Treatment of postpartum psychosis

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INTRODUCTION

During the postpartum period, females are at increased risk of new or recurrent psychiatric illness including mood, anxiety, and psychotic disorders. Postpartum psychosis (or puerperal psychosis) typically presents with rapid onset of psychotic symptoms including hallucinations and delusions, bizarre behavior, confusion, and disorganization which may mimic delirium. Symptom onset is typically within four weeks of delivery.

The syndrome is most often seen in patients who have been or subsequently are diagnosed with bipolar disorder. Less frequently it occurs in individuals with a diagnosis of major depression with psychosis, schizophrenia, or schizoaffective disorder. Fifty percent or more of females with postpartum psychosis have no prior psychiatric history and in many cases this is the first manifestation of an underlying psychiatric illness [1,2]. A small subset of females experience isolated postpartum psychosis that does not progress to mood or psychotic episodes outside the postpartum time period [3].

This topic and the associated algorithm discuss the treatment of postpartum psychosis in individuals without a prior diagnosis of a mood disorder (eg, bipolar disorder, major depression with psychosis) or a psychotic disorder (algorithm 1). Treatment of psychosis in the postpartum period in individuals with mood disorder or in individuals with schizophrenia are discussed elsewhere. The epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis of postpartum psychosis are reviewed separately.

- (See "Postpartum psychosis: Epidemiology, clinical features, and diagnosis".)

- (See "Psychosis in adults: Epidemiology, clinical manifestations, and diagnostic evaluation".)
- (See "Schizophrenia in adults: Maintenance therapy and side effect management".)
- (See "Mild to moderate postpartum unipolar major depression: Treatment".)
- (See "Severe postpartum unipolar major depression: Choosing treatment".)
- (See "Postpartum unipolar major depression: General principles of treatment".)
- (See "Bipolar disorder in postpartum women: Treatment".)
- (See "Teratogenicity, pregnancy complications, and postnatal risks of antipsychotics, benzodiazepines, lithium, and electroconvulsive therapy".)
- (See "Breastfeeding infants: Safety of exposure to antipsychotics, lithium, stimulants, and medications for substance use disorders".)
- (See "Antenatal exposure to selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs): Neonatal outcomes".)

INITIAL TREATMENT

Our initial treatment priorities in individuals with postpartum psychosis include ensuring the safety of the patient and their children and initiating medication. Postpartum psychosis constitutes a medical emergency requiring rapid identification and intervention (algorithm 1). (See 'Ensure safety' below and 'Initiating medication' below.)

Further discussion of the need for early identification and treatment of postpartum psychosis and assessment of risks to mother and baby are described separately. (See "Postpartum psychosis: Epidemiology, clinical features, and diagnosis", section on 'Clinical features' and "Postpartum psychosis: Epidemiology, clinical features, and diagnosis", section on 'Risk of suicide and infanticide'.)

Ensure safety — Our first priority in all cases of postpartum psychosis is to ensure the safety of the individual and their children. While separation of mother and baby at this critical time is not optimal, we typically hospitalize these individuals. We do not leave the mother alone with their children. An individual experiencing postpartum psychosis will generally not be able to care for themselves or their children without significant support. When the psychosis has lessened to the point that the patient is no longer a risk to themselves or their child, the visitation restrictions are relaxed. In rare cases where the individual's level of disorganization is mild and a reliable support is available to monitor the individual, we agree to outpatient treatment with daily checks; however, this is the exception. (See "Postpartum psychosis: Epidemiology, clinical features, and diagnosis", section on 'Risk of suicide and infanticide'.)

Uncommonly, hospitals may make provisions for supervised daytime visits with the infant. Some countries including the United Kingdom and Australia have inpatient mother-baby psychiatric units, though these units are not widely available internationally.

Initiating medication

Combined treatment for most — Our preferred pharmacologic treatment for individuals with postpartum psychosis who do not have an established psychiatric history is with a combination of an antipsychotic and lithium [4-6]. Our rationale is that individuals with postpartum psychosis have a high likelihood of subsequent diagnosis of bipolar disorder. This differs from our preferred treatment for individuals with psychosis in general (ie, nonpostpartum psychosis) in whom we typically do not begin lithium unless there are clear signs of mood dysregulation (eg, hypomania, mania). Postpartum treatment of individuals with an established psychiatric history is described elsewhere (algorithm 1).

