Unipolar major depression in pregnant women: General principles of treatment

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INTRODUCTION

Unipolar major depression is common in pregnant women, but is often not treated [1]. In a nationally representative survey in the United States that identified pregnant and nonpregnant women with major depression, pregnant women were less likely to receive mental health treatment than nonpregnant women (49 versus 57 percent) [2]. Untreated disease causes maternal suffering and is associated with poor nutrition, comorbid substance use disorders, poor adherence with prenatal care, postpartum depression, impaired relationships between the mother and her infant and other family members, and an increased risk of suicide [3,4].

Barriers to treatment of antenatal depression include cost, opposition to treatment (eg, fear of exposing the fetus to antidepressant medication or lack of interest in psychotherapy), unavailability of psychotherapy, and stigma [3,4]. In addition, many clinicians are reluctant to use pharmacotherapy because they lack sufficient expertise [5], and the large literature is often inconsistent [6].

This topic reviews the general principles of treating antenatal unipolar major depression. Other topics discuss choosing a specific treatment for antenatal major depression; the risks of antidepressants during pregnancy; and the epidemiology, clinical features, assessment, and diagnosis of antenatal depression.

- (See "Mild to moderate episodes of antenatal unipolar major depression: Choosing treatment".)
- (See "Severe antenatal unipolar major depression: Choosing treatment".)
- (See "Antenatal use of antidepressants and the potential risk of teratogenicity and adverse pregnancy outcomes: Selective serotonin reuptake inhibitors".)
- (See "Antenatal use of antidepressants and risks of teratogenicity and adverse pregnancy outcomes: Drugs other than selective serotonin reuptake inhibitors".)
- (See "Antenatal exposure to selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs): Neonatal outcomes".)
- (See "Unipolar major depression during pregnancy: Epidemiology, clinical features, assessment, and diagnosis".)

DEFINITION OF UNIPOLAR MAJOR DEPRESSION

Unipolar major depression (major depressive disorder) is diagnosed in patients who have suffered at least one major depressive episode and have no history of mania or hypomania [7]. An episode of unipolar major depression is a period lasting at least two weeks, with five or more of the following symptoms: depressed mood, loss of interest or pleasure in most or all activities, insomnia or hypersomnia, change in appetite or weight, psychomotor retardation or agitation, low energy, poor concentration, thoughts of worthlessness or guilt, and recurrent thoughts about death or suicide (table 1). Additional information about the clinical presentation and diagnosis of unipolar major depression is discussed separately. (See "Unipolar depression in adults: Clinical features" and "Unipolar depression in adults: Assessment and diagnosis".)

GENERAL PRINCIPLES

Patients with antenatal depression are usually best served by a multidisciplinary team that includes an obstetrician or internist and psychiatrist [4,8,9]. Communication among all of the involved clinicians is important to give consistent messages to increase uptake of treatment.

The sections below describe some general principles and issues that are involved in treating unipolar major depression during pregnancy. Information about the principles of treating unipolar depression in the general population of adults is discussed separately. (See "Unipolar depression in adults and initial treatment: General principles and prognosis", section on 'General principles'.)

Setting — Most women who are considering treatment for perinatal depression prefer to receive help at their obstetrics clinic, either from the obstetrician or a mental health clinician located at the clinic [10]. Randomized trials indicate that depressed patients, including women with perinatal depressive symptoms, can benefit from collaborative (integrated) care that is administered at an obstetrics and gynecology clinic [11,12]. Collaborative care involves a team of clinicians, such as an obstetrician, case manager, and mental health specialist, who work together to provide pharmacotherapy and/or psychotherapy.

Severe major depression often requires hospitalization. In a nationally representative survey of pregnant women with unipolar major depression in the United States (n = 375), inpatient care was reported by 7 percent [13].

History of prior treatment — It is important assess the benefit of previous treatment in order to guide treatment selection. If psychotherapy is indicated and the patient was successfully treated with a particular psychotherapy prior to pregnancy, the same therapy is used during pregnancy. Similarly, if pharmacotherapy is indicated and the patient was successfully treated with a particular antidepressant prior to pregnancy, the same drug is used during pregnancy.

