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# Use of lurasidone in pregnant patient with bipolar/schizoaffective disorder and comorbid obesity

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## Abstract

We report on a pregnant patient G3P2 with differential diagnosis of schizoaffective disorder and bipolar disorder with psychotic features and comorbid obesity with a significant past medical and mental health history including borderline personality disorder, posttraumatic stress disorder, preeclampsia, and morbid obesity. The patient was in her third trimester of pregnancy with an increased risk for recurrence of preeclampsia. She presented with symptoms of bipolar depression, anxiety, homicidal thoughts, and both auditory and visual hallucinations. She was taking haloperidol 15 mg oral daily; however, it did not control her mood symptoms. Lurasidone has minimal metabolic side effects compared to other SGAs and has lower potential for orthostatic hypertension, hyperprolactinemia, and adverse effects of drug-induced parkinsonism. Therefore, after thorough evaluation and considering the risk/benefit ratio in fetal drug exposure and the degree of severity of maternal psychiatric illness, the treatment team decided to discontinue haloperidol and administer lurasidone 20 mg oral daily. Additional large, controlled studies are needed to determine the safety and efficacy of lurasidone as the treatment of choice for childbearing women with bipolar disorder and/or schizoaffective disorder with comorbid obesity.

## Keywords

pregnancy; schizoaffective disorder; bipolar disorder; morbid obesity; lurasidone.

## Introduction

Bipolar disorder (BD) is a very common mental illness affecting up to 4.9 million people in the United States and approximately 60 million people worldwide [1]. It is characterized by at least one episode of mania and symptoms of depression. Notably, it can pose negative implications to females with BD during their reproductive years. For example, pregnancy is associated with 71% increased risk of recurrence of bipolar disorder [2]. The risk for preterm labor is increased by 50% regardless of whether the expecting

mother is being treated pharmacologically or not [3]. Other adverse pregnancy outcomes associated with BD include increased rates of labor induction and cesarean section and increased risk for postnatal mood disorder. Hyperglycemia, gestational hypertension, and antepartum hemorrhage also occur at a higher rate in women with BD [4]. In addition to adverse effects on the mother, babies born to mothers with BD are also highly impacted. They are more likely to have an extremely small gestational age that falls less than the second percentile [4]. Children, later in life, have higher rates of memory and attention disturbances, impaired social functioning, behavioral and emotional problems, and severe psychiatric disorders [5]. In light of this, the question of whether to treat with medication in the setting of pregnancy or not can be raised. Mothers who are not treated with mood stabilizers during pregnancy do not have an increased risk of infants with congenital abnormalities; however, the baby is still at risk for recurrent episodes of neonatal hypoglycemia until the age of 5 and microcephaly which can lead to other downstream impairments [6]. Babies born to mothers who are treated with mood stabilizers are at risk for congenital anomalies and extrapyramidal and withdrawal symptoms. Overall, it is generally recommended to continue previous therapy in women who become pregnant while on antipsychotics [6]. One complication a physician may encounter is patients who are also morbidly obese (BMI > 35 kg/m$^2$). Comorbid obesity is common in women with BD (up to 68%) due to illness-related, treatment-related, and lifestyle-related predicaments [7]. Thus, there are significant limitations to other treatment options in cases where the current pharmacotherapy such as first-generation antipsychotics are no longer effective in controlling symptoms of bipolar disorder, primarily due to the metabolic effects and/or teratogenicity of many treatment options.

Schizoaffective disorder (SAD) is a disorder whose symptoms overlap with those of schizophrenia (SCH), mood disorder (MD), and/or BD. SAD is characterized by criterion A for the diagnosis of schizophrenia accompanied by a major mood episode (manic or depressive) for most of the illness. SAD also involves a delusional or hallucinogenic episode without major mood symptoms for a duration of two weeks or longer [8]. The proper diagnosis of SAD can be complex as it encompasses both SCH and MD. Some studies have described SAD as an intermediate step between SCH and MDs while other studies stated it is as an atypical form of either SCH with a comorbidity of MD or vice versa [9]. Goghari et al. emphasized the importance of temporality in differentiating SAD from SCH and BD. The lifetime prevalence of the SAD is 0.3% with 30% of the cases falling within the category of women ages 25 to 35 [10]. Studies on the fetal impact of SAD are minimal. Gunduz et al. found no obstetric complications in patients with SAD when compared to pregnant women without SAD [11]. We present a case where a trial of lurasidone was used to control bipolar/schizoaffective disorder in a pregnant patient with comorbid obesity.

