Bipolar disorder in postpartum women: Treatment

AUTHOR: Victoria Hendrick, MD
SECTION EDITOR: Paul Keck, MD
DEPUTY EDITOR: David Solomon, MD

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Oct 2023.**
This topic last updated: **Aug 23, 2023.**

INTRODUCTION

A large, nationally representative survey of the United States general population estimated that among postpartum women, the 12-month prevalence of bipolar disorder was 3 percent [1]. Many postpartum bipolar patients require treatment to prevent or remedy acute mood episodes [2,3].

This topic reviews maintenance prophylaxis and acute treatment for postpartum bipolar mood episodes. The epidemiology, pathogenesis, clinical manifestation, assessment, and diagnosis of postpartum bipolar disorder is discussed separately, as is the general treatment of bipolar disorder, treatment of postpartum unipolar major depression, and an overview of postpartum care:

- (See "Bipolar disorder in postpartum women: Epidemiology, clinical features, assessment, and diagnosis".)
- (See "Bipolar mania and hypomania in adults: Choosing pharmacotherapy".)
- (See "Bipolar major depression in adults: Choosing treatment".)
- (See "Bipolar disorder in adults: Choosing maintenance treatment".)
- (See "Mild to moderate postpartum unipolar major depression: Treatment".)
- (See "Severe postpartum unipolar major depression: Choosing treatment".)
- (See "Overview of the postpartum period: Disorders and complications", section on 'Mental health issues'.)

TERMINOLOGY

Bipolar disorder is characterized by episodes of mania (table 1), hypomania (table 2), and major depression (table 3) [4]. The subtypes of bipolar disorder include bipolar I and bipolar II. Patients with bipolar I disorder experience manic episodes, and nearly always experience major depressive and hypomanic episodes. Bipolar II disorder is marked by at least one hypomanic episode, at least one major depressive episode, and the absence of manic episodes. Additional information about the clinical features and diagnosis of bipolar disorder is discussed separately. (See "Bipolar disorder in adults: Clinical features" and "Bipolar disorder in adults: Assessment and diagnosis", section on 'Diagnosis'.)

Onset of postpartum bipolar mood episodes occurs within a limited time period following birth of a live child. However, there is no established cutoff that separates postpartum-onset mood episodes from subsequent nonpostpartum episodes [5]; definitions of the puerperium range from the first 1 to 12 months following a live birth [4,6,7]. (See "Bipolar disorder in postpartum women: Epidemiology, clinical features, assessment, and diagnosis", section on 'Definition of the postpartum period'.)

MANAGEMENT

General principles — Postpartum bipolar mood episodes are usually treated by perinatal or general psychiatrists in collaboration with obstetricians, primary care clinicians, and neonatologists or pediatricians [2,8-12].

For postpartum bipolar patients, treatment is based upon randomized trials for the general treatment of bipolar patients, as well as observational studies and clinical experience with postpartum patients [13]. Factors involved in choosing a drug regimen include past response to medications, whether the patient is breastfeeding, side effect profiles, patient preference, comorbid general medical conditions, potential for drug-drug interactions, and cost.

We try to avoid medications associated with weight gain and sedation (eg, olanzapine) in postpartum bipolar patients. New mothers typically want to lose weight that was gained during pregnancy, and need to remain alert for their infants' cries.

Family meetings can accomplish several tasks, such as educating family members about the illness, providing support and allaying their concerns, obtaining additional history about prior treatment, and recruiting them to support patient adherence with treatment [14].

Setting — The setting for treatment of postpartum bipolar patients depends upon the type and severity of symptoms, level of psychosocial functioning, and available support. Inpatient hospitalization may be required for safety and stabilization, particularly for severely ill patients with one or more of the following features [15-17]:

- Suicidal or homicidal ideation or behavior
- Aggressive behavior
- Psychotic features (delusions or hallucinations)
- Substance dependence that is exacerbating the mood episode
- Impaired functioning (inability to care for oneself)
- Poor judgement that places the patient or others at imminent risk of being harmed (eg, neglecting the infant)

In addition, the threshold for admission is lower in patients with poor social support or previous severe mood episodes [14]. It may be feasible to treat moderately ill postpartum bipolar patients in a partial hospital (day) program, including patients with suicidality that does not pose an imminent risk (eg, fleeting thoughts of killing oneself with vague or nonexistent plans and no intent). An outpatient clinic may be suitable for less acutely ill patients (eg, thoughts that family members would be better off if the patient was dead, with no plan or intent to commit suicide).

Monitoring the patient — We typically monitor postpartum bipolar patients most closely (eg, weekly) during the first several weeks (eg, four) following parturition, when the large majority of mood episodes occur [18-20].