- (See "Bipolar disorder in postpartum women: Treatment", section on 'Psychotic mania'.)
- (See "Severe postpartum unipolar major depression: Choosing treatment", section on 'Psychotic depression'.)
- (See "Schizophrenia in adults: Maintenance therapy and side effect management".)
- (See "Psychosis in adults: Initial management".)
- (See "Bipolar disorder in postpartum women: Epidemiology, clinical features, assessment, and diagnosis", section on 'Epidemiology'.)

We encourage individuals who plan on breastfeeding (and whose level of psychosis or disorganization does not preclude breastfeeding) to take antipsychotics, lithium, or antidepressants as indicated. (See 'Breastfeeding' below.)

Initiating lithium

- **Pretreatment evaluation** – Prior to beginning lithium we screen for renal disease, thyroid dysfunction and obtain an electrocardiogram in individuals with coronary risk factors (eg, diabetes mellitus, hypertension, dyslipidemia, smoking). Further discussion of pretreatment testing for lithium is described elsewhere. (See "Bipolar disorder in adults and lithium: Pharmacology, administration, and management of adverse effects", section on 'Laboratory tests and monitoring'.)

- **Dose, titration, and monitoring** – For individuals without contraindications to lithium, we typically begin lithium at a dose of 300 mg on the first day then 300 mg two times a day beginning the second day. We check serum lithium levels five days after any adjustment and adjust the dose accordingly. We aim to maintain lithium levels within the established

therapeutic window for lithium. Our treatment with lithium, including dose, titration, and monitoring for individuals with postpartum psychosis is the same as treatment with lithium in adults with bipolar disorder. Treatment with lithium in adults with bipolar disorder is discussed elsewhere. (See "Bipolar disorder in adults and lithium: Pharmacology, administration, and management of adverse effects", section on 'Prescribing lithium' and "Bipolar mania and hypomania in adults: Choosing pharmacotherapy".)

Choosing, initiating, and monitoring antipsychotics

- **Choosing and initiating antipsychotic** – Our choice among antipsychotics is not dependent on the individual's plan for breastfeeding. Our preference is based on the same factors as those we use in choosing among antipsychotics in nonpostpartum periods. We prefer to treat individuals with a second-generation antipsychotic (SGA) rather than a first-generation antipsychotic. This is based on lower rates of extrapyramidal symptoms [7] and tardive dyskinesia [8] associated with SGAs. Among SGAs our preference is based on patient comorbidity, psychiatric symptoms such as level of agitation, and property of the specific medication that is desired (eg, sedation, weight gain, metabolic dysregulation). Further discussion on selection of antipsychotics is found elsewhere (See "Psychosis in adults: Initial management", section on 'Selection'.)

  We titrate from initial dose of the chosen medication to the therapeutic range as quickly as tolerated. For example, in an individual who we are beginning on olanzapine, we typically begin at a dose of 5 to 10 mg, orally, at night. We titrate in 5 mg increments every two days to initial dose range of 10 to 20 mg. We monitor for two or three days and if symptoms persist, we titrate to the maximum oral dose of 30 mg. If using lurasidone, we begin at 40 mg daily and titrate to 80 mg daily after three days. We monitor for two or three days and if symptoms persist, we titrate to the maximum oral dose of 160 mg over the next week. We adjust the dose for individuals with hepatic or renal insufficiency. Initial dose and titration of antipsychotic medications are found on the associated table (table 1).

- **For those requiring parenteral formulations** – We use intramuscular (IM) antipsychotics for acute stabilization of individuals who present with agitation or aggression and who are too disorganized to take or refuse to take medications orally. Our preference is to use the first-generation antipsychotic haloperidol. When using haloperidol we typically use 0.5 to 2 mg IM for mild agitation, 2 to 5 mg IM for moderate agitation and up to 10 mg IM for severe agitation. This can be repeated every 30 minutes until desired level of sedation is achieved. Olanzapine IM is a reasonable alternative. Further discussion of emergency

management of agitated or violent adults can be found elsewhere. (See "Assessment and emergency management of the acutely agitated or violent adult" and "Psychosis in adults: Initial management".)

