

MANAGEMENT OF BIPOLAR DISORDERS DURING & AFTER PREGNANCY

The management of bipolar disorders during & after pregnancy requires careful consideration of the benefits & harms to both mother & fetus. The patient & support member(s) should be involved in the decision making process prior to conception.

SHOULD MOOD STABILIZERS BE USED BEFORE, DURING OR AFTER PREGNANCY? ^{1,2,3,4,5}

- It depends on the patient's previous & current mental health status.
- Asymptomatic females who are at **low risk of relapse**: may consider tapering mood stabilizer over ≥ 4 weeks. Ideally taper occurs prior to conception. Work with patient & family/support member(s) to monitor closely for signs of relapse. If patient is on more than one mood stabilizer, aim for monotherapy.
- Females who are at **high risk of relapse** (e.g. history of relapse with previous cessation of therapy, postpartum psychosis): continue their mood stabilizer during & after pregnancy. If on **valproic acid/divalproex**, consider using another mood stabilizer before & during pregnancy.

WHAT IS THE RISK OF RELAPSE DURING PREGNANCY & POSTPARTUM? ^{3,6,7,8}

- Pregnancy itself does not contribute to, or offset, the risk of relapse; however, pregnant women are more likely to discontinue their medication due to concerns of teratogenicity. **80-100% of women who discontinue their mood stabilizer during pregnancy relapse**, especially when therapy is stopped abruptly; risk of relapse is 2-3x greater than those who continue therapy during pregnancy.
- **The greatest risk of relapse for untreated women is during the postpartum period**, which occurs 3.5x more often than during pregnancy. Childbirth can trigger or exacerbate existing bipolar mood disorders, as there is a rapid \downarrow of estrogen after delivery followed by dopamine down-regulation. The most frequent time relapse occurs is during the first two weeks after delivery.
- Relapses during & after pregnancy tend to be of depressive or mixed episodes, & there is \uparrow risk of postpartum psychosis see page 2.
- There is also a risk of relapse if & when medications are switched.

IS THERE ANY HARM IN NOT TREATING BIPOLAR DISORDER DURING PREGNANCY & POSTPARTUM? ^{4,9,10}

- **Untreated bipolar disorder can put the mother & fetus/baby at risk, with suicide & infanticide being the major concern.**
- Other concerns with untreated bipolar disorder include:
 - **Lifestyle**: \uparrow risk of risky behaviour/accidents, substance abuse, poor self-care, inadequate nutrition/vitamins, & bonding issues
 - **Obstetric**: \uparrow risk of intrauterine growth retardation, prematurity, & antepartum hemorrhage
 - **Neonatal**: \uparrow risk of low birth weight, \uparrow levels of cortisol & catecholamines, & \uparrow rates of neonatal intensive care unit admissions

WHAT IS THE ROLE OF NON-PHARMACOLOGIC THERAPIES DURING PREGNANCY & POSTPARTUM? ^{3,4,5,10,11,12}

- **Psychotherapy** (interpersonal psychotherapy, cognitive behavioural therapy [CBT] or cognitive remediation) may be helpful as an adjunct for the management of bipolar symptoms \pm depressive features. It may be considered as monotherapy in patients with bipolar disorder & **mild depressive symptoms** see page 2.
- **Electroconvulsive therapy** (ECT) is considered safe & effective in pregnant women. It may be considered as an adjuvant to medication in patients with severe depression, severe mixed episodes or bipolar mania; although this is based on limited data.
- **Psychosocial support** is required during & early after pregnancy. Daily activities should be structured to minimize sleep deprivation & mood lability. Try to ensure a support person is available in the home to allow for adequate sleep, e.g. partner take paternity leave. Potential stressors should be avoided, e.g. home renovations, moving, excessive visitors, etc.

WHICH MOOD STABILIZERS ARE CONSIDERED THE SAFEST TO USE DURING PREGNANCY see Table on pages 3 & 4 for additional info on individual medications ¹³⁻³⁰

