Postpartum unipolar depression: Prevention

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INTRODUCTION

Although delivering a baby is typically a happy event, some postpartum women become depressed [1-3]. Interventions to prevent postpartum unipolar major depression are indicated for euthymic women who are at increased risk of developing postpartum depression.

This topic reviews prevention of postpartum unipolar depression. Other topics discuss the clinical features, diagnosis, and treatment of postpartum unipolar major depression; clinical features and management of postpartum blues; safety of infant exposure to psychotropic drugs through lactation; and the diagnosis and treatment of postpartum paternal depression and antepartum unipolar depression:

- (See "Postpartum unipolar major depression: Epidemiology, clinical features, assessment, and diagnosis".)
- (See "Postpartum unipolar major depression: General principles of treatment".)
- (See "Mild to moderate postpartum unipolar major depression: Treatment".)
- (See "Severe postpartum unipolar major depression: Choosing treatment".)
- (See "Postpartum blues".)
- (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 "Postpartum paternal depression".)

TERMINOLOGY

- **Postpartum period** – We define the postpartum period as the first 12 months after birth. Definitions of the puerperium range from the first 1 to 12 months following a live birth. (See "Postpartum unipolar major depression: Epidemiology, clinical features, assessment, and diagnosis", section on 'Definition of postpartum period'.)

- **Postpartum blues** – During the puerperium, mild, transient depressive symptoms such as dysphoria, insomnia, emotional lability, and decreased concentration occur in many women. The clinical features and management of postpartum blues are discussed separately. (See "Postpartum blues".)

- **Postpartum depression** – The diagnostic criteria for postpartum major depression are the same criteria that are used to diagnose nonpuerperal major depression (table 1) [4]. (See "Postpartum unipolar major depression: Epidemiology, clinical features, assessment, and diagnosis", section on 'Diagnosis' and "Unipolar depression in adults: Assessment and diagnosis", section on 'Unipolar major depression'.)

INDICATIONS

Interventions to prevent postpartum unipolar major depression are indicated for euthymic women who are at increased risk of developing the disorder. Although many risk factors for postnatal depressive syndromes have been identified, the factors that have the largest effect and are most consistently associated with postpartum depression are:

- A past history of either perinatal or nonperinatal depression

- Depressive symptoms during the current pregnancy

Prevention is especially indicated for postpartum women at increased risk of major depression who are manifesting prodromal symptoms.

Additional information about risk factors for postpartum depression is discussed separately. (See "Postpartum unipolar major depression: Epidemiology, clinical features, assessment, and diagnosis", section on 'Risk factors'.)

CHOOSING TREATMENT

For euthymic postpartum patients with an increased risk of developing unipolar major depression due to a prior history of depression (see 'Indications' above), the choice of treatment for preventing an episode of depression depends upon the prior treatment history, as described in the subsections below.

Prior history of successful treatment with antidepressants — For euthymic, postpartum patients who were successfully treated for major depression with antidepressants in the past, including women who discontinued successful maintenance pharmacotherapy for depression shortly before or during pregnancy, and are now at risk of developing major depression due to a prior history of depression, we suggest prophylaxis with the previously used antidepressants [5]. Women with a prior history of depression frequently prefer antidepressants for prevention of recurrences [6]. Although concerns have been raised about using antidepressants in women who are breastfeeding their infants, the general consensus is that the risks of a depressive episode outweigh the risks of infant exposure. (See "Postpartum unipolar major depression: Epidemiology, clinical features, assessment, and diagnosis", section on 'Adverse consequences' and "Safety of infant exposure to antidepressants and benzodiazepines through breastfeeding" and "Severe postpartum unipolar major depression: Choosing treatment", section on 'Initial treatment'.)

We generally resume the previous regimen in the third trimester (eg, two to four weeks prior to delivery), to ensure patients are at a therapeutic dose at time of delivery. Doses typically are titrated up as is done for initial treatment. Higher doses may be required in the third trimester to offset decreased maternal serum drug concentrations that can occur due to expanded plasma volume, hepatic enzyme induction, and increased drug clearance [7,8]. However, a reasonable alternative is to resume antidepressants after delivery when postpartum patients are medically stable. Information about prescribing antidepressants during pregnancy is discussed separately. (See "Unipolar major depression in pregnant women: General principles of treatment", section on 'Prescribing antidepressants'.)