For postpartum bipolar patients who suffer a mood episode, the frequency of visits depends upon the patient's clinical status. Hospitalized patients are assessed daily, and patients with active suicidal ideation, a specific plan, and intent to kill themselves may require constant observation. Outpatients are commonly seen on a weekly basis until they have responded (ie, the patient's safety has stabilized and the number, intensity, and frequency of psychotic and mood symptoms has improved substantially). Following response, patients can be seen every two to four weeks until they remit.

For postpartum bipolar patients who remit and remain stable, monitoring can be tapered, with progressively longer intervals between assessments. As an example, a patient who is seen every two weeks at the time of remission can be seen every two weeks for one to three more visits, then every month for one to three visits, and then every two months for one to three visits. Continuously stable patients can be seen every three to six months. More frequent visits should

be scheduled for patients who develop symptoms or side effects (eg, sedation that interferes with infant care).

Parenting — Bipolar symptoms (eg, impulsivity) can render patients incapable of safely parenting [14]. If clinicians are uncertain about the safety of children, child welfare agencies should be notified to determine the:

- Level of social support (eg, availability of relatives and visiting nurses to care for the patient and infant)
- Risks of a newborn remaining with the bipolar parent
- Risks of removing the child from the home

Feeding the infant — For postpartum bipolar patients who are treated with pharmacotherapy and have sufficient resources, we often suggest formula feeding the baby to avoid exposure to medications through breast milk [11,21]. All psychotropic drugs appear to be excreted in breast milk at varying concentrations [22]. Although breastfeeding has many potential benefits for both the mother and child, the mother's clinical status and need for pharmacotherapy should take priority over the method of feeding the infant [23].

However, breast milk is a reasonable alternative to formula for postpartum bipolar patients treated with pharmacotherapy. There are several benefits to breastfeeding, and many patients would rather forego medications than breastfeeding. We attempt to use drugs compatible with breastfeeding and doses at the low end of the therapeutic range, especially for infants less than three months of age, because their capacity to metabolize and clear medications is less than that of older infants [24]. Exposure to psychotropic agents through breastfeeding should also be minimized in premature infants, because their decreased ability to metabolize and/or eliminate medications increases steady state plasma concentrations [25,26].

Postpartum bipolar patients should attempt to recruit family and friends to help with the newborn's nighttime feedings, to prevent sleep deprivation and the associated risk of recurrent mood episodes [11,13,23,27,28]. Newborns fed with formula during the day are fed formula at night. Infants who are breastfed during the day can be fed at night with breast milk expressed while awake earlier in the day, or with supplemental formula.

The use of psychotropic medications in breastfeeding patients is discussed separately. (See "Safety of infant exposure to antidepressants and benzodiazepines through breastfeeding" and "Management of epilepsy during preconception, pregnancy, and the postpartum period", section on 'Breastfeeding'.)

EUTHYMIC PATIENTS

We typically prescribe maintenance treatment for euthymic, postpartum bipolar patients to delay or prevent recurrent mood episodes. Among postpartum patients, relapse occurs after approximately 37 percent of deliveries [29].

Evidence for the efficacy of treatment is based upon:

- Randomized trials that did not focus upon postpartum patients [30,31]. (See "Bipolar disorder in adults: Choosing maintenance treatment", section on 'Pregnancy'.)
- Observational studies that suggest recurrent mood episodes are less frequent among postpartum bipolar patients who are treated with maintenance medications, compared with untreated patients. As an example, a meta-analysis of eight prospective and retrospective observational studies found that postpartum mood episodes occurred in fewer patients who received maintenance pharmacotherapy (n = 98), compared with patients who remained medication free (n = 107; 29 versus 65 percent) [29].

Prophylactic treatment of postpartum bipolar patients is consistent with treatment guidelines from the United Kingdom National Institute for Health and Clinical Excellence [32,33] and is standard practice for many perinatal psychiatrists [3,22,34-37].

Choosing a medication — Selecting a medication for euthymic, postpartum bipolar depends upon several factors, including treatment history and the decision to breastfeed.

Patients not breastfeeding — For euthymic bipolar patients who are receiving intrapartum maintenance pharmacotherapy and are not breastfeeding, we continue the same medications after delivery. However, doses should generally be decreased. Prenatal physiologic changes (eg, increased renal elimination, volume of distribution, and cardiac output) reverse after parturition, which typically causes serum drug concentrations to increase [38]. Lamotrigine levels are especially likely to increase after delivery. A prospective observational study of bipolar patients (n = 6) who were treated with lamotrigine during pregnancy found that within five weeks of delivery, serum concentrations increased approximately 150 percent, compared with the third trimester [39]. Lithium levels, which tend to decrease during pregnancy, are also likely to increase postpartum [40].

For euthymic bipolar patients who discontinued maintenance pharmacotherapy prior to conception or during pregnancy, are medication-free at the time of delivery, and are not

breastfeeding, we typically resume the previous regimen after childbirth when patients are medically stable.