Educating patients and families — For antenatal unipolar major depression, we recommend psychoeducation for the patient and family despite limited evidence of its efficacy in this population [9,14,15]. Educating childbearing women about depression is consistent with multiple treatment guidelines [16-20]. Psychoeducation includes information about the symptoms and course of depression, as well as treatment options [8]. The discussion about depression during pregnancy should include information about the potential risks of untreated depression. (See "Severe antenatal unipolar major depression: Choosing treatment", section on 'Unplanned pregnancies and discontinuing antidepressants during pregnancy' and "Antenatal depression: Pregnancy and neonatal outcomes" and "Antenatal depression: Risks of abnormal infant and child development" and "Antenatal depression: Risks of cognitive impairment and psychopathology in the offspring".)

Antidepressant medications are one option for some patients with antenatal depression; however, the risks of antenatal exposure to antidepressants are not established due to the lack of randomized trials. Nevertheless, to the extent that medications are associated with adverse outcomes, the absolute risks appear to be low [21-23]. (See "Antenatal use of antidepressants and the potential risk of teratogenicity and adverse pregnancy outcomes: Selective serotonin reuptake inhibitors" and "Antenatal use of antidepressants and risks of teratogenicity and adverse pregnancy outcomes: Drugs other than selective serotonin reuptake inhibitors" and "Antenatal exposure to selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs): Neonatal outcomes".)

As part of psychoeducation, patients are also encouraged to get adequate rest, maintain a consistent sleep-wake cycle, utilize supports, reduce stressors when possible, and continue pre-pregnancy exercise routines. (See "Exercise during pregnancy and the postpartum period".)

Adherence — Poor adherence is common among patients with psychiatric disorders, including prenatal depression. Barriers to care include cost, logistics, not trusting clinicians, and stigma [24].

Monitoring symptoms — We recommend routinely monitoring symptoms of perinatal depression during treatment with the self-report, 10-item Edinburgh Postnatal Depression Scale (figure 1A-B) [25]. The scale can be completed in less than five minutes in the waiting room immediately before seeing the clinician. Although the instrument was originally developed as a screening tool, we find it is also useful for monitoring response to treatment. Items asking about the somatic symptoms of depression such as sleep and appetite are not included in the scale because these symptoms are common in pregnant women who are not depressed [26]. The scale is acceptable to most women and clinicians [27], easy to score, and is available in over 50 languages [28]. Responses are scored 0, 1, 2, or 3, with a maximum score of 30. In studies that evaluated the instrument as a screening tool, scores ≥12 or 13 identified most women with major depression. However, many studies used a cutoff score of ≥10 [29].

An alternative to the Edinburgh Postnatal Depression Scale is the self-report, nine-item Patient Health Questionnaire (table 2). However, the Patient Health Questionnaire includes items about changes in appetite, energy, and sleep, which may reflect the physical effects of pregnancy rather than depression [1].

General information about monitoring depressive symptoms during treatment is discussed separately. (See "Using scales to monitor symptoms and treat depression (measurement based care)".)

Prescribing antidepressants — Pregnant patients with major depression need to weigh various risks when deciding whether to use an antidepressant medication. (See "Severe antenatal unipolar major depression: Choosing treatment", section on 'Weighing the risks'.)

Antenatal major depression is frequently managed with pharmacotherapy. In a nationally representative survey in the United States that identified pregnant women who were treated for major depression (n = 375), the most common form of treatment was medications (received by 40 percent) [13]. In addition, it is estimated that among all pregnant women in the United States, antidepressants are used by more than 7 percent [30,31]. However, the stigma and shame that is associated with depression can be exacerbated during pregnancy, and may lead women to avoid using pharmacotherapy [22,32].

Although it is not clear if the effectiveness of antidepressants is the same in pregnant and nonpregnant women, we generally look to the data from the general population of adults. One indication that antidepressants have their expected effect in antenatal depression is the observation that discontinuation of antidepressants during pregnancy is associated with depressive relapses. (See "Severe antenatal unipolar major depression: Choosing treatment", section on 'Unplanned pregnancies and discontinuing antidepressants during pregnancy'.)

