Management of bipolar disorder over the perinatal period

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Background

Women with bipolar disorder have a high risk of relapse following childbirth. The risk of relapse can be reduced by mood stabilisers, but they are potentially harmful to the developing fetus.

Objective

The objective of this article is to provide an up-to-date review of the strategies for managing women with bipolar disorder over the perinatal period.

Discussion

Discussing the risks of taking mood stabilisers or having a medication-free pregnancy is essential for women with bipolar disorder. The latter, with careful monitoring, is suggested for women with less severe illness and good supports. Full or partial prophylaxis with a mood stabiliser is recommended for women at higher risk of relapse. Careful monitoring during pregnancy, psychosocial interventions and planning for the postnatal period will aid in preventing bipolar disorder relapse. The general practitioner is ideally placed to take a key management role in liaising with the obstetric and mental health teams, and planning for the postnatal period.

For women with bipolar disorder, the perinatal period poses a risk of relapse and/or harm to the developing fetus. Careful planning with an analysis of the risks and benefits of different management strategies is essential to ensure the best outcome for the woman and her infant. In this article, we provide a review of the management issues specific to women with bipolar disorder while they are pregnant.

The risk of relapse

Childbirth can trigger a relapse of bipolar disorder in 37% of women with the disorder. This figure rises to 66% if the women are unmedicated and 23% if they are on prophylactic medication.[1] Relapse is increased among women with more severe bipolar disorder and recent episodes of the illness, whereas women with a long period of euthymia and good social supports are less likely to have a relapse. Prophylactic mood stabilisers can significantly reduce the risk of relapse,[1] but introduces the problem of medication safety in pregnancy.

Managing the risks

When women are first given a diagnosis of bipolar disorder, the psychiatry team has a pivotal role, in collaboration with the general practitioner (GP), to help them accept the diagnosis and need for ongoing medication. The GP will also be involved in discussions about contraception (to prevent any unwanted pregnancy during a manic episode), and ensuring that women are on medications that have a low risk of harm to a developing fetus (eg avoiding sodium valproate). In many instances the GP will be actively involved with long-term management of a woman's bipolar disorder and be the first person she turns to for family planning.

Ideally, women with bipolar disorder will plan their pregnancy. In cases of unplanned pregnancy, the woman will require an urgent clinical and medication review. Medication should not be abruptly ceased as this poses a risk of relapse. If the woman is on valproate, it should be tapered down over a week, and another medication substituted, along with taking folate. Referral to, or discussion with, a perinatal psychiatrist is ideal.

Pregnancy planning

Pregnancy planning allows parents to make an informed decision about having a baby. For women with bipolar disorder, the perinatal psychiatrist should be actively involved in this process in liaison with the GP.

First, the bipolar disorder diagnosis needs to be confirmed as women who are misdiagnosed have different risks to manage.[2] Second, there needs to be an assessment of the severity of the patient's bipolar disorder (eg frequency and number of episodes); treatment compliance; basic social factors that could affect the patient's ability to care for her baby (eg housing, finances, lifestyle); social network; and

capacity to care for her baby. Third, the management options over the perinatal period, particularly the use and risks of medications, need to be discussed.

Mood stabilisers during pregnancy

Mood stabilisers can be teratogenic; these risks are reviewed in depth elsewhere.[3] Of particular concern is sodium valproate; 10–11% of infants exposed in utero will have major congenital malformations[4] and be at risk of significant intellectual impairment.[5] For this reason, valproate should not be used as a first-line mood stabiliser in women of childbearing age.[6] Carbamazepine is also linked to fetal abnormalities, but not with intellectual impairment, and should not be used during pregnancy.[4] Lamotrigine poses a lower risk during pregnancy and can be prescribed to breastfeeding mothers, with 2.7% of babies having congenital abnormalities; however, it has limited efficacy in preventing mania.

