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The use of psychotropic medications in pregnancy and lactation

Pregnant and breastfeeding women who experience significant psychiatric illness may need to use benzodiazepines, antipsychotics, mood stabilizers, or other drugs to protect themselves and their infants.

ABSTRACT: The decision to use a psychotropic medication of any kind during pregnancy or in the postpartum period always requires a careful weighing of the risks and benefits to both the mother and her fetus or newborn. There are several factors that must be considered, including the possible teratogenic effects of the medication, the safety of the medication during labor and delivery, the possible long-term neurobehavioral effects on childhood development, and the effects of ongoing exposure during breastfeeding.

When considering a treatment plan for a pregnant or breastfeeding woman with a psychiatric disorder, the risks to the mother and the fetus or newborn from both the illness and the treatments must be assessed. Medications that should not be used during pregnancy are listed in **Table 1**. If possible, psychotropic medications in general should be avoided during the first 12 weeks of pregnancy, as this is the time of the most active organ development in the fetus. However, for a woman who is already taking a medication at the time of conception, by the time the pregnancy is confirmed, most or all of the organogenesis has often already occurred. If this is the case, there is wisdom in not panicking. Abrupt discontinuation of medications can precipitate a relapse, and this can result in the need for further medication exposure to stabilize the mother.

Psychotropic medication use during pregnancy

Psychotropic medications in pregnancy are indicated for women who develop a significant psychiatric illness during the pregnancy, women who experience an exacerbation of a pre-existing illness during pregnancy,

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Table 1. Medications to avoid during pregnancy

Pregnancy phase	Medication
First trimester	Carbamazepine Valproic acid Lithium (if possible) Low-potency typical antipsychotics
Third trimester and labor and delivery	High-dose benzodiazepines
All trimesters	Monoamine oxidase inhibitors (MAOIs)

and women who have experienced a rapid deterioration of their condition after discontinuing medication. An international epidemiological survey conducted 12 years ago indicated that the prevalence of psychotropic drug use during pregnancy was approximately 3.5%.[1] At the time, benzodiazepines accounted for the most exposure; however, the increasing use of antidepressants, particularly the selective serotonin reuptake inhibitors (SSRIs), has made this the most commonly used category of psychotropic medications in pregnancy in recent years. When a medication of any kind is prescribed in pregnancy, the lowest possible dose that will provide com-

Table 2. Effects of exposure to psychotropic medications during pregnancy.

Medication	Effects	References
Benzodiazepines • lorazepam (short) • clonazepam (med) • alprazolam (short) • diazepam (long)	Exposure to high-dose benzodiazepines in utero has been associated with newborn withdrawal symptoms, including irritability and restlessness, apnea, cyanosis, lethargy, and hypotonia. No long-term effects have been reported, although data are limited. Drugs with a short or medium half-life (lorazepam, clonazepam) at the lowest effective doses should be used.	2, 3
Tricyclic antidepressants (TCAs) • clomipramine • desipramine • imipramine • amitriptyline • nortriptyline	The tricyclic antidepressants are most commonly used for comorbid conditions and when other treatments have failed. TCAs, which were once the treatment of choice for depression and panic, remain effective and are not associated with teratogenesis. Doses may need to be adjusted as the pregnancy proceeds. While data analysis has shown that exposure in pregnancy does not increase the incidence of teratogenesis, neonatal withdrawal symptoms have been associated with these medications, so careful monitoring of the newborn is essential.	2, 4-6
Monoamine oxidase inhibitors (MAOIs)	The MAOIs are contraindicated in pregnancy, based on animal studies that have reported increased rates of congenital abnormalities.	2
Other non-SSRI antidepressants • buproprion • mirtazapine • trazodone	Limited data are available on the use of these medications during pregnancy.	None
Atypical antipsychotics • olanzapine • risperidone • clozapine • quetiapine • ziprasidone	Low-potency dopamine blockade neuroleptics have been associated with an increased rate of congenital abnormalities. High-potency dopamine blockade antipsychotic medications have not been associated with congenital abnormalities. However, data are limited, and little or no information is available on clozapine, ziprasidone, and quetiapine. Ziprasidone is not yet available in Canada, but to date there are no reports of increased risk with exposure.	2, 7, 8
Typical antipsychotics • haloperidol • loxapine • trifluoperazine • chlorpromazine • thioridazine	Low-potency typical antipsychotics (e.g., thioridazine) have been associated with increased risk of mild malformations. High-potency typical antipsychotics (e.g., haloperidol) have not been associated with increased risk.	8
Mood stabilizers • lithium • valproic acid • carbamazepine • lamotrigine • topiramate • gabapentin	Limited information is available regarding lamotrigine, topiramate, and gabapentin use in pregnancy. Carbamazepine and valproic acid use during the first trimester has been associated with an increased risk of neural tube defects, as well as minor and major fetal malformations, low birth weight, and thrombocytopenia. Lithium use in pregnancy has been associated with a pronounced increase in the rate of Ebstein anomaly; however, recent literature suggests that this rate is much lower than previously reported (1 in 4000 vs 1 in 400). If lithium is continued in pregnancy, because of the risk of decompensation, drug levels should be monitored carefully. The dose may need to be increased by as much as 100% in pregnancy to maintain symptom control, but should be decreased by at least 50% at the time of delivery to avoid toxicity in both mother and newborn.	2, 9, 10