For depressed, pregnant women who are treated with antidepressants, we suggest that clinicians attempt to minimize fetal exposure by using monotherapy and doses at the low end of the therapeutic range, especially during the first trimester [4,8,33,34]. As an example, in managing depression with insomnia, it may be feasible to select a sedating antidepressant, rather than a more activating drug combined with trazodone or a benzodiazepine [35].

We suggest initiating antidepressants at low doses (eg, citalopram or fluoxetine at 10 mg/day, or sertraline at 25 mg/day) [36]. One reason is that the gastrointestinal side effects of some antidepressants may be aggravated during pregnancy. However, in prescribing the lowest effective dose, it is important to strive for remission and to avoid inadequate doses [8,22,36,37]. There is little to no evidence that lower doses decrease the risk of adverse obstetrical and neonatal outcomes. In addition, undertreatment exposes the fetus to both the medication and the mother's persistent depression.

Antidepressant drug doses may need to be increased as the pregnancy progresses, because prenatal pharmacokinetic changes may decrease antidepressant serum concentrations and possibly diminish treatment effects, especially during the third trimester. A literature review of prospective and retrospective studies found that pregnancy was associated with increased activity of hepatic enzymes induced by hormones, as well as an increased volume of distribution and increased hepatic and renal blood flow [38]. Thus, dose increases within the therapeutic dose range may be indicated for antidepressants such as certain selective serotonin reuptake inhibitors (SSRIs; eg, citalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline) and tricyclics (eg, clomipramine, imipramine, and nortriptyline).

In addition to monitoring symptoms (see 'Monitoring symptoms' above) to guide dosing, clinicians should monitor serum drug concentrations for certain medications (eg, desipramine, imipramine, and nortriptyline) with established therapeutic ranges [38]. (See "Tricyclic and tetracyclic drugs: Pharmacology, administration, and side effects", section on 'Plasma levels and therapeutic response'.)

Serum levels of SSRIs are typically not assayed because the relationship between serum concentrations and therapeutic effects is not well established [38]. However, it is reasonable to

use a serum level obtained prior to pregnancy during a period of euthymia as a target level during pregnancy. In addition, therapeutic reference ranges for SSRIs have been suggested by practice guidelines. (See "Selective serotonin reuptake inhibitors: Pharmacology, administration, and side effects", section on 'Medical tests and plasma levels'.)

Antidepressants that are prescribed during the third trimester are generally maintained through delivery; following delivery, we continue to use the same dose that was prescribed before delivery [36,38]. There is no evidence that tapering or discontinuing antidepressants at term reduces the risk of neonatal complications, and tapering or stopping antidepressants can increase the maternal risk of perinatal relapse. It is generally agreed the risks of postnatal depression (especially recurrent episodes) exceed the risks of neonatal complications [8]. (See "Postpartum unipolar major depression: Epidemiology, clinical features, assessment, and diagnosis", section on 'Adverse consequences' and "Antenatal exposure to selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs): Neonatal outcomes", section on 'Neonatal effects'.)

Some health care systems obtain a high resolution ultrasound in all pregnant patients at approximately week 18 of the pregnancy. For pregnant patients who are treated with antidepressants in health care systems that do not routinely monitor patients with ultrasounds, this should be discussed with the obstetrician. We recommend an ultrasound if the patient has a personal or family history of cardiac disease, or is receiving paroxetine. Echocardiography is also obtained if there is any suspicion of fetal cardiac disease or when paroxetine is used. Paroxetine may possibly be associated with a small absolute risk of congenital cardiac defects. Additional information about routine prenatal ultrasonography and the risk of antenatal paroxetine is discussed separately. (See "Antenatal use of antidepressants and the potential risk of teratogenicity and adverse pregnancy outcomes: Selective serotonin reuptake inhibitors", section on 'Paroxetine'.)

Managing nonresponse — If patients with antenatal unipolar major depression do not respond to initial treatment, we suggest the following steps:

- Verify that the patient has unipolar major depression rather than a different condition. (See "Unipolar major depression during pregnancy: Epidemiology, clinical features, assessment, and diagnosis", section on 'Differential diagnosis' and "Unipolar depression in adults: Assessment and diagnosis", section on 'Differential diagnosis'.)