Lithium is the most effective mood stabiliser,[6] with demonstrated efficacy in the prophylaxis of postpartum relapse,[7] and should be considered for women with severe bipolar disorder. The absolute risk for Ebstein's anomaly is low,[8] despite having an increased relative risk (Table 1). There is an increased risk of other cardiac anomalies; however, the rates (odds ratio [OR]: 4.75) are lower than was previously thought.[9] If lithium is used during pregnancy, fetal echocardiography and level 2 ultrasonography are recommended.[10]

Regularly monitoring the serum lithium levels during pregnancy is essential as the levels can change with changing maternal fluid volume. It is essential to maintain a therapeutic level of 0.6–0.8 mmol/L.[11] Reducing the dose of lithium at around 38 weeks gestation will reduce the risk of the infant having high serum lithium levels; however, a full therapeutic dose must be restored immediately following delivery. Electrolyte and urea levels should also be monitored, and thyroid function tests should be regularly performed as lithium can induce hypothyroidism.

Second-generation antipsychotics, such as quetiapine or olanzapine, are used as alternatives in the treatment of bipolar disorder. They are generally considered safe for use in pregnancy; however, they may increase the risk for gestational diabetes and large babies.[12]

Clarification of the use of psychotropic medication can be discussed with a perinatal psychiatrist. Up-to-date web resources also provide good information:

- Pregnancy and breastfeeding medicines guide, https://thewomenspbmg.org.au
- Mothersafe, www.mothersafe.org.au
- Breastfeeding – Lactmed, https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm

Management strategies

The goals of management are to maintain maternal wellbeing, ensure fetal safety and prepare for the postpartum period. Good antenatal care is crucial, ideally in a specialist clinic. There needs to be regular communication between the GP, obstetric team and treating psychiatrist. Medication will need to be carefully managed at delivery.[11] This should be coupled with ensuring that the patient maintains a healthy lifestyle (eg healthy diet, smoking cessation, avoiding illicit drugs).

Pharmacological

Three pharmacological strategies can be considered, depending on the severity of the patient's bipolar disorder and her psychosocial circumstances. The first strategy is a medication-free pregnancy and postpartum period, if asymptomatic. This option should be reserved for patients who have had few episodes of the disorder, long periods of mood stability (at least one year), low risk of self-harm, good support network, and are able to identify early warning signs, along with a strategy to seek early help. Women will need to be slowly (over two to six weeks) discontinued from their mood stabiliser, at a time of minimal stress and time of year when relapse is unlikely, prior to conception.

The second strategy is partial prophylaxis. The aim is to have a medication-free first trimester after discontinuation of mood stabilisers prior to conception. A mood stabiliser, generally lithium, is reintroduced after organogenesis is completed and an ultrasound is unable to detect any cardiac defect. Some women may prefer to be medication-free throughout their pregnancy, in which case, lithium prophylaxis can be initiated immediately following delivery, starting at the pre-pregnancy effective dose.[7]

The third strategy is full prophylaxis with a mood stabiliser maintained throughout pregnancy.[10] The patient needs to be aware of the risks to the developing fetus, consent to taking a mood stabiliser, have an ultrasound and a clear plan as to what will happen if there is a significant fetal abnormality, and not breastfeed if she is taking lithium (with careful monitoring).[11] A second-generation antipsychotic or sodium valproate (provided she has adequate contraception) could be used as an alternative while she breastfeeds, but lithium should be reinstated following weaning.

Regular reviewing and monitoring of the patient's clinical state, medication dose and serum levels for lithium (aiming for the lowest effective dose), and side-effects during the course of the pregnancy are essential. Any symptoms suggesting a relapse of bipolar disorder require prompt assessment and treatment. The treatment will depend on the symptom severity and context. Emergent hypomanic symptoms, such as irritability, increased energy and sleep disturbance can be managed with short-term use of a sedating second-generation antipsychotic to restore a stable sleep–wake cycle. Psychosocial treatments (eg cognitive behavioural therapy [CBT]) are indicated for mild-to-moderate symptoms, and pharmacotherapy for moderate-to-severe symptoms.

Psychosocial

In addition to monitoring symptoms, review sessions should focus on planning for the postpartum period, making use of psychosocial strategies.[13]

A major risk factor for relapse is sleep deprivation.[14,15] A regular bedtime, wake-up time and evening mealtime during the pregnancy (key features of social rhythm therapy) may help to prevent relapse. Planning how to maintain regular sleep postpartum is also crucial. Strategies include expressing milk (if breastfeeding) during the day, to allow others (eg partner, mother) to feed the infant overnight. CBT is helpful in reducing emergent anxiety and depressive symptoms, and behavioural strategies are very helpful in dealing with the demands of caring for an infant.