Some postpartum women who are at risk for recurrences of major depression may want to avoid pharmacotherapy. Reasonable alternatives to antidepressants include psychotherapy (eg, cognitive-behavioral therapy or interpersonal psychotherapy), psychosocial interventions (eg, home visits), or close monitoring (eg, clinical interviews every one to four weeks, depending upon clinical urgency).

No history of successful antidepressant treatment — For euthymic, postpartum patients who are at highest risk of developing postpartum major depression due to a prior history of depression (see 'Indications' above), and who have not been successfully treated with antidepressants in the past, we suggest prophylaxis with either cognitive-behavioral therapy or

interpersonal psychotherapy, depending upon availability. This approach is consistent with guidance from the US Preventive Services Task Force, which found that cognitive-behavioral therapy or interpersonal psychotherapy can prevent perinatal depression [9]. A reasonable alternative is a psychosocial intervention such as home visits by clinicians (eg, nurses) or telephone support by nonprofessionals.

In addition, either pharmacotherapy or watchful waiting are reasonable alternatives. Pharmacotherapy is more widely available than cognitive-behavioral therapy and interpersonal psychotherapy. We generally initiate an antidepressant regimen in the third trimester (eg, two to four weeks prior to delivery).

EVIDENCE OF EFFICACY

Randomized trials that excluded pregnant and lactating women have demonstrated that maintenance treatment with antidepressant drugs is efficacious in preventing unipolar major depression. (See "Unipolar depression in adults: Continuation and maintenance treatment", section on 'Antidepressant medications'.)

In addition, randomized trials in postpartum women indicate that nonpharmacologic interventions, such as psychotherapy (eg, cognitive-behavioral therapy [CBT] or interpersonal psychotherapy) or psychosocial interventions (eg, home visits), can prevent postnatal unipolar depression. As an example:

- In a meta-analysis of 20 randomized trials (n >14,000) that compared nonpharmacologic treatment (eg, psychotherapy or psychosocial interventions) with control conditions (eg, usual care), the risk of depressive symptoms was reduced in patients who received active treatment (relative risk 0.8, 95% CI 0.7-0.9) [10]. However, heterogeneity across studies was moderate to large.

- A meta-analysis of 10 randomized trials (nine prevention trials and one treatment trial; n >18,000 antenatal and postpartum women) found a significant, but clinically small effect favoring active interventions over usual care [11].

- Another meta-analysis (28 studies, nearly all randomized trials, sample size not reported) compared control conditions with a variety of interventions that were nearly all nonpharmacologic (eg, psychotherapy, enhanced standard obstetric care, or social support) and found a 30 percent reduction in depressive episodes among patients who received active interventions (odds ratio 0.7, 95% CI 0.6-0.9) [12]. However, heterogeneity across studies was moderate to large.

Evidence of efficacy that is specific to psychotherapy and to psychosocial interventions is discussed below. (See 'Psychotherapy' below and 'Psychosocial interventions' below.)

Antidepressants — Randomized trials that excluded pregnant and lactating women have demonstrated that maintenance treatment with antidepressant drugs is efficacious in preventing unipolar major depression. (See "Unipolar depression in adults: Continuation and maintenance treatment", section on 'Antidepressant medications'.)

In addition, a 20-week trial compared sertraline (final dose 75 mg/day) with placebo in euthymic postpartum women with a past history of postpartum depression; the study treatments were started 24 hours after birth [13]. Relapse of depression occurred in fewer patients who received sertraline than placebo (1/14 versus 4/8 [7 versus 50 percent]). However, dizziness and drowsiness occurred more often with sertraline than placebo.

Postpartum antidepressants are not a contraindication to breastfeeding and patients should not be discouraged from breastfeeding. Antidepressants are generally compatible with breastfeeding, and most studies demonstrate low or undetectable serum levels of medication in infants. Nevertheless, uncommon adverse effects may occur, and infants should be monitored for sedation, difficulty feeding, and/or difficulty sleeping. (See "Safety of infant exposure to antidepressants and benzodiazepines through breastfeeding".)

Psychotherapy — Randomized trials in the general population of patients with unipolar major depression have demonstrated that maintenance treatment with psychotherapy is efficacious in delaying or preventing recurrent episodes. (See "Unipolar depression in adults: Continuation and maintenance treatment", section on 'Psychotherapy'.)

High quality studies have also found that psychotherapy can prevent onset of postpartum depression:

- A meta-analysis of eight randomized trials (n >3000) compared psychotherapy (primarily interpersonal psychotherapy) with control conditions and found that postpartum depressive symptoms were less likely to occur in patients treated with psychotherapy (relative risk 0.61, 95% CI 0.39-0.96) [10].