- Ask about adherence with treatment because nonadherence is common during treatment of psychiatric disorders; improving adherence with pharmacotherapy or psychotherapy homework can convert nonresponders to responders.

- Determine whether there are significant life stressors (eg, nonsupportive partner) that need to be addressed.

- Establish if comorbid psychopathology (eg, anxiety disorder, personality disorder, or substance use disorder) is present (see "Unipolar depression in adults: Clinical features", section on 'Psychiatric'). If a disorder other than major depression is more salient, treatment should refocus upon the primary problem.

Making referrals — Primary care clinicians and obstetricians often treat pregnant patients with major depression. However, the diagnosis may not be clear or these clinicians may not be comfortable managing antenatal depression and thus refer patients to psychiatrists; referrals are also made if requested by patients. In addition, referral is usually indicated for patients with [4,9,16,39]:

- Severe depression (see "Severe antenatal unipolar major depression: Choosing treatment", section on 'Severity of illness')

- Suicidal ideation or behavior (see "Suicidal ideation and behavior in adults")

- Aggressive behavior (see "Assessment and emergency management of the acutely agitated or violent adult")

- Psychotic features (eg, delusions or hallucinations) (see "Unipolar major depression with psychotic features: Epidemiology, clinical features, assessment, and diagnosis")

- Catatonia (see "Catatonia in adults: Epidemiology, clinical features, assessment, and diagnosis")

- Poor judgement that places the patient or others at imminent risk of harm (including her other children)

- Psychiatric comorbidity, such as anxiety disorders, eating disorders, or substance use disorders (see "Unipolar depression in adults: Clinical features", section on 'Psychiatric')

- Nonresponse to pharmacotherapy and psychotherapy

- Bipolar major depression (see "Bipolar disorder in adults: Assessment and diagnosis", section on 'Unipolar major depression')

In addition, referral to social work may be appropriate; indications include problematic social circumstances, such as intimate partner violence or other trauma, unemployment, poverty, or homelessness. Social workers may also facilitate treatment uptake.

CHOOSING SPECIFIC TREATMENTS

Choosing specific treatments for antenatal unipolar major depression is discussed separately. (See "Mild to moderate episodes of antenatal unipolar major depression: Choosing treatment" and "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".)

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

SUMMARY

- Most women who are considering treatment for perinatal depression prefer to receive help at their obstetrics clinic, either from the obstetrician or a mental health clinician

located at the clinic. (See 'Setting' above.)

- It is important to assess the benefit of previous therapies in order to guide treatment selection. (See 'History of prior treatment' above.)

- We educate patients with antenatal unipolar major depression and families about the symptoms of depression, treatment options, and the potential risks of untreated depression and of antenatal exposure to antidepressants. In addition, we encourage patients to get adequate rest, maintain a consistent sleep-wake cycle, utilize supports, reduce stressors when possible, and continue prepregnancy exercise routines. (See 'Educating patients and families' above.)

- Clinicians are encouraged to routinely monitor symptoms of perinatal depression during treatment. We typically use the self-report, 10-item Edinburgh Postnatal Depression Scale (figure 1A-B). (See 'Monitoring symptoms' above.)

- Pregnant patients with major depression need to weigh various risks when deciding whether to use an antidepressant drug. If antidepressants are prescribed, doses may need to be increased, especially late in pregnancy. (See 'Prescribing antidepressants' above.)

- If patients with antenatal unipolar major depression do not respond to initial treatment, we suggest verifying the diagnosis, asking about adherence, and determining whether there are life stressors and/or comorbid psychiatric disorders that require attention. (See 'Managing nonresponse' above.)

- Although primary care clinicians and obstetricians can treat pregnant patients who are depressed, many patients are referred to psychiatrists. Indications for referral include severe major depression, suicidal ideation and behavior, psychotic features, and nonresponse to initial treatment. (See 'Making referrals' above.)

- Selecting a specific treatment depends in part upon the severity of the depressive syndrome. (See "Mild to moderate episodes of antenatal unipolar major depression: Choosing treatment" and "Severe antenatal unipolar major depression: Choosing treatment".)

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