Anticipatory problem-solving for difficulties that could arise postpartum is crucial. This involves posing a series of 'What if …?' scenarios and going through a problem-solving process so that the patient has a suite of coping strategies in place.

Table 1. Comments on the perinatal use of commonly used medications for bipolar disorder[3,6,11,12]

Medication	Comments in pregnancy	Comments in breastfeeding	Safety*
Lithium	• Cautious use in pregnancy • Risk of heart defect – need for fetal echocardiography • Regular monitoring and dose adjustment during pregnancy to maintain therapeutic level	Contraindicated for breastfeeding	–
Anticonvulsant mood stabilisers			
Sodium valproate	Contraindicated in pregnancy	Considered safe for breastfeeding (contraception essential)	+
Carbamazepine	Not recommended – increased risk of fetal abnormalities and nuchal tube defects (folate recommended)	High levels in breast milk – limited data on safety	+/–
Lomotrigine	Not contraindicated in pregnancy		+
Second generation antipsychotics (SGAs)			
Clozapine	May increase risk of gestational diabetes	Monitor infant for agranulocytosis	+/–
Olanzapine	May increase risk of gestational diabetes	Maternal over sedation may impact on nocturnal feeds	+
Quetiapine	May increase risk of gestational diabetes	Maternal over sedation may impact on nocturnal feeds	+
Risperidone	Hyperprolactinaemia – may lead to difficulties conceiving		+
Ziprasidone			0
Aripriprazole			0
First-generation antipsychotics			
Haloperidol	No major abnormalities noted – possible risk of infant having extrapyramidal side effects		+
Antidepressants			
Selective serotonin reuptake inhibitors (SSRIs)	• A small increased risk for heart defect (low absolute risk), generally considered safe to use in pregnancy • Avoid paroxetine and fluoxetine • Risk of poor neonatal adaptation syndrome (advise neonatologists)	Fluoxetine can lead to infant becoming jittery	+
Serotonin and noradrenaline reuptake inhibitors (SNRIs)	Risk of poor neonatal adaptation syndrome (advise neonatologists)	Fluoxetine can lead to infant becoming jittery.	+/–
Tricyclic antidepressants (TCAs)	Risk of poor neonatal adaptation syndrome (advise neonatologists)	Postural hypotension can be a problem especially getting up for nocturnal feeds	+

**Breastfeeding safety:*
- *+ considered safe*
- *– Contraindicated*
- *0 insufficient information*

Relapse

Patients should be encouraged to identify early warning signs of relapse and work on strategies for what to do if they emerge,[16] especially when and how to seek urgent help. There is no use identifying early warning signs if the patient is unable to access care. These should be written down and discussed with her partner and the treating team.

The risk of relapse is highest during the first month postpartum, when vigilance regarding early warning signs is essential and a plan to get immediate access to care formulated. If available, the patient can be referred to perinatal outreach services.

If an acute relapse does occur, then hospital treatment (involuntary admission if there are safety concerns), ideally in a mother and baby unit, is essential for the safety of the woman and her infant. If a mother and baby unit is unavailable, alternative care should be organised; for the infant, this should preferably be with a family member. Management of the relapse is dependent on the pole of illness.[17]

Managing a relapse of the bipolar disorder also involves the mother's bond with her baby. When safe and possible, the patient should be able to be with her infant to allow for the healthy development of the relationship. If there are prolonged separations from her infant, the GP can review the quality of the mother–infant relationship when reunited, and support the development of a secure attachment relationship.

The patient's partner needs to be included in the management plan. He may be distressed and stressed by what is happening to the patient, especially if they have to take on primary care for the infant. Additionally, the partner will require education about the patient's illness and support from the GP, as well as a review of their own mental wellbeing. The partner can also be a valuable ally in the patient's management.

In summary, women with bipolar disorder have a high risk of relapse following childbirth. They need to be aware of this risk as an essential part of psychoeducation at the time of diagnosis, along with contraceptive advice and avoiding teratogenic medications.

Management over the perinatal period requires a careful risk–benefit analysis of treatment options, regular review and monitoring of symptoms and medication doses, training in psychosocial risk-reduction strategies, and planning for the postpartum period. A team approach (eg GP, obstetric and psychiatry teams) is encouraged, with an emphasis on rapid access to treatment should a relapse occur.

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