## Case Description

We present a case of a 26-year-old Hispanic female patient, gravida 3, para 1-1-0-2 with significant past medical history including bipolar disorder, borderline personality disorder, posttraumatic stress disorder, preeclampsia in a prior pregnancy, and morbid obesity (BMI > 60.1 kg/m$^2$) who was admitted to the inpatient psychiatric unit for suicidal and homicidal ideation.

On initial psychiatric assessment, the patient was 28 weeks pregnant. Though the patient was a poor historian, she endorsed symptoms of depression including lack of sleep, poor concentration, low energy, poor appetite and suicidal ideations, homicidal thoughts, and thoughts of self-harm. The patient also

endorsed symptoms of mania including distractibility and racing thoughts. She also endorsed symptoms of anxiety such as excessive worry about her unborn child and delusional intrusive thoughts that her baby will be taken away after delivery by Child Protective Service (CPS).

She had a history of parasuicidal behavior including cutting herself with glass and taking an unknown amount of antipsychotic medication. Her psychosocial history included the following: she lived alone; she reported a history of sexual abuse at the age of 13; she had no relationship with her children's father and her support system consisted solely of her aunt.

Additionally, she had an open case with her 9-month-old infant son, who was under her aunt's custody. The patient endorsed homicidal ideations towards CPS regarding her unborn child but had no intent or plan. The patient also admitted to auditory hallucinations of birds chirping and visual hallucinations of shadows that followed her. The patient's prior psychiatric medication trials included aripiprazole and quetiapine. However, she had been taking haloperidol 5 mg daily and 10 mg at night for the past 3 years.

The patient reported the current pharmacotherapy did not help her auditory and visual hallucinations, so the decision was made to discontinue haloperidol, start on lurasidone 20 mg daily, and continue prenatal vitamins. Lurasidone was selected because, compared to other first and second-generation antipsychotics, lurasidone is relatively safer (pregnancy category B) and lower risk. During her hospitalization, the patient was also treated with diphenhydramine 50 mg and trazodone 50 mg for insomnia as well as lorazepam 1 mg for anxiety. The day following the patient's first dose of lurasidone 20 mg, she denied auditory and visual hallucinations. The patient also denied excessive worrying and suicidal and homicidal ideations. However, the patient did complain of chest pain. An EKG and troponin were negative for acute coronary syndrome. No other side effects were reported. On the day of discharge, the patient demonstrated improved symptoms of mania and anxiety. She denied any suicidal or homicidal ideations, plan, or intent. She reported the medication had improved her intrusive thoughts. The patient's symptoms of depression improved. She no longer endorsed visual or auditory hallucinations. Outpatient treatment components were established including outpatient psychiatrist, therapist, and continued monitoring for safety, efficacy, and complications of pregnancy by her obstetrician.

## Discussion

This case demonstrates difficulties associated with treating pregnant patients with BD/SAD, complicated by morbid obesity. BD and/or SAD are usually treated with mood stabilizers, antipsychotics, and antidepressant medication [12,13]. However, benefits and treatment-related teratogenicity are factors necessary to consider with the different therapeutic classes used to treat BD/SAD [14].

**Mood stabilizers:** Mood stabilizers such as lithium and lamotrigine can cause a range of abnormalities (e.g., Ebstein's anomaly, polyhydramnios, diabetes insipidus, thyroid dysfunctions, and floppy baby syndrome caused by lithium; and neural tube defects as well as cleft lip or palate caused by lamotrigine); and therefore, are not recommended for use during pregnancy [15]. Carbamazepine and valproate, antiepileptics used as mood stabilizers in BD/SAD, also pose higher risk for congenital anomalies, with carbamazepine specifically causing neonatal hepatotoxicity [15]. There is also a relative risk of neural tube defects and valproate exposure in-utero puts the baby at increased risk for developmental delay [16].

**Antidepressants:** Antidepressants are known to induce manic episodes, so they are usually prescribed in conjunction with a mood stabilizer or antipsychotic [17]. However, birth defects (e.g., anencephaly, cardiac defects, omphalocele) are two to three times more likely to occur in babies who are exposed to SSRI medications in pregnancy [18].

**First-generation antipsychotics:** In contrast to second-generation antipsychotics (SGAs), metabolic risks rarely appear in patients being treated with first-generation antipsychotics (FGA). Because FGAs are less harmful, it is the choice of treatment in drug-naive pregnant women with bipolar disorder [19,20]. Although haloperidol is most effective in treating acute mania during pregnancy compared to other agents, our patient was titrated to a therapeutic dose that was ineffective in addressing her symptoms of bipolar depression. In addition, there have been reports of haloperidol causing increased rates of premature labor and in some cases, spontaneous abortions, cardiovascular and respiratory complications, and fetal akinesia in pregnant patients taking haloperidol [6].