- **Monitoring on an antipsychotic** – SGAs vary in their side effect profiles. However, the rate of adverse effects from any antipsychotics is comparable to that in nonpuerperal psychotic disorders.

  Treatment with SGAs is associated with hyperglycemia, hyperlipidemia, and weight gain. Additionally extrapyramidal symptoms have been reported. We monitor individuals treated with antipsychotics for emergent side effects at regular intervals. Adverse effects and monitoring for metabolic dysregulation are discussed elsewhere and presented on the associated tables (table 2 and table 3). (See "Second-generation antipsychotic medications: Pharmacology, administration, and side effects" and "Schizophrenia in adults: Maintenance therapy and side effect management".)

Evidence basis for treatment of postpartum psychosis

- **Mood stabilizers/lithium** – Our preference for using lithium in postpartum psychosis is based on clinical trials demonstrating efficacy of mood stabilizers in the treatment of bipolar disorder in nonpostpartum females, reports of successful treatment with lithium in postpartum psychosis, and our clinical experience [5,9].

  In a retrospective report including 64 in-patients who received stepped care for postpartum psychosis, 47 of the 48 individuals who did not respond to acute treatment with benzodiazepines and antipsychotics remitted following the addition of lithium [5]. Of those that continued lithium monotherapy or augmentation for nine months, 83 percent showed sustained remission.

- **Antipsychotics** – Our preference for using antipsychotic medications in the treatment of females with postpartum psychosis is based on published reports suggest their use is common and effective in treating the syndrome, and our clinical experience [3,10]. Evidence is limited to small uncontrolled studies or case reports [5]. Indirect evidence includes randomized trials of medications for the underlying psychotic disorders in nonpostpartum samples [11-14]. There are no known differences among antipsychotics in their efficacy for reducing psychosis. Efficacy of antipsychotics in the treatment of psychosis is discussed elsewhere. (See "Psychosis in adults: Initial management" and "Schizophrenia in adults: Maintenance therapy and side effect management".)

Monotherapy for specific circumstances

Individuals who cannot take lithium — For individuals who cannot take lithium (eg, renal insufficiency) we begin treatment with an SGA as monotherapy at the same dose and titration schedule described above (see 'Choosing, initiating, and monitoring antipsychotics' above). Subsequent treatment for inadequate response in individuals who cannot take lithium is discussed below. (See 'Inadequate response to monotherapy' below.)

Individuals with mild level of disorganization — For individuals with mild levels of disorganization that do not lead to agitation, insomnia or other psychosocial disruption we occasionally begin treatment with lithium monotherapy. These individuals may not require an antipsychotic. This is the exception rather than the rule. We monitor these individuals closely while on lithium. We check regular serum levels and adjust lithium accordingly. (See "Bipolar mania and hypomania in adults: Choosing pharmacotherapy", section on 'Medication doses and side effects'.)

For individuals with concurrent depressive symptoms — For individuals without a prior psychiatric history who present with postpartum psychosis with prominent symptoms of major depression (eg, anhedonia, decreased appetite, thoughts of self-harm), our preference is treatment with lithium, an antipsychotic and an antidepressant (ie, selective serotonin reuptake inhibitor [SSRI]). In these cases, to avoid beginning all three medications at once, we begin with lithium and the antipsychotic and monitor for one week. At that time, unless symptoms are adequately treated, we add the SSRI.

However, in individuals with emotional lability (rapid fluctuations in mood) or excessive irritability we do not add an SSRI. These symptoms may reflect a mixed state or (ie, mixed depression and mania) or rapidly cycling moods. We are extremely vigilant to identify these patients, as addition of an antidepressant may precipitate a manic episode. (See "Bipolar major depression in adults: Efficacy and adverse effects of antidepressants", section on 'Risk of switching to mania'.)