- A meta-analysis of 13 studies (nearly all randomized trials, sample size not reported) compared psychotherapy (eg, CBT or interpersonal psychotherapy) with control conditions and found a 40 percent reduction in depressive episodes among patients who received psychotherapy (odds ratio 0.6, 95% CI 0.4-0.8) [12].

In addition, a meta-analysis of 14 randomized trials (total n >1400 women) compared psychotherapy with control conditions for preventing unipolar major depression or minor depression during pregnancy or the postpartum period (perinatal depression) [14]. All of the women were at increased risk for perinatal depression, and psychotherapy in nearly all of the studies consisted of cognitive-behavioral therapy or interpersonal psychotherapy. Perinatal depression occurred less often with psychotherapy (relative risk 0.6, 95% CI 0.4-0.7).

Cognitive-behavioral therapy — CBT is a time-limited psychotherapy that combines cognitive therapy and behavioral therapy. Cognitive therapy attempts to modify the dysfunctional thoughts and beliefs about oneself, the world, and the future (eg, "I'm no good"); behavioral therapy focuses upon modifying the patient's problematic behavioral responses (eg, inactivity) to environmental stimuli or dysfunctional thoughts through techniques such as problem solving, stimulus control, and exposure with response prevention.

Randomized trials indicate that CBT can prevent postpartum depressive episodes and that individual treatment is the preferred method of administration. As an example, a meta-analysis of 12 studies (primarily randomized trials, sample size not reported) compared CBT with a control condition; most of the studies administered the study treatments during pregnancy. CBT reduced the risk of postpartum depressive episodes by 40 percent (odds ratio 0.6, 95% CI 0.5-0.9) [15]. In addition, the benefit was greater for individual therapy than group therapy.

Information about the administration of CBT as well as its efficacy in preventing recurrences in the general population of patients with major depression is discussed separately. (See "Overview of psychotherapies", section on 'Cognitive and behavioral therapies' and "Unipolar depression in adults: Continuation and maintenance treatment", section on 'Cognitive-behavioral therapy'.)

Interpersonal psychotherapy — Interpersonal therapy is a time-limited psychotherapy that addresses interpersonal difficulties that lead to psychiatric disorders; the therapy focuses upon the patient's interpersonal life in four problem areas: grief over loss, role disputes, role transitions, and interpersonal deficits.

Randomized trials indicate that interpersonal psychotherapy can prevent postpartum depression:

- A meta-analysis of five trials (total n = 366 women) compared interpersonal psychotherapy with usual care and found a significant but clinically small effect favoring active treatment [10].

- A subsequent trial compared interpersonal psychotherapy with usual care in 197 pregnant patients [16]. Active treatment included four group sessions, education, homework, and one individual postpartum booster session. Within six months of delivery, onset of postpartum depression occurred in fewer patients who received interpersonal psychotherapy than standard care (16 versus 31 percent).

- Another subsequent trial compared interpersonal psychotherapy with an educational (control) program in 106 primiparous adolescents [17]. Both interventions provided five prenatal sessions and one postpartum booster session. Onset of postpartum depression within six months of delivery occurred in fewer patients who received interpersonal psychotherapy than education (13 versus 25 percent). Although the difference between treatments was not statistically significant, a difference of this magnitude, if real, would be clinically meaningful.

Information about the administration of interpersonal psychotherapy, as well as its efficacy in preventing recurrences in the general population of patients with major depression, is discussed separately. (See "Interpersonal Psychotherapy (IPT) for depressed adults: Specific interventions and techniques" and "Interpersonal Psychotherapy (IPT) for depressed adults: Indications, theoretical foundation, general concepts, and efficacy".)

Mindfulness based cognitive therapy — Mindfulness based cognitive therapy is a group program that combines the clinical application of mindfulness meditation with elements of CBT. The treatment is generally used to delay or prevent recurrence of unipolar major depression, based upon randomized trials in the general population of patients with depression. (See "Unipolar major depression: Treatment with mindfulness-based cognitive therapy".)

In addition, other studies suggest that mindfulness based cognitive therapy can prevent postpartum depression [18]. One randomized trial compared the therapy (eight sessions) with usual care in 86 pregnant patients with a prior history of major depression [19]. The use of pharmacotherapy or other psychotherapies was permitted in both treatment groups. Recurrence of depressive episodes during the postpartum period occurred in fewer patients treated with mindfulness based cognitive therapy than usual care (5 versus 35 percent).