For euthymic postpartum bipolar patients who were not receiving preconception or prenatal maintenance pharmacotherapy and are not breastfeeding, we suggest maintenance treatment with lithium, a first-line drug for the general maintenance treatment of bipolar disorder based upon meta-analyses of randomized trials that did not focus upon postpartum patients. In addition, observational studies support the use of lithium for postpartum bipolar patients [37,41,42]:

- A four-week prospective study of patients who were stable throughout pregnancy found that relapse occurred in 2 of the 26 (8 percent) patients who received prophylactic postpartum medications (lithium monotherapy for the large majority), and one of the five (20 percent) patients who did not [3].
- A 12-week retrospective study of 27 patients found that relapse occurred in fewer patients who received maintenance lithium (1 of 14 [7 percent]), compared with patients who did not (8 of 13 [62 percent]) [43].
- A retrospective study of 17 patients found that relapse occurred in fewer patients who received maintenance lithium for a minimum of three months (two of nine [22 percent]) compared with patients who did not (six of eight [75 percent]) [44].

The efficacy of lithium for the general maintenance treatment of bipolar disorder is discussed separately, as are the pharmacology, administration, and side effects of lithium, and use of lithium at the time of delivery. (See "Bipolar disorder in adults and lithium: Pharmacology, administration, and management of adverse effects" and "Bipolar disorder in women: Preconception and prenatal maintenance pharmacotherapy", section on 'Refractory patients' and "Bipolar disorder in adults: Choosing maintenance treatment", section on 'Lithium'.)

A reasonable alternative to lithium is lamotrigine, another first-line drug for the general maintenance treatment of bipolar disorder based upon a meta-analysis of randomized trials that did not focus upon postpartum patients. The efficacy of lamotrigine is discussed separately, as are the dose schedule, pharmacology, and side effects (table 4 and table 5). (See "Bipolar disorder in adults: Choosing maintenance treatment", section on 'Lamotrigine' and "Antiseizure medications: Mechanism of action, pharmacology, and adverse effects", section on 'Lamotrigine'.)

For euthymic bipolar patients who were not receiving preconception or prenatal maintenance pharmacotherapy, are not lactating, and are unresponsive to or intolerant of lithium and

lamotrigine, we suggest in order of preference risperidone, aripiprazole, divalproex, quetiapine, olanzapine, or carbamazepine, based upon efficacy and side effect profiles in randomized trials that did not focus upon postpartum patients [2]. Risperidone has the most evidence supporting its use and carbamazepine the least, there is more evidence for aripiprazole than divalproex and quetiapine, and quetiapine is sedating. Although multiple trials have consistently found that olanzapine is efficacious, it is often avoided due to metabolic effects and excess sedation. The efficacy of risperidone, aripiprazole, divalproex, quetiapine, olanzapine, and carbamazepine in randomized trials that did not focus upon postpartum patients is discussed separately, as are the pharmacology, administration, and side effects of these drugs. (See "Bipolar disorder in adults: Choosing maintenance treatment" and "Second-generation antipsychotic medications: Pharmacology, administration, and side effects" and "Antiseizure medications: Mechanism of action, pharmacology, and adverse effects".)

Small, prospective observational studies of maintenance treatment of postpartum bipolar patients with olanzapine and valproate have found the following results:

- A four-week study found that recurrent mood episodes occurred in 2 of the 11 (18 percent) patients who received olanzapine (mean dose 6 mg each night) and 8 of the 14 (57 percent) patients who received other medications or none at all [45].

- A 20-week study found that recurrent mood episodes occurred in 10 of the 15 (67 percent) patients who received divalproex (target serum concentration 50 to 100 mcg/mL) plus clinical monitoring (psychoeducation and weekly assessments) and 8 of the 11 (73 percent) patients who received clinical monitoring alone [46].

Breastfeeding patients — For maintenance treatment of postpartum bipolar patients who breastfeed, choosing a specific drug depends primarily upon treatment history and whether a drug is compatible with lactation:

- For patients who discontinued maintenance pharmacotherapy prior to conception or during pregnancy, and are medication-free at the time of delivery, we typically resume the prior regimen after childbirth when patients are medically stable, provided the medications are compatible with lactation.

- For patients who are receiving intrapartum maintenance pharmacotherapy, we usually continue the same regimen after delivery, provided the medications are compatible with breastfeeding. However, doses should generally be decreased because serum drug concentrations increase after delivery [38].

- For patients whose preconception or prenatal maintenance pharmacotherapy is often avoided during breastfeeding, and for patients who never received maintenance treatment, we suggest using medications that are regarded as compatible with breastfeeding. Thus, we prefer valproate or carbamazepine, based upon efficacy in randomized trials that did not focus upon postpartum patients and compatibility with lactation in several studies [9,47]. Although there are more data supporting the efficacy of lithium and lamotrigine than valproate or carbamazepine, lithium is often avoided for breastfeeding patients, and there are concerns about using lamotrigine during lactation.

