Postpartum Depression: Part 2

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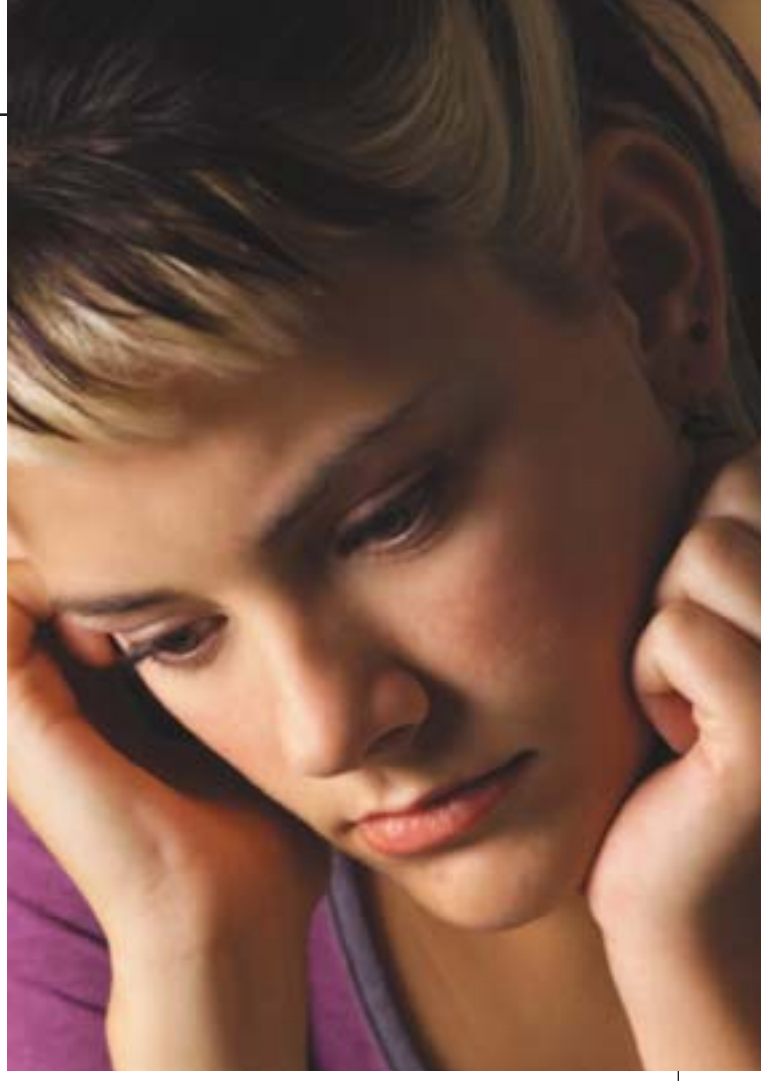

For most women, pregnancy is a time of well-being. For the vulnerable woman, however, pregnancy may precipitate or exacerbate a previous depression. Although changes in sleep, appetite and fatigue are symptoms associated with pregnancy, these changes may also herald the onset of depression. Patients who experience a two-week history of depressed mood with loss of interest, accompanied by changes in sleep, energy, concentration, appetite and memory, may be suffering from depression. Pregnancy often can exacerbate depressive symptoms. Untreated depression during pregnancy may interfere with the patient's day-to-day functioning and impair quality of life. Depression during pregnancy may impact the developing fetus. Babies born to mothers who are depressed tend to have low birth weights and are born prematurely.

What Causes Depression During Pregnancy?

Many factors can contribute to the onset of depression during pregnancy, the most common of which are underlying biological factors attributed to changes in brain chemistry. Women with a previous, or family, history of depression are at a high risk for developing depression during pregnancy. The various psychological and physical changes associated with pregnancy also can trigger the onset of depression.

Treatment of Depression During Pregnancy

Although depression can be a serious medical disorder, growing evidence shows that in addition to specific counseling and education treatments, antidepressants are safe for the mother and the growing baby.