Psychosocial interventions — Psychosocial interventions for preventing postpartum depression include home visits by clinicians (eg, nurses) or telephone support by nonprofessionals. These interventions, which are administered during pregnancy or soon after delivery, may prevent postpartum depression, but the benefit is often small:

- A meta-analysis of 12 randomized trials (n >11,000 postpartum women) compared psychosocial interventions with usual care and found that the risk of postpartum

depressive symptoms was reduced modestly by 17 percent in the active treatment groups (relative risk 0.83, 95% CI 0.70-0.99); heterogeneity across studies was moderate [10]. In particular, efficacy was greater for home visits by nurses or midwives than usual care (two trials, n >1000 women; relative risk 0.6, 95% CI 0.4-0.7). Other analyses suggested that interventions initiated postnatally may be superior to interventions with an antenatal-only component or antenatal plus postnatal components.

- Another meta-analysis (seven randomized trials, n >17,000 antenatal and postpartum women) found a significant, but clinically small effect favoring psychosocial interventions over usual care [11].

- A randomized trial compared an action-oriented behavioral intervention with usual care in postpartum women (n = 495) [20]. The behavioral intervention addressed risk factors for depression such as maternal physical symptoms (eg, vaginal bleeding and pain), poor social support, lack of resources, and infant factors (eg, colic). Usual care included routine postpartum education and a list of community resources. Both treatment groups received two sessions within two weeks of delivery. Clinically significant depressive symptoms during the six months following delivery occurred less often with active treatment than usual care (odds ratio 0.6, 95% CI 0.4-0.9).

Randomized trials also suggest that interventions that are relatively simple, practical, and focus upon both the mother and infant, rather than solely the mother (eg, teaching parenting skills), may help prevent postpartum depressive symptoms [21,22]. As an example:

- One trial compared a prevention program with usual care in new parents (n = 770 families); active treatment included information about infant sleep and crying as well as settling techniques, along with one telephone consultation and one parent group meeting, each of which encouraged parents or caregivers to develop management plans (eg, routine infant bedtimes) to address problems [23]. At the six-month follow-up, clinically significant depressive symptoms occurred less often in caregivers who received the prevention program than usual care (8 versus 13 percent).

- A second trial compared a postpartum prevention program with usual care in 54 mother-infant dyads [22]. Active treatment, called Practical Resources for Effective Postpartum Parenting, consisted of four sessions with a psychologist during the third trimester and first six weeks postpartum, in which mothers learned to change the infant's crying and fussing behavior. Usual care consisted of two sessions with a psychologist, during which symptoms of postpartum depression were discussed and patients received referrals for psychiatric care. Assessment at six weeks postpartum found that rating scale scores for

depression and for anxiety were each lower in patients who received active treatment than usual care. However, assessments 10 weeks postpartum found that symptoms were comparable in the two groups.

Education alone does not seem to be an effective psychosocial intervention for preventing postpartum depression [24]. A meta-analysis of four randomized trials (nearly 1500 women) compared antenatal and postnatal group classes with usual care; the active interventions included content about maternal and newborn health problems, depression, enhancing social support, and problem solving [10]. The risk of postpartum depression in the education and usual care groups was comparable. In addition, a review of six randomized trials in nearly 3000 women found that in five of the trials, education without counseling or extensive support provided no advantage over control conditions for preventing perinatal depression (depressive disorders during pregnancy or the postpartum period) [14].

TREATMENTS WITH LITTLE TO NO BENEFIT

Supplements — Multiple reviews of randomized trials have concluded that neither omega-3 fatty acids nor selenium prevent postpartum depression [25,26]:

- **Omega-3 fatty acids** – A review of four randomized trials found that in each trial, the benefit of omega-3 fatty acids and placebo was comparable [26]: As an example:
  - One trial compared fish oil rich in docosahexaenoic acid (800 mg/day) with vegetable oil placebo in pregnant women (n = 2399); study drugs were taken from the second trimester until birth [27]. Postpartum depression was comparable for the two groups (10 and 11 percent of patients).
  - Another trial randomly assigned pregnant patients (n = 126) to fish oil rich in docosahexaenoic acid (900 mg/day), fish oil rich in eicosapentaenoic acid (1060 mg/day), or soy oil placebo; study drugs were taken from the second trimester until six to eight weeks after delivery [28]. Postpartum depressive symptoms in the three groups were comparable.