  For patients who want to switch treatment from a drug that may be problematic during lactation, we typically taper and discontinue the drug over one week, and at the same time start and titrate up a compatible medication. The discontinued drug is usually tapered by the same amount for each dose decrease. As an example, lithium 1200 mg per day is decreased by 300 mg per day, every one to two days. Patients should pump breast milk and dispose of it until they have completed the switch.

  For breastfeeding patients who are resistant to or intolerant of valproate or carbamazepine, a reasonable alternative in order of preference is risperidone, aripiprazole, quetiapine, or olanzapine, based upon efficacy in randomized trials that did not focus upon postpartum patients and compatibility with lactation [48]. (However, there is less experience using second-generation antipsychotics in lactating patients, compared with valproate and carbamazepine.) Risperidone has the most evidence supporting its use, there is more evidence for aripiprazole than quetiapine, and quetiapine is sedating. Although multiple trials have consistently found that olanzapine is efficacious, it is often avoided due to metabolic effects and excess sedation.

The safety of valproate, carbamazepine, lithium, lamotrigine, risperidone, aripiprazole, quetiapine, and olanzapine with breastfeeding is discussed separately, as is the maintenance efficacy, pharmacology, administration, and side effect profile of these drugs. (See "Breastfeeding infants: Safety of exposure to antipsychotics, lithium, stimulants, and medications for substance use disorders" and "Antiseizure medications: Mechanism of action, pharmacology, and adverse effects" and "Second-generation antipsychotic medications: Pharmacology, administration, and side effects" and "Bipolar disorder in adults: Choosing maintenance treatment", section on 'Pregnancy'.)

Adjunctive psychotherapy — For postpartum bipolar patients, we suggest adjunctive psychoeducation or cognitive-behavioral therapy (CBT), based upon randomized trials that did not focus upon postpartum patients. Although no head-to-head trials have compared these psychotherapies, we generally choose psychoeducation because there are more data

supporting its use, it is easier to administer than CBT and thus usually more available, and psychoeducation is generally an element of CBT. The evidence of efficacy for reducing recurrent mood episodes with other psychotherapies, such as family therapy and interpersonal and social rhythm therapy, is not as compelling. (See "Bipolar disorder in adults: Choosing maintenance treatment", section on 'Choosing adjunctive psychotherapy'.)

PSYCHOTIC MANIA

Postpartum patients with psychotic mania typically require hospitalization for management by psychiatrists and other mental health clinicians. Patients can breastfeed their babies provided that nursing staff are present; however, many patients are too disorganized and impulsive to breastfeed. The safety of using psychotropic drugs during breastfeeding is discussed separately. (See "Safety of infant exposure to antidepressants and benzodiazepines through breastfeeding", section on 'Benzodiazepines' and "Breastfeeding infants: Safety of exposure to antipsychotics, lithium, stimulants, and medications for substance use disorders".)

For patients with postpartum mania with psychotic features, we suggest the following treatment algorithm. Patients initially receive step 1 and progress through each step until they respond. The algorithm is largely based upon a standardized treatment protocol evaluated in an observational study [49]:

- **Step 1** – Benzodiazepine monotherapy (eg, clonazepam or lorazepam) at bedtime for up to three nights, to ascertain whether sleep restoration and treatment of anxiety or mild agitation improves the syndrome. However, for patients with moderate to severe agitation, or patients with assaultive or grossly disorganized behavior, treatment commences at step 2. In addition, step 1 is skipped for patients who were treated with an antipsychotic immediately prior to admission. Patients unresponsive to benzodiazepine monotherapy are treated with step 2 therapy.

  For patients who remit with benzodiazepine monotherapy, a different drug (eg, lithium) for maintenance treatment is started and titrated up. After the dose of the second drug is in the therapeutic range, the benzodiazepine is tapered and discontinued. Choosing a drug for maintenance treatment is discussed elsewhere in this topic. (See 'Choosing a medication' above.)

- **Step 2** – Benzodiazepine plus an antipsychotic for two to three weeks. However, antipsychotic monotherapy is a reasonable alternative to combination treatment, especially for patients who do not tolerate benzodiazepines, are breastfeeding and

concerned about the risks to their infants, and patients with substance use disorders. Either first-generation antipsychotics (eg, haloperidol) or second-generation antipsychotics (eg, olanzapine, quetiapine, or risperidone) can be used.