Our choice among the antidepressants are the SSRIs. Our preference from among SSRIs is partially determined by whether the individual will be breastfeeding. The literature on using SSRIs are generally reassuring regarding short-term adverse effects [15,16]. Among the SSRIs our preference is treatment with sertraline; however, fluoxetine is a reasonable alternative. Both sertraline and fluoxetine are among the most widely studied medications and appear to be associated with few adverse effects in infants exposed through breast milk [15,17]. Exposure to SSRI antidepressant medications in breast milk in general appears to be low and with minimal adverse effects [18,19]. (See 'Breastfeeding' below and "Safety of infant exposure to antidepressants and benzodiazepines through breastfeeding".)

Clinical trials have found the combination of an antidepressant and antipsychotic to be efficacious in nonpostpartum patients with major depression with psychotic features [20-24].

SUBSEQUENT TREATMENT

An algorithm discusses the treatment of postpartum psychosis (algorithm 1).

For robust response — For individuals who have responded to treatment with lithium and a second-generation antipsychotic (SGA) we suggest the following:

- **Antipsychotic** – We continue treatment with the antipsychotic for a minimum of three to six months. Our decision is based on ongoing stability of symptoms in the context of stable psychosocial functioning.

- **Lithium** – We continue lithium monotherapy for up to a year in most cases. At least one cohort study supports the use of lithium for at least nine months, suggesting that the rate of sustained remission is higher for individuals maintained on lithium than those maintained on antipsychotic [5].

Individuals who have responded to pharmacologic treatment who discontinue their medication soon after hospital discharge are at increased risk for recurrence.

In individuals with prior underlying psychiatric history or in those with risk factors such as suicidality, we often treat indefinitely. Discussion of maintenance treatment for bipolar disorder, mood disorders, or psychotic disorders is found elsewhere. (See "Schizophrenia in adults: Maintenance therapy and side effect management" and "Bipolar disorder in adults: Choosing maintenance treatment" and "Unipolar major depression with psychotic features: Maintenance treatment and course of illness".)

- **Adjunctive psychotherapy** – Once the psychotic symptoms are under control, we recommend adjunctive psychotherapy. In our clinical experience, psychotherapy can provide useful adjunctive treatment, focusing on psychoeducation, support, coordination, and encouraging/monitoring adherence to medication. We coordinate with other providers to ensure a coherent uniform plan for monitoring the individual's status and reinforcing the need for medication adherence.

  There are no clinical trials investigating the role of psychotherapy or other psychosocial treatments in postpartum psychosis.

For inadequate response

Inadequate response to monotherapy — For individuals who have begun on monotherapy (see 'Monotherapy for specific circumstances' above) our subsequent treatment is as follows:

- **For individuals started on lithium monotherapy** – For individuals who have started on lithium monotherapy (rather than combined treatment with an antipsychotic), who do not respond to lithium monotherapy despite therapeutic trial, we add an SGA. (See 'Monotherapy for specific circumstances' above.)

- **For individuals started on SGA monotherapy** – For individuals who are unable to take lithium who do not respond to treatment with an SGA monotherapy, our next choice is valproate. Valproate is efficacious in nonpostpartum individuals with bipolar disorder. While little evidence supports significant clinical effect on newborn exposure to valproate in breast milk, our preference is to avoid using valproate beyond the initial stabilization period due to teratogenicity in future pregnancy. (See 'Breastfeeding' below and "Bipolar mania and hypomania in adults: Choosing pharmacotherapy", section on 'Anticonvulsants'.)

Prominent insomnia — For patients with postpartum psychosis who experience insomnia/disrupted sleep or agitation despite treatment with antipsychotic medication and lithium, we suggest augmentation with a benzodiazepine rather than other medications. Early intervention to promote sleep in postpartum psychosis may attenuate the psychotic episode.

In selecting among benzodiazepines, we favor those with a short half-life and no active metabolites, such as lorazepam [25,26]. Our preference is to begin lorazepam at a dose of 0.5 to 2 mg orally or intramuscularly in conjunction with the antipsychotic.

Our preference for benzodiazepines in the treatment of prominent insomnia in the context of postpartum psychosis comes from case reports, small studies and our clinical experience supporting their use, particularly to promote sleep, in psychosis and mania [27]. A retrospective report described treatment of 64 inpatients treated for postpartum psychosis using a four-step algorithm: beginning with benzodiazepines, followed by the addition of antipsychotics, then lithium, then electroconvulsive therapy (ECT). Only 6 percent of patients responded to benzodiazepine treatment alone; a majority of patients responded to a combination of medications including benzodiazepines [5]. Benzodiazepines are considered relatively safe during breastfeeding, though sedation is a potential side effect in the infant.

