics, LAIs have demonstrated greater efficacy in preventing psychiatric hospitalization. Additional advantages of LAIs include heightened awareness among clinicians regarding medication adherence, reduced risk of overdose, and improved, standardized interaction between clinicians and patients.[12] The majority of available data suggest that the adverse effects of LAI drugs are comparable to those of oral counterparts, except for long-acting olanzapine, which necessitates a three-hour observation period following administration to watch for signs of post-injection sedation syndrome.[13] Pregnant women with a history of hospitalizations due to non-adherence to oral antipsychotic medication are ideal candidates for (LAI) antipsychotic medication during pregnancy.[4,14] Similarly, women with a history of frequent and prolonged psychiatric hospitalizations associated with schizophrenia, schizoaffective disorder, and, in certain cases, bipolar disorder, should also be considered.[15] Factors such as psychiatric decompensation during prior pregnancies or in the immediate postpartum period, as well as a history of illicit substance use, serve as additional clinical risk indicators favoring the use of LAIs over oral antipsychotics in clinical decision-making.[16]

This case report underscores the use of LAIs pre-conception, antepartum, and postpartum in a woman who presented with mania after discontinuing a lithium mood stabilizer. It emphasizes the importance of discussing and evaluating the potential risks and benefits of long-acting injectables with the patient and caregiver.[17] Pregnant individuals frequently express apprehension regarding the use of long-acting injectable antipsychotic medication during pregnancy, citing concerns about potential harm to the fetus.[18] Our patient harbored similar concerns upon commencing antipsychotic treatment. However, non-adherence to antipsychotic medication during the first trimester among women with severe psychiatric illness poses an almost twofold greater risk of relapse compared to adherent individuals.[18] Notably, severe psychiatric symptoms during pregnancy have adverse outcomes for both mother and infant.[19,20] Untreated schizophrenia or bipolar disorder is considered an independent risk factor for congenital malformations in newborns, while antepartum psychosis can lead to a denial of pregnancy.[21]

In the United States, there are presently six antipsychotics available in a long-acting injectable (LAI) form: aripiprazole, fluphenazine, haloperidol, olanzapine, paliperidone, and risperidone.[21] Long-acting injectable formulations feature varied dosing schedules, ranging from biweekly to several months for the more recent extended-release formulations.[22] When evaluating pregnant patients, it is imperative to meticulously assess the known and potential risks versus the known and potential benefits associated with the prescription of LAIs during pregnancy. Critical considerations for the treating psychiatric clinician comprise the prior efficacy of the oral formulation, the patient's capacity to comply with the necessary overlap time with the oral formulation, potential side effects, and cost. Recently, zuranolone, a 14-day oral medication, has been used to treat postpartum depression.[23] A double blind phase 3 clinical trial demonstrated statistically significant improvement in depressive symptoms as assessed by change from baseline HAM-D scores at day 15, in the zuranolone group compared with the placebo group.[23] However, since the patients were only followed for 45 days, the long-term efficacy and safety of zuranolone in women with PPD are unknown.[23] Additionally, patients were not permitted to breastfeed, so the effect of zuranolone on lactation and its relative infant dose were not evaluated.[23]

The current safety data on antipsychotics and lactation is somewhat limited; however, the benefits of breastfeeding may outweigh the potential risks associated with antipsychotic exposure through breast milk.[24]

Conclusion

In the case of long-acting injectable antipsychotics (LAIs), there is a greater tendency for clinicians either not to begin or to discontinue LAI prescriptions during pregnancy. Given the prevalence of significant psychiatric conditions and their associated risks of decompensation during the perinatal period, healthcare providers must be at ease with the use of antipsychotic medications during pregnancy. While acknowledging the limited safety data on long-acting injectable (LAI) formulations during pregnancy, we recommend transcending apprehensions related to prescribing LAIs to pregnant women when substantial risks of psychiatric decompensation outweigh the absence of data.

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