Patients who do not respond to the benzodiazepine plus antipsychotic within two to three weeks or do not tolerate the antipsychotic are switched to a different antipsychotic. If the failed antipsychotic was a first generation drug, the new antipsychotic is generally a second generation drug; if the failed drug was a second generation drug, the new drug may be either a first or second generation antipsychotic. The antipsychotics are switched by tapering and discontinuing the failed drug at the same time that the new drug is titrated up.

For patients who remit with a benzodiazepine plus an antipsychotic, the benzodiazepine is tapered and discontinued, and the antipsychotic is maintained. If patients do not respond to step 2, treatment advances to step 3.

- **Step 3** – Combination treatment with a benzodiazepine, antipsychotic, and lithium. However, a reasonable alternative is use valproate rather than lithium, or to administer an antipsychotic plus lithium or valproate without a benzodiazepine. Valproate may be preferred by breastfeeding patients.

  For patients who do not respond to a benzodiazepine, antipsychotic, and lithium after approximately two to three weeks, the antipsychotic is switched to a different one. However, a reasonable alternative is to switch lithium to valproate (if valproate was used initially, it is switched to lithium). Drugs are switched by tapering and discontinuing the failed drug at the same time that a new drug is titrated up. After two to three weeks, unresponsive patients receive a third round of step 3 treatment, either by switching lithium to valproate or switching antipsychotics. If patients do not respond to step 3 within 6 to 10 weeks, treatment advances to step 4.

  For patients who remit with a benzodiazepine, antipsychotic, and lithium or valproate, the benzodiazepine is tapered and discontinued. Thereafter the antipsychotic or lithium (or valproate) is tapered and discontinued, depending upon the patient's prior treatment history and medication side effects.

- **Step 4** – Electroconvulsive therapy (ECT). Benzodiazepines are usually tapered and discontinued prior to administration of ECT, and other drugs are often discontinued as well. (See "Overview of electroconvulsive therapy (ECT) for adults", section on 'Concurrent medications' and "Bipolar disorder in adults: Indications for and efficacy of electroconvulsive therapy".)

Evidence supporting the use of this algorithm includes randomized trials that included patients with mania or hypomania, and did not focus upon postpartum psychotic mania; the trials found that benzodiazepines, antipsychotics, and lithium are efficacious. The efficacy, administration, and side effects of these drugs are discussed separately. (See "Bipolar mania and hypomania in adults: Choosing pharmacotherapy".)

In addition, this algorithm was adapted (with small modifications) from a standardized treatment protocol that was evaluated in a nine month observational study [49]. The study included patients with postpartum psychosis (n = 64) who were initially admitted to a specialty mother-baby inpatient unit; psychotic mania was present in 42 patients (66 percent). Treatment consisted of a four-step standardized protocol in which patients initially received step 1; unresponsive patients progressed through each step until they responded. Step 1 involved lorazepam for three nights; step 2 involved lorazepam plus an antipsychotic for an additional two weeks; in step 3, lithium was added to lorazepam and the antipsychotic for an additional 10 weeks; in step 4, pharmacotherapy was discontinued and ECT was to be administered. Among the patients with postpartum psychosis (n = 64), the cumulative rate of remission at each step was 6, 25, and 98 percent of patients; none of the patients received step 4 (ECT).

MANIA (NONPSYCHOTIC) AND HYPOMANIA

Despite clinical differences between nonpsychotic manic episodes and hypomanic episodes (hypomania is less severe than mania), for the purpose of treatment they are considered to be similar and thus treated with the same medications [15,16,50].

Patients not breastfeeding — The treatment of mania or hypomania in postpartum patients who are not breastfeeding is similar to the treatment in nonpostpartum patients, which is discussed separately. (See "Bipolar mania and hypomania in adults: Choosing pharmacotherapy".)

Breastfeeding patients — For patients with mania (without psychotic features) or hypomania who are breastfeeding, we suggest a first-generation antipsychotic; we prefer haloperidol based upon randomized trials that did not focus upon postpartum patients [51]. The efficacy of haloperidol is comparable to risperidone and olanzapine, and superior to carbamazepine and valproate. First- and second-generation antipsychotics are generally not contraindicated in lactating patients, but there is more experience with first-generation antipsychotics [9,52,53]. Other first-generation antipsychotics that are reasonable alternatives to haloperidol include chlorpromazine, fluphenazine, perphenazine, thiothixene, and trifluoperazine. The efficacy, administration, pharmacology, and side effects (table 6) of first-generation antipsychotics are

discussed separately, as is their use during lactation. (See "Bipolar mania and hypomania in adults: Choosing pharmacotherapy" and "First-generation antipsychotic medications: Pharmacology, administration, and comparative side effects" and "Safety of infant exposure to antidepressants and benzodiazepines through breastfeeding".)

