Aripiprazole Combined with Other Psychotropic Drugs in Pregnancy: Two Case Reports

Vesna Pirec, MD, PhD,[1] Aarti Mehta, MD,[2] and Sittanur Shoush, MD[3]

[1] *Insight Behavioral Health Centers and Women's Mental Health, University of Illinois at Chicago, Chicago, Illinois, U.S.A.*
[2] *General Adult and Reproductive Psychiatrist, Chicago, Illinois, U.S.A.*
[3] *Women's Mental Health and Women's Mental Health Fellowship,University of Illinois at Chicago, Chicago, Illinois, U.S.A.*

ABSTRACT

Maternal exposure to second generation antipsychotics during pregnancy has been associated with some negative effects for both mothers and infants. Aripiprazole is becoming more readily used, although data regarding its use in pregnancy are limited. Additionally there are limited data with regards to the impact of polypharmacy on pregnancy outcomes. Given the relative paucity of information related to aripiprazole use in pregnancy it is difficult to counsel women on potential risks or side effects. We present two cases that illustrate the use of aripiprazole as a part of a polypharmacy regimen in pregnancy and describe the pregnancy outcomes in an effort to help clinicians facing complex treatment decisions in pregnancy.

While the study of antidepressant use in pregnancy has received substantial attention in the past decade, both in research and in the media, less is known about the use of second generation antipsychotics (SGA). Despite this, the use of SGAs in pregnancy is steadily increasing.

While there is literature on the use of SGAs as a class, there is limited information on specific SGAs use in pregnancy, especially newer ones such aripiprazole (1, 2). Aripiprazole is one of the newer SGAs that has unique pharmacological activities: partial agonist at dopamine 2 receptors and antagonist at serotonergic 5HT1A receptors. Aripiprazole has demonstrated its efficacy in stabilizing symptoms of psychosis and mania, as well as augmenting antidepressive effect of other medications. It has been prescribed more commonly due to novel mechanism of action and what was thought (3) to be a relatively lower risk for metabolic syndrome. However, aside from a few published case reports, its use in pregnancy has not been well studied. Lack of available data makes it difficult to counsel women on potential risks or side effects. Additionally, there is limited data with regards to the impact of polypharmacy on pregnancy outcomes (4). While the goal is to limit polypharmacy in pregnancy, this is not always possible. We present two cases that illustrate the use of aripiprazole and polypharmacy in pregnancy and describe the pregnancy outcomes in an effort to help clinicians facing complex treatment decisions while medicating expecting mothers.

CASE 1:

Ms. M was a 26 year–old woman who presented at 36 weeks gestational age into her first pregnancy for management of her bipolar illness. She had diabetes mellitus type II and hypothyroidism, both well controlled with insulin and levothyroxine respectively. She did not use illicit substances.

Ms. M has had multiple hospital admissions most of which were for mania with psychotic features. Prior to conceiving she was stable on aripiprazole 15 mg daily, but self-discontinued upon discovering pregnancy around 4 weeks gestational age. Due to partial response to aripiprazole, lamotrigine was added and slowly titrated up to 150 mg daily at 25 weeks gestational age. Despite medication adjustment, Ms. M developed another manic psychotic episode and was admitted to inpatient psychiatry at 31 weeks gestational age. In the hospital lamotrigine was discontinued and clonazepam and haloperidol were added.

On discharge from the hospital she was taking aripiprazole 15 mg daily and clonazepam 1 mg at bedtime. Due to remaining hypomanic symptoms aripiprazole was titrated up to 10 mg twice daily and clonazepam 1 mg at bed time was continued. Ms. M's symptoms were stabilized on this regimen.

She delivered a term infant by cesarean due to breech presentation. The infant was 5-10th percentile with APGARs of 9/9. Although initially vigorous the infant developed

Address for Correspondence: ✉ Vesna Pirec, MD, PhD,Chief Medical Director, Insight Behavioral Health Centers, Women's Mental Health 333 North Michigan Avenue, Suite 1900 Chicago, IL 60601, U.S.A. vpirec@insightillinois.com

poor feeding and hyperbilirubinemia of unknown etiology and on day two was admitted to the neonatal intensive care unit with nasogastric tube for feeding supplementation. The hyperbilirubinemia resolved spontaneously after a couple of days and the infant's feeding improved. They were discharged from the hospital on day five. Ms. M chose to bottle feed the infant. On subsequent pediatrician follow up for three months the infant was developing well, apart from having an umbilical hernia and hemangioma on the thigh.