Further information about the safety of benzodiazepines the management of psychosis and in individuals who are breast feeding is reviewed separately. (See "Safety of infant exposure to antidepressants and benzodiazepines through breastfeeding" and "Psychosis in adults: Initial management".)

For inadequate response to combination therapy — For patients with postpartum psychosis who do not respond to antipsychotic medication and mood stabilizers, we often change to another SGA medication while simultaneously beginning to discuss and arrange treatment with ECT [5]. (See 'Choosing, initiating, and monitoring antipsychotics' above.)

Response to ECT is generally more rapid compared with response to medication; thus, ECT may be useful if a rapid response is needed to prevent harm (eg, the woman is at high risk for suicide or infanticide, is catatonic, or is acutely agitated). The number of treatments will depend on the severity of the symptoms.

There are no randomized clinical trials on the efficacy of ECT in postpartum psychosis. Clinical trials have found ECT to be efficacious in the treatment of nonpostpartum patients with major depression [28-31], to suggest efficacy for bipolar depression [32,33], and to show mixed results for bipolar mania [34-38]. (See "Bipolar disorder in adults: Indications for and efficacy of electroconvulsive therapy" and "Unipolar major depression in adults: Indications for and efficacy of electroconvulsive therapy (ECT)", section on 'Efficacy'.)

Data from an uncontrolled trial, two retrospective matched-cohort studies, and case series, totaling more 300 patients treated with ECT for postpartum psychosis, provide preliminary support for efficacy [39-42]. As an examples:

- In a retrospective study, ECT was associated with a higher rate of “marked improvement” or symptom resolution among 58 females with postpartum psychosis compared with 56 matched nonpuerperal females with psychosis (65 versus 33 percent) [42].
- In a retrospective study using the Swedish nationwide population-based registry, ECT was associated with a higher response rate among 185 females who received treatment within six months of giving birth compared with 185 matched nonpuerperal females (87 versus 74 percent) [43]. The risk of relapse after ECT was found to be lower for 180 patients with puerperal psychiatric illness compared with the risk in 180 matched nonpuerperal females, although the risk of relapse was still substantial in both groups [44].

ECT has a relatively low rate of adverse effects in the general population, including time-limited neurocognitive effects, rare cardiovascular or pulmonary compromise, and risks associated with general anesthesia [29]. (See "Medical evaluation for electroconvulsive therapy".)

BREASTFEEDING

Based upon the limited evidence and our clinical experience, we encourage females with postpartum psychosis who plan on breastfeeding to take antipsychotic medications, antidepressants, or lithium as indicated. Some females will only take their medications if they are allowed to breastfeed. In such cases, the benefits of medication may supersede concerns about use of the drug in lactation.

However, some females with more severe illness may be too disorganized or present too great a risk to the child to safely breastfeed.

While all psychotropic medications taken by the mother are transferred into breast milk and are passed on to the nursing infant, the exposure to antipsychotic and antidepressant medications in breast milk appears to be low and clinically insignificant [18,19].

There is no clear consensus on the safety of lithium in breastfeeding females [45]. We use lithium in individuals who can participate in a discussion of the risks and benefits of using the medication while breastfeeding.

The effects of antipsychotics, benzodiazepines, anticonvulsants, and lithium on exposure through breast milk are discussed elsewhere. The literature remains scant and more research is needed to make evidence based recommendations [46].

- (See "Safety of infant exposure to antidepressants and benzodiazepines through breastfeeding".)
- (See "Breastfeeding infants: Safety of exposure to antipsychotics, lithium, stimulants, and medications for substance use disorders".)
- (See "Management of epilepsy during preconception, pregnancy, and the postpartum period", section on 'Breastfeeding'.)
- (See "Severe postpartum unipolar major depression: Choosing treatment", section on 'Choosing treatment for breastfeeding patients'.)