In our clinical experience, postpartum patients with mania or hypomania often do not respond to or tolerate haloperidol. (Response is defined as stabilizing the patient's safety and substantial improvement in the number, intensity, and frequency of symptoms.) For these resistant patients, we suggest in order of preference risperidone or olanzapine, based upon their efficacy and acceptability in randomized trials that did not focus upon postpartum patients [51]. The efficacy of risperidone and olanzapine is superior to carbamazepine and valproate. In addition, risperidone and olanzapine are generally not contraindicated during lactation [9,47,53]. To switch drugs, haloperidol is tapered and discontinued over one week while at the same time risperidone is started and titrated up. We generally taper haloperidol by the same amount for each dose decrease. As an example, haloperidol 8 mg per day is decreased by 2 mg per day, every day. The efficacy, administration, pharmacology, and side effects of risperidone and olanzapine (table 6) are discussed separately, as is their use in breastfeeding patients. (See "Bipolar mania and hypomania in adults: Choosing pharmacotherapy" and "Second-generation antipsychotic medications: Pharmacology, administration, and side effects" and "Safety of infant exposure to antidepressants and benzodiazepines through breastfeeding".)

Based upon clinical experience, manic and hypomanic episodes in breastfeeding patients often respond to sequential trials of haloperidol, risperidone, and olanzapine. However, for refractory patients who do not respond, we suggest in order of preference carbamazepine or valproate, based upon their efficacy and acceptability in randomized trials that did not focus upon postpartum patients [51]. The efficacy of carbamazepine for mania episodes may be superior to valproate. Carbamazepine and valproate are generally regarded as compatible with breastfeeding [9,47]. The efficacy, administration, pharmacology, and side effects (table 4 and table 5) of carbamazepine and valproate are discussed separately, as is their use in breastfeeding patients. (See "Bipolar mania and hypomania in adults: Choosing pharmacotherapy" and "Antiseizure medications: Mechanism of action, pharmacology, and adverse effects" and "Breastfeeding infants: Safety of exposure to antipsychotics, lithium, stimulants, and medications for substance use disorders", section on 'Anticonvulsants'.)

For breastfeeding patients with moderate to severe mania that does not respond to sequential trials of haloperidol, risperidone, olanzapine, carbamazepine, and valproate, we suggest electroconvulsive therapy (ECT) [37,54], based upon studies that did not focus upon postpartum

patients. (See "Bipolar disorder in adults: Indications for and efficacy of electroconvulsive therapy", section on 'Mania'.)

Using ECT for patients with postpartum mania who are breastfeeding is consistent with practice guidelines from the American Psychiatric Association [54]. Additional information about treating postpartum bipolar patients with ECT is discussed elsewhere in this topic. (See 'Electroconvulsive therapy' below.)

BIPOLAR MAJOR DEPRESSION

Patients not breastfeeding — The treatment of bipolar major depression in postpartum patients who are not breastfeeding is similar to the treatment in nonpostpartum patients, which is discussed separately. (See "Bipolar major depression in adults: Choosing treatment".)

Breastfeeding patients — For patients with bipolar major depression who are breastfeeding and are not psychotic, we suggest valproate, based upon randomized trials that did not focus upon postpartum patients. Although there are more data supporting the efficacy of quetiapine and olanzapine, valproate is generally regarded as compatible with lactation and there is more experience with valproate during breastfeeding than quetiapine and olanzapine [9,47]. In addition, monotherapy is preferred over medication combinations (eg, fluoxetine plus olanzapine) to minimize infant exposure [47]. For patients with bipolar major depression with psychotic features who are breastfeeding, we suggest the antipsychotics quetiapine or olanzapine, rather than the anticonvulsant valproate. The efficacy, administration, pharmacology, and side effects (table 4 and table 5) of valproate are discussed separately, as is its use in breastfeeding patients. (See "Bipolar major depression in adults: Choosing treatment" and "Antiseizure medications: Mechanism of action, pharmacology, and adverse effects" and "Breastfeeding infants: Safety of exposure to antipsychotics, lithium, stimulants, and medications for substance use disorders", section on 'Anticonvulsants'.)

In our clinical experience, lactating bipolar patients with major depression often do not respond to or tolerate valproate. (Response is defined as stabilizing the patient's safety and substantial improvement in the number, intensity, and frequency of symptoms.) For these resistant patients, we suggest in order of preference quetiapine and olanzapine, based upon their efficacy and side effects in randomized trials that did not focus upon postpartum patients. There is more evidence supporting quetiapine than olanzapine, and olanzapine typically causes more adverse metabolic effects. Both drugs are generally not contraindicated during lactation [9,47,53]. To switch drugs, valproate is tapered and discontinued over one week while at the same time quetiapine is started and titrated up. We generally taper valproate by the same

amount for each dose decrease. As an example, valproate 1500 mg per day is decreased by 250 to 500 mg per day, every one to two days. The efficacy, pharmacology, administration, and side effects (table 6) of quetiapine and olanzapine are discussed separately, as is their use in breastfeeding patients. (See "Second-generation antipsychotic medications: Pharmacology, administration, and side effects" and "Safety of infant exposure to antidepressants and benzodiazepines through breastfeeding" and "Bipolar major depression in adults: Choosing treatment".)