**Second-generation antipsychotics:** SGAs such as olanzapine, aripiprazole, and quetiapine are known to cause metabolic side effects such as weight-gain, hyperglycemia, and dyslipidemia. Specifically, aripiprazole increases leptin and quetiapine increases cholesterol levels [21]. Aripiprazole is effective against SAD and does not cause fetal harm [22,23]. Other SGAs such as paliperidone and risperidone have no major congenital abnormalities in a small subset of pregnant women with SAD [12,24,25]. According to Gentile et al., babies born to mothers taking SGAs have significantly higher mean birth weight compared to those exposed to first-generation antipsychotics [7]. This patient was morbidly obese and already at risk for developing gestational metabolic complications. Therefore, this therapeutic option posed higher risk than benefit to the patient and her unborn child. Our patient also had an increased risk for preeclampsia and preterm delivery with her current pregnancy due to her history of preeclampsia with her previous pregnancy and risks associated with BD, discussed previously. Thus, most SGAs were not the appropriate treatment option in this case.

Lurasidone has been shown to be more effective than first generation antipsychotics. Furthermore, it has been shown that individuals taking lurasidone do not experience metabolic nor prolactin-related adverse effects [26]. Potkin et al. confirmed there are no effects on weight, metabolism, or cardiac function with the use of lurasidone during pregnancy [27].

## Conclusion

When treating expecting mothers with BD/SAD, providers must also consider which medications fall under each safe pregnancy category established by the Food and Drug Administration (FDA) and American College of Obstetricians and Gynecologists (ACOG) guidelines. Lithium, valproate, and carbamazepine (mood stabilizers) fall under category D. Most antidepressants, all typical antipsychotics, and most atypical antipsychotic medications (risperidone, olanzapine, quetiapine, ziprasidone, aripiprazole, asenapine) are category C according to ACOG guidelines [28]. Lastly, lurasidone and clozapine fall under category B. The risks for clozapine are unclear and lack large-scale studies. Also, clozapine is usually the last treatment option when two other antipsychotic medication trials have failed. Thus, in this case, lurasidone was the safest treatment option.

The differential of SAD would be a challenge to confirm in this patient's case due to the short-term observation by the treatment team, as time plays a role in confirming a diagnosis. Although she presented with symptoms which satisfies the criterion for SAD during the primary encounter (e.g., mania, depressed mood, hallucinations, and delusions), the duration of those symptoms was not available [8,29]. These temporal factors necessary for diagnosing SAD make the confirmation of SAD in this patient difficult. Treatment options for SAD have not been extensively explored. The literature tends to link treatment of SAD with SCH or BD. Such treatments have generally focused on atypical antipsychotics, mood stabilizers, and antidepressants [12]. However, these treatments are derived from studies mainly focusing on SCH and BD with only a small subsection of the patients in the studies being primarily diagnosed with SAD [12]. Moreover, lurasidone provides a safe treatment option for both the patient and the fetus as it does not impact weight gain nor metabolic parameters [27].

Although discontinuation of therapy is an option, abrupt discontinuation results in higher risks of new morbidity (e.g., early depressive, and dysphoric states) in women with BD/SAD. Untreated manic episodes may be severe and lead to expectant mothers attempting suicide and/or infanticide. While Yinglin et al. reports nimodipine to be useful in controlling mood swings of BD and is reportedly most effective in young patients with rapid cycling disease, our patient did not present with rapid cycling BD symptoms [30,31]. Further, nimodipine is more difficult to use than lurasidone requiring dosing every 4 hours. Interestingly, long-acting injectable aripiprazole is reportedly safe for pregnancy in BD; however, as previously mentioned it increases the risk for metabolic syndrome and is considered pregnancy safety category C. There are limited case reports on electroconvulsive therapy during pregnancy, and little is known about psychotherapy effectiveness in pregnant women.

Pregnancy is not protective in BD/SAD. It is also evident that treatment for bipolar depressive episodes and schizophrenic-like hallucinations in pregnancy, particularly in women who are morbidly obese, is complicated. In this case, lurasidone was useful in controlling mood symptoms of BD/SAD; it has minimal metabolic side effects compared to other SGAs. Lurasidone may also be associated with lower potential for orthostatic hypertension, hyperprolactinemia, and adverse effects of drug-induced parkinsonism [32]. In sum, treatment selection should include a careful evaluation of the following: risk/benefit ratio of fetal drug exposure, maternal psychiatric illness severity, and safety/efficacy profile of drugs [33]. Future large-scale studies are needed to determine safety and efficacy of lurasidone in pregnant females with BD/SAD and comorbid obesity.

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