There are no known effects of electroconvulsive therapy (ECT) on breast milk. The American Psychiatric Association Task Force on ECT recommends that the informed consent process include a discussion with the mother of potential risks to the infant from breastfeeding during a course of ECT [47]. Anesthetic medications administered during ECT treatment generally pose little risk to breastfeeding infants [48]. Exposure can be minimized by delaying breastfeeding for a few hours after ECT therapy or by collecting and storing breast milk the day prior to ECT. Further discussion of ECT in the postpartum period can be found elsewhere (See "Severe postpartum unipolar major depression: Choosing treatment", section on 'Choosing treatment for breastfeeding patients'.)

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: Psychotic disorders".)

SUMMARY AND RECOMMENDATIONS

- **Postpartum psychosis** – Postpartum psychosis presents with rapid onset of psychotic symptoms including hallucinations and delusions, bizarre behavior, confusion, and disorganization. (See 'Introduction' above.)

  Postpartum psychosis is most often seen in individuals who have been or subsequently are diagnosed with bipolar disorder. (See 'Introduction' above.)

- **Ensure safety** – Postpartum psychosis constitutes a medical emergency, generally requiring rapid identification and intervention.

  We typically hospitalize individuals with postpartum psychosis. While separation of mother and baby at this critical time is not optimal, we do not leave the mother alone with their children. (See 'Ensure safety' above.)

- **Initiating medication** – An algorithm discusses the treatment of postpartum psychosis (algorithm 1).

  - **Combined treatment for most** – For individuals with postpartum psychosis with no established psychiatric history, we suggest initial treatment with a combination of an antipsychotic medication and lithium, rather than either treatment alone (**Grade 2C**). (See 'Combined treatment for most' above.)

    As in other settings, we prefer treatment with a second-generation antipsychotic (SGA) rather than a first generation antipsychotic due to their lower rate of extrapyramidal symptoms. (See 'Choosing, initiating, and monitoring antipsychotics' above.)

  - **Monotherapy for specific circumstances** – We use an antipsychotic as monotherapy for those who cannot take lithium. We infrequently use lithium monotherapy for individuals with very mild disorganization that does not cause psychosocial disruption. (See 'Monotherapy for specific circumstances' above.)

- **For individuals with concurrent depression** – For individuals with postpartum psychosis and prominent symptoms of depression, we suggest combination treatment with a selective serotonin reuptake inhibitor (SSRI) in addition to lithium and an antipsychotic (**Grade 2C**).

  However, we do not treat individuals with emotional lability or excessive irritability with an SSRI, as these individuals may be at increased risk for precipitating a manic episode. (See 'For individuals with concurrent depressive symptoms' above.)

- **Subsequent treatment**

  - **For robust response** – For individuals with a robust response to treatment with lithium and an SGA, we continue the antipsychotic for a minimum of three to six months and lithium for a minimum of nine months.

    For individuals that respond to initial pharmacologic management, we suggest adjunctive psychotherapy focusing on psychoeducation and encouraging adherence to medication (**Grade 2C**). (See 'For robust response' above.)

  - **For inadequate response to monotherapy** – We add an SGA for individuals who do not respond to initial monotherapy treatment with lithium. (See 'Inadequate response to monotherapy' above.)

    For individuals who are unable to take lithium who do not respond to initial treatment with SGA monotherapy, our next choice is valproate. We avoid using valproate beyond the initial stabilization period. (See 'Inadequate response to monotherapy' above.)

  - **For prominent insomnia** – For patients with postpartum psychosis who experience insomnia/disrupted sleep despite initial treatment, we suggest augmentation with a benzodiazepine rather than other medications (**Grade 2C**). (See 'Prominent insomnia' above.)

- **For inadequate response to combined treatment** – For patients with postpartum psychosis who do not respond to or tolerate combined treatments, we often change to another SGA medication while simultaneously beginning to arrange treatment with electroconvulsive therapy. (See 'For inadequate response to combination therapy' above.)

- **Breastfeeding** – Based upon the limited evidence and our clinical experience, we encourage females with postpartum psychosis who plan on breastfeeding to take antipsychotic medications, antidepressants, or mood stabilizers as indicated. However, some females with more severe illness may be too disorganized or present too great a risk

to the child to safely breastfeed. (See 'Breastfeeding' above and 'Combined treatment for most' above.)

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