  In addition, a meta-analysis of two randomized trials compared omega-3 fatty acids with placebo (total n = 204) for preventing depressive disorders during pregnancy or the postpartum period, and found that omega-3 fatty acids provided no benefit [14].

  Information about the benefit of omega-3 fatty acids for treating the general population of patients with depression is discussed separately. (See "Unipolar depression in adults:

Investigational and nonstandard treatment", section on 'Omega-3 fatty acids'.)

- **Selenium** – One trial compared selenium (100 micrograms/day) with placebo, taken from the first trimester until delivery [29]. Although the study investigators found a statistically significant advantage favoring selenium in preventing depressive symptoms, an analysis conducted by a systematic review showed only a trend favoring selenium [25]. In addition, the study was marked by a high rate of attrition; 179 patients were randomly assigned to a study treatment, but outcome data were available for less than half (n = 85).

Exercise — There is no compelling evidence that exercise during pregnancy prevents postpartum depression:

- A meta-analysis of three randomized trials in 1200 women found that the benefit of exercise and the control conditions was comparable for preventing depressive disorders during pregnancy or the postpartum period (relative risk 0.5, 95% CI 0.2-1.6) [9].

- A subsequent study randomly assigned pregnant women between 16 and 20 weeks gestation (n = 639) to exercise or to no intervention [30]. The exercise program consisted of supervised aerobic and resistance training for one hour, three times per week, for 16 weeks. Adherence to exercise was poor, and the rate of depressive episodes during the first three postpartum months was comparable in the exercise and control groups (6 and 9 percent of patients).

BREASTFEEDING

The safety of infant exposure to psychotropic medications through breastfeeding is discussed separately. (See "Safety of infant exposure to antidepressants and benzodiazepines through breastfeeding", section on 'Antidepressants' and "Breastfeeding infants: Safety of exposure to antipsychotics, lithium, stimulants, and medications for substance use disorders".)

POSTPARTUM BLUES

Management of postpartum blues (transient, mild depressive symptoms) is discussed separately. (See "Postpartum blues", section on 'Management'.)

ANTENATAL UNIPOLAR MAJOR DEPRESSION

Treatment of unipolar depression during pregnancy is discussed separately. (See "Severe antenatal unipolar major depression: Choosing treatment".)

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: Depressive disorders" and "Society guideline links: Postpartum care".)

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: Coping with high drug prices (The Basics)" and "Patient education: Depression during and after pregnancy (The Basics)")
- Beyond the Basics topics (see "Patient education: Coping with high prescription drug prices in the United States (Beyond the Basics)")

In addition, several lay groups offer support and education to women with postpartum mood disorders and to family members. One such group is Postpartum Support International (available at the website or call 1-800-944-4773), which holds local, state, national, and international meetings. Educational information is also available at the National Women's Health Information Center (available at the website).

SUMMARY AND RECOMMENDATIONS

- Interventions to prevent postpartum unipolar major depression are indicated for women who are at increased risk of developing the disorder. Risk factors that have the largest effect and are most consistently associated with postpartum depression include a past history of either perinatal or nonperinatal depression and/or depression during the current pregnancy. (See 'Indications' above.)

- For postpartum patients who were successfully treated for major depression with antidepressants in the past, we suggest prophylaxis with antidepressants rather than no treatment (**Grade 2C**). The antidepressant of choice depends upon patient's past response to antidepressants.

- We generally start the antidepressant in the third trimester, but it is reasonable to start the drug after delivery when postpartum patients are medically stable. Reasonable alternatives to pharmacotherapy include psychotherapy (eg, cognitive-behavioral therapy or interpersonal psychotherapy), psychosocial interventions (eg, home visits), or watchful waiting (clinical interviews every one to four weeks). (See 'Prior history of successful treatment with antidepressants' above and 'Evidence of efficacy' above.)

- For patients who are at risk of developing postpartum major depression and have not been successfully treated with antidepressants in the past, we suggest prophylaxis with psychotherapy or psychosocial interventions, rather than no treatment (**Grade 2B**). We typically prefer cognitive-behavioral therapy, interpersonal psychotherapy, or mindfulness based cognitive therapy depending upon availability. However, either pharmacotherapy or watchful waiting are reasonable alternatives. (See 'No history of successful antidepressant treatment' above and 'Evidence of efficacy' above.)

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