- The patient's disease severity, clinical course & gestational age of the fetus need to be considered when tailoring drug therapy during pregnancy. Ideally, risks & benefits of treating/not treating bipolar disorder are discussed with the patient prior to conception.
- Mood stabilizers differ in their risk of teratogenicity & type of malformations.
- When possible, use monotherapy at the lowest effective dose. **Risk of malformations \uparrow with polytherapy & is dose-dependent.**
- The majority of safety data on antiepileptics use during pregnancy is based on females with epilepsy, & there is some debate as to whether epilepsy itself can increase the risk of fetal harm.
- **Antipsychotics** are thought to have a low potential for fetal harm, but this class of medication also has the least amount of pregnancy & breastfeeding safety data among treatment options.
- **Lamotrigine** appears to have the lowest risk of malformations among the antiepileptics (risk of cleft palate abnormalities is $\sim 8/1000$), but is less effective for certain types of bipolar disorder phases (e.g. mania). Requires cautious dose titration ($\uparrow 50\text{mg/day}$ q1-2 weeks) to \downarrow risk of severe skin reaction.
- **Carbamazepine** use during 1st trimester has been linked to malformations (neural tube, fetal carbamazepine syndrome & cardiac defects) & risk ranges from 3.4%-8.7%.
- **Valproic acid/divalproex** has the highest incidence of malformations e.g. neural tube defects with 1st trimester exposure & has been associated with neurodevelopmental impairments in infants/children exposed to valproic acid during 2nd & 3rd trimesters.
- **Lithium** has been linked to fetal cardiac malformations, however the risk is lower than originally thought \rightarrow cardiac malformations 8/1000 & Ebstein's anomaly 10/20,000.
- Due to pharmacokinetic changes during pregnancy, lithium & antiepileptic doses may need to be \uparrow in 2nd &/or 3rd trimesters. Consider \downarrow to the pre-pregnancy dose after delivery especially if dose was \uparrow quite a bit during pregnancy; balance risk of toxicity with risk of relapse.
- Refer to the Table on pages 3 & 4 for additional information on the above medications & use before, during & after pregnancy.

HOW SHOULD BIPOLAR DISORDER & DEPRESSIVE SYMPTOMS BE MANAGED DURING PREGNANCY?^{1,5}

- The majority of bipolar episodes during pregnancy are depressive.
- **Mild depressive symptoms:** non-pharmacological therapy (e.g. interpersonal therapy, CBT)
- **Moderate depressive symptoms:** CBT ± pharmacotherapy *see below*
- **Severe depressive symptoms:** pharmacotherapy *see below* ± CBT
- Pharmacotherapy options for moderate to severe depressive symptoms:
 - Quetiapine **SEROQUEL** can be used as monotherapy for both bipolar disorder & depression, OR
 - Antidepressant + mood stabilizer: for the antidepressant, a selective serotonin reuptake inhibitor (SSRI, except for paroxetine **PAXIL** due to minimal/no benefit in bipolar disorders ^{CANMAT 2013}) or bupropion **WELLBUTRIN** is recommended
 - **Antidepressants may trigger or worsen mania; CANMAT²⁰¹³ advises against the use of tricyclic antidepressants & venlafaxine **EFFEXOR** as these agents have an ↑ risk of manic switch.**
 - Monitor closely for manic & hypomanic symptoms; discontinue the antidepressant if these symptoms develop.
 - If the patient is concerned about the potential teratogenic harm of her mood stabilizer & prefers monotherapy with an antidepressant during pregnancy, consider (re)starting a mood stabilizer after the 1st trimester.
 - Also see the RxFiles Q&A *Are Antidepressants Safe During Pregnancy & Lactation* for additional information: <http://www.rxfiles.ca/rxfiles/uploads/documents/Antidepressants-PregnancyandBreastfeeding-QandA.pdf>

HOW SHOULD ACUTE MANIC EPISODES BE MANAGED DURING PREGNANCY?^{1,5}

- **If the patient is not currently on therapy:** start a mood stabilizer using the lowest effective dose. **CANMAT²⁰¹³ recommends lithium or an atypical antipsychotic** e.g. olanzapine, quetiapine, risperidone as 1st line agents for the management of acute mania in the general population; valproic acid/divalproex also recommended as 1st line, but should only be used during pregnancy if patient has failed other agents in the past. 2nd line agents: carbamazepine, haloperidol.
- **If the patient is currently on prophylactic therapy:** assess medication adherence, consider ↑ the dose (note: pharmacokinetic changes during 2nd & 3rd trimester ↑ drug clearance & may lead to loss of medication efficacy), discontinue any antidepressants, &/or switch to a 1st line agent if not already on one. If there is no response after the above measures & if mania is severe, consider ECT or, if necessary, combination therapy (preferably after 1st trimester).

SHOULD FEMALES WITH BIPOLAR DISORDER BREASTFEED?^{1,8,13,31}

- The benefits of breastfeeding must be balanced against the **risk of relapse due to major stressors such as sleep deprivation** &, if on a mood stabilizer, the potential impact of the medication on the breastfed infant.
- As mentioned on page 1, the risk of relapse is greatest immediately postpartum.
- **Tips for minimizing sleep deprivation:**
 - Have a family/support member feed the baby during the night using breast milk obtained via a breast pump &/or formula.
 - Offer the mother a night-time sedative during the first postpartum week, e.g. zopiclone 7.5mg po HS PRN or quetiapine 12.5-25mg po HS PRN. Note: there is minimal safety data for zopiclone or quetiapine during lactation. Hold breastfeeding overnight if hypnotic used.
- If breastfeeding causes undue stress & the patient is at high risk of relapse, it may be in the mother's best interest not to breastfeed.
- Compatibility of mood stabilizers with breastfeeding: (refer to Table on pages 3 & 4 for additional information)
 - All mood stabilizers are excreted into breast milk, but to varying degrees.
 - **Carbamazepine & valproic acid:** compatible with breastfeeding.
 - **Antipsychotics:** appear safe, but have the least amount of safety data during breastfeeding.
 - **Lamotrigine:** infant serum levels are ~30% of the maternal dose. No reports of adverse events, but monitor infant for rash.
 - **Lithium:** a small study (n=10) found that infant serum levels were only ¼ of the maternal serum concentrations.