Psychosocial Treatments

Treating depression during pregnancy can be challenging. Various risks and benefits of each treatment must be clearly discussed with the individual and family members. In most cases of mild depression with little disability, medications should be avoided, and supportive psychotherapy and education

should be offered as the major treatment. In more moderate to severe cases, where most of the diagnostic symptoms are met and dysfunction is evident, cognitive behavioural therapy and interpersonal therapy (IPT) are recommended.[1] IPT has been proven effective in at least one study.[2] IPT may be ideal for the pregnant, depressed woman who has feelings of guilt, has difficulty adjusting to her role as mother and experiences interpersonal problems. Psychotherapy may be combined with pharmacotherapy to treat moderate to severe depression during pregnancy.[1]

Summary

Postpartum Depression

- Any use of medication in pregnant, depressed patients must involve weighing the risk of exposing the developing fetus to medications *versus* the effects of untreated depression on the mother and fetus.
- Medications and electroconvulsive therapy (ECT) generally appear to be safe during pregnancy, postpartum and while breastfeeding.
- While the evidence for the safety of antidepressant medication is emerging, there is a need for longitudinal studies to further support existing evidence.

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Pharmacotherapy

Over half of pregnancies are unplanned.[3] The majority of pregnancies are documented at six to eight weeks of gestation and, in many cases, patients have been taking medications since conception.[3] In ideal circumstances, medication should be avoided, especially during the first 12 weeks when the baby's organ formation occurs. Various circumstances, however, do not make this a practical option. Any use of medication in pregnant, depressed patients must involve weighing the risk of exposing the developing fetus to medications *versus* the effects of untreated depression on the mother and fetus. Women with clearly documented bouts of depression, or those who have experienced an exacerbation of an underlying depression during pregnancy, should either continue taking their medications or consider taking one of the "safer antidepressants," such as selective serotonin reuptake inhibitors (SSRIs) or venlafaxine. Furthermore, women who are stable while taking medication, but demonstrate a rapid decompensation upon discontinuation, should be reinitiated on antidepressant medication. Guidelines for pregnant women who may have had one serious episode of depression, but have recovered, are less clear.

Potential risks to the fetus for medication exposure include organ malformation (teratogenecity), neonatal toxicity (perinatal syndromes) and postnatal behavioural sequelae (behavioural teratogenecity). The baseline incidence of major congenital malformation is 2% to 4%, and as high as 10% if minor malformations are involved.[4,5] The U.S. Food and Drug Administration (FDA) "Use in Pregnancy Rating System" is one of the standards used to determine and select appropriate medication during pregnancy (Table 1). Most psychotropic medications are "category C," indicating that more human data is needed and that they pose potential risks to the fetus. There is encouraging data, however, that most of the newer antidepressants, as well as tricyclic

Table 1

Key to FDA Use-in-Pregnancy Ratings

The U.S. FDA's use-in-pregnancy rating system weighs the degrees to which available information has ruled out the risk to the fetus against the drug's potential benefit to the patient. The ratings and their interpretation are as follows:

Category	Interpretation
A	*Controlled studies show no risk:* Adequate, well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester of pregnancy.
B	*No evidence of risk in humans:* Adequate, well-controlled studies in pregnant women have not shown increased risk of fetal abnormalities, despite adverse findings in animals, or, in the absence of adequate human studies, animal studies show no fetal risk. The chance of fetal harm is remote, but remains a possibility.
C	*Risk cannot be ruled out:* Adequate, well-controlled human studies are lacking, and animal studies have shown a risk to the fetus or are lacking, as well. There is a chance of fetal harm if the drug is administered during pregnancy, but the potential benefits may outweigh the potential risks.
D	*Positive evidence of risk:* Studies in humans, or investigational or post-marketing data, have demonstrated fetal risk. Nevertheless, potential benefits from the use of the drug may outweigh the potential risk. For example, the drug may be acceptable if needed in a life-threatening situation or serious disease for which safer drugs cannot be used or are ineffective.
X	*Contraindicated in pregnancy:* Studies in animals or humans, or investigational or post-marketing reports, have demonstrated positive evidence of fetal abnormalities or risk, which clearly outweighs any possible benefit to the patient.