Based upon clinical experience, bipolar major depression in breastfeeding patients often does not respond to sequential trials of valproate, quetiapine, and olanzapine. For refractory patients who do not respond, we suggest adding fluoxetine to olanzapine, based upon efficacy and side effects of the combination in randomized trials that did not focus upon postpartum patients. In addition, these drugs are generally not contraindicated during lactation [9,47,53]. The efficacy, dose, pharmacology, and side effects of fluoxetine and olanzapine are discussed separately, as is their use in breastfeeding patients. (See "Selective serotonin reuptake inhibitors: Pharmacology, administration, and side effects" and "Second-generation antipsychotic medications: Pharmacology, administration, and side effects" and "Safety of infant exposure to antidepressants and benzodiazepines through breastfeeding" and "Bipolar major depression in adults: Choosing treatment".)

Electroconvulsive therapy — For lactating patients with bipolar major depression (with or without psychotic features) that does not respond to sequential trials of valproate, quetiapine, olanzapine, and fluoxetine plus olanzapine, we suggest electroconvulsive therapy (ECT), based upon randomized trials that did not focus upon postpartum patients [37,54]. (See "Bipolar disorder in adults: Indications for and efficacy of electroconvulsive therapy", section on 'Bipolar major depression'.)

Additional evidence includes a retrospective study (with blind ratings) of ECT for depressive and psychotic disorders in postpartum females (n = 58) and in nonpostpartum females (n = 56) [55]. Symptoms improved more in the postpartum patients.

ECT is generally safe and there are no absolute contraindications, even in patients whose general medical status is compromised [54]. However, safety concerns regarding ECT necessitate preprocedure medical consultation. Medical consultation for ECT, the use of ECT for patients with general medical conditions, ECT side effects (eg, cardiopulmonary events), and additional information about ECT are discussed separately. (See "Medical evaluation for electroconvulsive therapy" and "Overview of electroconvulsive therapy (ECT) for adults".)

Electrode placement and other aspects of ECT technique for treating bipolar disorder have not been standardized. Thus, ECT is typically administered with the same technique used for other indications and is generally given three times per week on alternating days. Most patients regardless of indication remit with 6 to 12 treatments, but some patients may require 20 or more. The technique for performing ECT is discussed separately. (See "Technique for performing electroconvulsive therapy (ECT) in adults".)

Breastfeeding typically is not interrupted during a course of ECT because of the minimal amounts of anesthetic drugs (eg, methohexital and succinylcholine) that enter breast milk and are subsequently absorbed from the infant's gastrointestinal tract [54]. However, other drugs that may be used during ECT, such as antihypertensives, antireflux drugs (eg, histamine-2 receptor antagonists), and analgesics may be excreted into breast milk. Exposure to medications can be decreased by delaying lactation for several hours after an ECT treatment, or alternatively, collecting and storing breast milk prior to ECT for bottle feeding.

Using ECT for patients with postpartum bipolar major depression who are breastfeeding is consistent with practice guidelines from the American Psychiatric Association [54].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Bipolar disorder".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Bipolar disorder (The Basics)" and "Patient education: Coping with high drug prices (The Basics)")

- Beyond the Basics topics (see "Patient education: Bipolar disorder (Beyond the Basics)" and "Patient education: Coping with high prescription drug prices in the United States (Beyond the Basics)")

These educational materials can be used as part of psychoeducational psychotherapy. (See "Bipolar disorder in adults: Choosing maintenance treatment", section on 'Pregnancy'.)

The National Institute of Mental Health also has educational material explaining the symptoms, course of illness, and treatment of bipolar disorder in a booklet entitled "Bipolar Disorder," which is available online at the website or through a toll-free number, 866-615-6464. The website also provides references, summaries of study results in language intended for the lay public, and information about clinical trials currently recruiting patients.

More comprehensive information is provided in many books written for patients and family members, including The Bipolar Disorder Survival Guide: What You and Your Family Need to Know, written by David J. Miklowitz, PhD (published by The Guilford Press, 2002); An Unquiet Mind: A Memoir of Moods and Madness, written by Kay Jamison, PhD (published by Random House, 1995); and Treatment of Bipolar Illness: A Casebook for Clinicians and Patients, by RM Post, MD, and GS Leverich, LCSW (published by Norton Press, 2008).

The Depression and Bipolar Support Alliance (available at their website or 800-826-3632) is a national organization that educates members about bipolar disorder and how to cope with it. Other functions include increasing public awareness of the illness and advocating for more research and services. The organization is administered and maintained by patients and family members, and has local chapters.