plete symptom control should be used. **Table 2** outlines the most commonly prescribed psychotropic medications and provides information on their use by pregnant women (see "The use of antidepressants in pregnancy and lactation" elsewhere in this issue for details about SSRI-type medications).

Psychotropic medication use during lactation

Data on the use of psychotropic medications in breastfeeding women are growing, and recent publications suggest that such medications are not associated with prolonged adverse effects in infants exposed to them through breast milk. However, all psychotropic medications *are* found in breast milk in varying amounts and are passed on to the nursing infant. Thus, when pharmacotherapy is indicated for a breastfeeding woman, the potential risks of medication exposure in the infant must be weighed against the risks of untreated maternal illness. **Table 3** outlines the most commonly prescribed psychotropic medications and provides information on their use by breastfeeding women (see "The use of antidepressants in pregnancy and lactation" elsewhere in this issue for details about SSRI-type medications).

Where to from here?

The existing literature on the use of psychotropic medications in pregnant and lactating women is limited to case reports and small studies, making it difficult to formulate any generalizations regarding the safety of these medications. However, the results of studies published to date are promising, with few adverse effects reported.

Table 3. Effects of exposure to psychotropic medications during lactation.

Medication	Effects	References
Benzodiazepines • lorazepam • clonazepam • alprazolam • diazepam	Case reports indicate that milk plasma concentrations vary from 0.1% to 0.5% of the maternal dose for different benzodiazepines. Sedation, lethargy, impaired respiration, and withdrawal have been reported in exposed infants after prolonged use. Therefore, if these medications are indicated, the minimum dose required for symptom relief should be used, and the infant should be monitored regularly.	3
Tricyclic antidepressants (TCAs) • clomipramine • desipramine • imipramine • amitriptyline • nortriptyline • doxepin	The tricyclic antidepressants appear to be safe for use by breastfeeding women. Occasional sedation has been reported in infants exposed to clomipramine and doxepin. The active metabolite of doxepin has the longest half-life of all TCAs, and should be avoided if possible because of the potential for excess accumulation in infant serum. A recent long-term study has reported no adverse developmental effects in infants exposed to TCAs through breast milk.	6
Monoamine oxidase inhibitors (MOAIs)	The MOAIs are not recommended for use by breastfeeding mothers because of profiles indicating extensive interaction with other medications.	2
Antipsychotics • olanzapine • risperidone • clozapine • quetiapine • ziprasidone	The long-term developmental effects of neuroleptic exposure on the infant dopamine system and receptors are still unclear. Recent data on haloperidol, olanzapine, and quetiapine are encouraging, with no adverse effects reported. Clozapine has been associated with sedation, irritability, and seizures in infants. There are limited data available on the other atypical neuroleptics, thus caution is recommended.	8, 11-13
Mood stabilizers • lithium • valproic acid • carbamazepine • lamotrigine • topiramate • gabapentin	Lithium has been reported to cross into breast milk at approximately 40% to 50% of the maternal levels. The use of lithium during lactation is contraindicated because the neonatal kidney is still immature and the risk for lithium accumulation is high. Low serum levels have been detected in infants exposed to carbamazepine and valproate through breast milk, suggesting that these drugs are compatible with breastfeeding. However, the possible association between these drugs and thrombocytopenia and hepatotoxicity indicates that close monitoring of the infant is necessary. Gabapentin has been reported to cross into breast milk at almost 100% of the maternal levels and is, therefore, not recommended for use in breastfeeding women. Little information exists on the use of lamotrigine and topiramate, so caution is advised.	14, 15

We continue to get information regarding the effects of psychotropic medications from women who conceive while on these drugs. The formation of drug registries and the sharing of information on infant outcomes among clinicians and researchers are essential. In addition, long-term follow-up studies that address possible developmental effects of medication exposure are critical to a better understanding of the safety of psychotropic medication exposure in fetuses and neonates.

When pharmacotherapy is indicated for a breastfeeding woman, the potential risks of medication exposure in the infant must be weighed against the risks of untreated maternal illness.

Competing interests

None declared.

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