CASE 2:

Ms. J was 23-year-old female with an atrial septal defect who was pregnant for the fifth time and had two live children, initially presented to an outside hospital two months post-partum and six weeks pregnant. She had prior history of bipolar disorder with psychotic features and was off all medication. On admission to the first hospital she presented with psychotic mania in the context of cocaine, marijuana and benzodiazepine use. Her initial medication regimen was ziprasidone 80 mg twice daily and oral haloperidol 10 mg twice daily. Her symptoms persisted and she was transferred to the second hospital. Per collateral history Ms. J's prior episode of post-partum psychosis was stabilized on aripiprazole.

Initial medication regimen was discontinued and aripiprazole and lithium were initiated. Ms. J's medications were slowly titrated up to 25 mg of aripiprazole daily and lithium 300 mg three times per day. At approximately 10 weeks gestational age Ms. J improved significantly and was discharged from the hospital in stable condition. Due to feeling overly sedated, Ms. J self-discontinued lithium at approximately 12 weeks gestational age without consulting her psychiatrist. She continued to be stable and monotherapy with aripiprazole 25 mg daily was continued throughout the pregnancy. Ms. J denied use of any illicit drugs after her initial presentation.

Ms. J gave birth to a term infant by vaginal delivery, with Apgar's of 9/9. The infant was in the 26th percentile for weight, 53rd percentile for length but <3rd percentile for head circumference. It was also noted that the baby had hypospadias. Ms. J chose not to nurse.

DISCUSSION

In both cases infants were exposed to multiple medications during various gestational stages. Thus it is difficult to draw any direct conclusion related to the infant outcomes and aripiprazole exposure. In both cases the women had term infants that were discharged from the hospital within five days from delivery and initial development was unremarkable. In Case 1 the infant's poor feeding may have been a result of antipsychotic withdrawals or neonatal benzodiazepine toxicity. It is unclear if the hyperbilirubinemia was related to medication exposure; however, it was time limited and did not require intervention. The infant in Case 2 had microcephaly and hypospadias. These malformations could have been attributed to any of the individual medications or a result of polypharmacy. However, since no previously published case reports of intrauterine exposure to aripiprazole showed any structural malformation in newborns (1, 2, 5, 6), it is more likely that fetal malformations in the second case were related to the exposure to polypharmacy. Additionally, in every pregnancy there is always a 1-3% chance of giving birth to an infant with major malformation regardless of medication exposure. And lastly, the fact that both women discontinued some of their medication without consulting their doctor, and possibly by doing that exacerbated their symptoms for a time period, could have contributed to infants' outcomes.

The debate over using psychotropic medication in pregnancy continues. Whenever possible, polypharmacy is discouraged in this patient population. Data regarding in utero exposure to some relatively newer medications such as aripiprazole alone or in the context of polypharmacy are sparse. Only one case report describes placental transfer of aripiprazole to be similar to that of risperidone or haloperidol (7). Meanwhile clinicians struggle to achieve stabilization of patients' symptoms while providing as safe an environment as possible for a growing fetus. Presented cases further highlight the need for more studies on the use of aripiprazole as well as on the potential impact of polypharmacy in pregnancy in order to help guide clinicians and patients in making informed treatment decisions.

References

1. Gentile S, Tofani S, Bellantuono C. Apiprazole and pregnancy: A case report and literature review. J Clin Psychopharmacol 2011;31:531-532.
2. Watanabe N, Kasahara M, Sugibayashi R, Nakamura T, Nakajima K, Watanabe O, Murashima A. Perinatal use of aripiprazole: A case report. J Clin Psychopharmacol 2011;31:377-379.
3. Newcomer JW. Second-generation (atypical) antipsychotics and metabolic effects: A comprehensive literature review. CNS Drugs 2005;19:1-93.
4. Einarson A, Choi J, Koren G, Einarson T. Outcomes of infants exposed to multiple antidepressants during pregnancy: Results of a cohort study. J Popul Ther Clin Pharmacol 2011;18:e390-396.
5. Lutz UC, Hiemke C, Wiatr G, Farger G, Arand J, Wildgruber D. Aripiprazole in pregnancy and lactation: A case report. J Clin Psychopharmacol 2010;30:204-205.
6. Mervak B, Collins J, Valenstein M. Case report of aripiprazole usage during pregnancy. Arch Women Ment Health 2008;11:249-250.
7. NguyenT, Teoth S, Hacket P., Illett K. Placental transfer of aripiprazole. Aust NZ J Psychiatry 2011;45:500-501.