The National Alliance on Mental Illness (available at their website or 800-950-6264) is a similarly structured organization devoted to education, support, and advocacy for patients with any mental illness. Bipolar disorder is one of their priorities.

SUMMARY AND RECOMMENDATIONS

- **Diagnosing bipolar disorder** – Bipolar disorder is characterized by episodes of mania (table 1), hypomania (table 2), and major depression (table 3). (See 'Terminology' above and "Bipolar disorder in adults: Assessment and diagnosis", section on 'Diagnosis'.)

- **Defining the postpartum period** – Onset of postpartum bipolar mood episodes occurs within a limited time period following birth of a live child; definitions of the puerperium range from the first 1 to 12 months following a live birth. (See "Bipolar disorder in postpartum women: Epidemiology, clinical features, assessment, and diagnosis", section on 'Definition of the postpartum period'.)

- **Feeding the infant** – Postpartum bipolar patients who are treated with pharmacotherapy and have sufficient resources are often encouraged to formula feed their infants to avoid exposure to medications through breast milk. However, breastfeeding is a reasonable alternative; we attempt to use drugs compatible with breastfeeding and doses at the low end of the therapeutic range. (See 'Feeding the infant' above.)

- **Euthymic patients**

  - **Who are not breastfeeding** – For euthymic bipolar patients who are receiving intrapartum maintenance pharmacotherapy and are not breastfeeding, we continue the same medications after delivery to prevent or delay recurrent mood episodes. However, doses should be decreased. For patients who discontinued maintenance pharmacotherapy prior to conception or during pregnancy, are medication-free at the time of delivery, and are not breastfeeding, we typically resume the previous regimen after childbirth when patients are medically stable. (See 'Patients not breastfeeding' above.)

    For euthymic, postpartum bipolar patients who were not receiving preconception or prenatal maintenance pharmacotherapy, and are not breastfeeding, we suggest maintenance treatment with lithium rather than other drugs (**Grade 2B**). However, lamotrigine is a reasonable alternative. Patients unresponsive to or intolerant of lithium and lamotrigine can be treated with risperidone, aripiprazole, divalproex, quetiapine, olanzapine, or carbamazepine. (See 'Patients not breastfeeding' above.)

  - **Who are breastfeeding** – For euthymic, postpartum bipolar patients who discontinued maintenance pharmacotherapy prior to conception or during pregnancy, are medication-free at the time of delivery, and are breastfeeding, we typically resume the prior regimen after childbirth when patients are medically stable, provided the medications are compatible with lactation. For patients who are receiving intrapartum maintenance pharmacotherapy and are breastfeeding, we usually continue the same regimen after delivery, provided the medications are compatible with breastfeeding. (See 'Breastfeeding patients' above.)

For euthymic, postpartum bipolar patients who are breastfeeding, and who never received maintenance treatment or who received preconception or prenatal maintenance pharmacotherapy that is often avoided during breastfeeding, we suggest valproate or carbamazepine, rather than other drugs (**Grade 2B**). Patients unresponsive to or intolerant of valproate and carbamazepine can be treated with risperidone, aripiprazole, quetiapine, or olanzapine. (See 'Breastfeeding patients' above.)

- **Psychotic mania** – For patients with postpartum psychotic mania, we suggest a four-step sequential treatment algorithm, rather than other treatment regimens (**Grade 2C**). Patients initially receive step 1 and progress through each step until they respond. Step 1 involves benzodiazepine monotherapy for up to three nights; step 2 a benzodiazepine plus an antipsychotic for two weeks; step 3 the combination of a benzodiazepine, antipsychotic, and lithium for 10 weeks, and step 4 electroconvulsive therapy (ECT). (See 'Psychotic mania' above.)

- **Nonpsychotic mania, hypomania, or major depression**

  - **Patients who are not breastfeeding** – The treatment of mania, hypomania, and bipolar major depression in postpartum patients who are not breastfeeding is similar to the treatment in nonpostpartum patients. (See "Bipolar mania and hypomania in adults: Choosing pharmacotherapy" and "Bipolar major depression in adults: Choosing treatment".)

  - **Patients who are breastfeeding** – For breastfeeding patients with mania (nonpsychotic) or hypomania, we suggest haloperidol rather than other drugs (**Grade 2B**). Patients unresponsive to or intolerant of haloperidol can be treated with risperidone or olanzapine. (See 'Breastfeeding patients' above.)

    For breastfeeding patients with bipolar major depression, we suggest valproate rather than other drugs (**Grade 2B**). Patients unresponsive to or intolerant of valproate can be treated with quetiapine or olanzapine. (See 'Breastfeeding patients' above.)

Topic 83170 Version 25.0

→