Adapted from: Medical Economics Company: *Physicians' Desk Reference*. Medical Economics Company, Montvale, NH, 2000.

antidepressants (TCAs), are generally safe for the fetus and do not increase the risk of neonatal malformation or behavioural teratogenecity.[1] SSRIs generally are recommended as first-line treatments of depression during pregnancy. No study involving SSRIs has revealed an increased risk for teratogenecity in those exposed, as compared to those not exposed. Although fluoxetine has the greatest evidence of safety *in utero*, similar data is emerging with the use of citalopram, paroxetine, sertraline and fluvoxamine.[1,6] A recent study also suggested venlafaxine was safe during pregnancy.[7] In women who did not respond or tolerate SSRIs or venlafaxine, TCAs (*e.g.*, imipramine, nortriptyline and clomipramine) are safe alternative options.[8,9] Regarding potential behavioural sequelae, a recent study involving *in utero* exposure to fluoxetine revealed no effect on global intelligence quotient (IQ), language development or behavioural development in children followed for seven years after they were born.[10] Since anxiety and insomnia are common symptoms associated with depression, a sedative hypnotic is often needed. Although benzodiazepines generally should be avoided in the first trimester, discriminate use of lorazepam or clonazepam is preferable over long-acting agents,

such as diazepam. Finally, electroconvulsive therapy continues to be the treatment of choice for women with severe depression with suicidal ideation, psychosis and who are unresponsive or intolerant to medication, or in cases where physical health is a concern.[11]

Postpartum Depression

Despite the high prevalence rates and disability associated with postpartum depression, there are relatively few good studies that evaluate the role of pharmacological and psychotherapeutic treatment interventions. The discussion of therapy for postpartum depression will be divided into psychosocial and biological treatments.

Psychosocial treatments. IPT and cognitive behavioural therapy (CBT) have been shown to be effective treatments of milder cases of postpartum depression.[1] The goal of therapy is to assist the new mother in addressing guilt and role transition issues, educate her partner about postpartum depression and provide support during a time of increased stress. Classically, medications and psychotherapy are combined for moderate to severe forms of postpartum depression. Because of the increased demand of caretaking, psychosocial intervention aimed at obtaining household help for the mother also may aid in the recovery from mild forms of depression. A recent study showed psychoeducation was beneficial for patients and their partners when offered jointly, as opposed to the patient alone.[12]

Biological treatments. One double-blind study of fluoxetine showed effective treatment for depression in the first six to eight weeks postpartum. In the same study, fluoxetine and CBT were both effective treatments, with the combination not conferring any additional benefit.[13] Several open studies have reported the efficacy of sertraline, venlafaxine or fluoxetine for treating postpartum depression.[1] In all of these studies, standard doses of antidepressants were effective and well tolerated. Recently, estradiol has been shown to be effective as an adjunct with antidepressants, as well as in preventing the recurrence of postpartum depression.[14,15] Despite the role of estrogen in postpartum depression, this treatment option usually is reserved for individuals who respond poorly to standard antidepressants. Estrogen's role as an augmenting agent with antidepressants is unclear.

Prophylactic treatment for women with previous postpartum depression is controversial. Despite limited and conflicting data, a recent expert's opinion guideline suggests the use of antidepressants or psychotherapy may be beneficial three to four weeks prior to delivery or shortly after delivery in women with a previous history of postpartum depression.[1]

Postpartum Psychosis

Postpartum psychosis is often a medical emergency necessitating immediate hospitalization with aggressive intervention. In most cases of postpartum psychosis, electroconvulsive therapy (ECT) is the recommended treatment. ECT poses a very low risk for the mother and the breastfeeding infant. In patients who refuse ECT, combination therapy with antidepressants and high-potency neuroleptics, such as haloperidol or the newer atypical agents (*e.g.*, olanzapine and risperidone) are options to consider.

Antidepressants and Lactation

Historically, women treated with antidepressants were discouraged from breastfeeding. Although the decision to breastfeed should be made after a risk-to-benefit analysis has been carried out, growing data supports the use of antidepressants in women who wish to breast-feed. Data with SSRIs, including fluoxetine, paroxetine, citalopram, sertraline and fluvoxamine, as well as venlafaxine and TCAs, suggest they are safe in the newborn infant.[16,17] In most of these studies, the amount of the parent compound and its metabolite were at low or at near undetectable levels in the infant's serum. These studies indicate no associated toxicity to infants, with no observable physical or behavioural problems. One should be cautious, however, since there are no studies on the long-term developmental effects of using these medications during lactation.

Conclusion

Depression during pregnancy and postpartum can mean significant consequences for the mother, the fetus and the family. Untreated depression in the mother has a negative impact on the fetus and newborn. There is a growing body of literature that supports the use of psychological and biological interventions for the treatment of depression during pregnancy and postpartum. More specifically, medications and electroconvulsive therapy generally appear to be safe during pregnancy, postpartum and while breastfeeding. While the evidence for the safety of antidepressant medication is emerging, there is a need for longitudinal studies to further support existing evidence. CME

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