SCREENING FOR BIPOLAR DISORDER DURING PREGNANCY & POSTPARTUM^{1,2,7,8,32,33,34}

- ~ ½ of females suffering from bipolar disorders after childbirth are misdiagnosed with postpartum depression.
- Postpartum depression is treated with antidepressants → can induce (hypo)mania, psychotic episodes or rapid cycling in a patient with bipolar disorder. Proper diagnosis is required for appropriate management.
- Currently, there is a lack of screening instruments for bipolar disorders in the peri-pregnancy period. The **Mood Disorder Questionnaire (MDQ)** may be helpful to identify patients with this mood disorder. A score of 7 is considered a positive result; however, an alternate cut-off score has been proposed for postpartum females (a score of 8 without the supplementary questions, sensitivity 88%, specificity 85%). Link to on-line MDQ form: <http://www.dbsalliance.org/pdfs/MDQ.pdf>
- The **Highs scale** can be used to identify postpartum hypomania symptoms *see On-Line Extras*.

HOW ARE POSTPARTUM BIPOLAR EPISODES DISTINGUISHED FROM OTHER POSTPARTUM MOOD DISORDERS?^{32,33,34}

- The majority of postpartum bipolar episodes are depressive, & are often mistaken for depression or the "baby blues".
- Onset & accompanying symptoms, when present, can be used to distinguish the different types of postpartum mood disorders.
- **Postpartum bipolar disorder symptoms surface within days of delivery. Baby blues** may occur postpartum days 3-4, & resolve by day 10. **Postpartum depression** peaks 6-8 weeks after childbirth.
- Postpartum bipolar disorder **hypomanic symptoms include** distractibility, goal-directed activity (e.g. taking on new projects), irritability, overtalkativeness, racing thoughts & ↓ sleep requirements.
- 25-50% of bipolar females are at risk of postpartum psychosis (risk ↑ to 60% in patients with a personal or family history of postpartum psychosis). ~4% commit infanticide. Use of mood stabilizers during & after pregnancy ↓ risk. If drug therapy is not used during pregnancy, start medication within 24 hours of delivery.
- If postpartum bipolar episode is severe, consider mood stabilizer therapy beyond one year after childbirth. Ensure patient is on a mood stabilizer during & after subsequent pregnancies.

RxFiles On-Line Extras: Q&A Management of Bipolar Disorders During & After Pregnancy

Highs Scale:

The following questionnaire can be used to identify postpartum hypomania symptoms:

Instructions:

As you have recently given birth, we would like to know how you have been feeling. **In the past 3 days**, have you felt any of the following conditions? If you answer yes to any of these questions, please indicate on which days these feelings were present – day 1 is the first day after your baby was born, day 2 the next day, etc.

	Yes, a lot (2 points)	Yes, a little (1 point)	No, have not experienced	On which days
Have you felt elated (high or unusually cheerful)?				
Have you felt more active than usual?				
Have you felt more talkative than usual, or a pressure to keep talking?				
Have your thoughts raced?				
Have you felt that you are a specially important person with special talents or abilities?				
Have you felt the need for less sleep?				
Have you had trouble concentrating because your attention keeps jumping to unimportant things around you?				
Total points for “Yes, a lot” & “Yes, a little”				

Scoring: 2 points for each “Yes, a lot” and 1 point for each “Yes, a little”. Must score a Yes on elation for inclusion. Score of ≥ 8 for a “case”.

Adapted from: Glover V, Liddle P et al. Mild hypomania (the Highs) can be a feature of the first postpartum week – association with later depression. *British Journal of Psychiatry*. 1994; 164:517-521.

RxFiles Related Documents:

Bipolar Disorder & Mood Stabilizer/Adjuvant Agent Comparison Chart <http://www.rxfiles.ca/rxfiles/uploads/documents/members/Cht-psyc-moodstabilizers.pdf>

Antipsychotic Comparison Chart <http://www.rxfiles.ca/rxfiles/uploads/documents/members/Cht-Psyc-Neuroleptics.pdf>

Antidepressant Comparison Chart <http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-Psyc-Antidepressant.pdf>

Peri-Pregnancy Chart <http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Peri-Pregnancy-DrugTx.pdf>

Q&A Are Antidepressants Safe during Pregnancy & Breastfeeding <http://www.rxfiles.ca/rxfiles/uploads/documents/Antidepressants-PregnancyandBreastfeeding-QandA.pdf>

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