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Postpartum depression

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Abstract

Postpartum depression (PPD) affects up to 15% of mothers. Recent research has identified several psychosocial and biologic risk factors for PPD. The negative short-term and long-term effects on child development are well-established. PPD is under recognized and under treated. The obstetrician and pediatrician can serve important roles in screening for and treating PPD. Treatment options include psychotherapy and antidepressant medication. Obstacles to compliance with treatment recommendations include access to psychotherapists and concerns of breastfeeding mothers about exposure of the infant to antidepressant medication. Further research is needed to examine systematically the short-term and long-term effect of medication exposure through breastmilk on infant and child development.

Keywords

antidepressant; postnatal depression; postpartum depression; psychotherapy; treatment

We reviewed selected studies about the diagnosis and treatment of postpartum depression (PPD). Despite methodologic limitations, the results of several studies can provide treatment options for women with PPD. Women face difficult dilemmas about the negative effects of untreated psychiatric disorder in the postpartum period vs the risks of exposure to the breastfeeding infant from psychotropic medication. We have included a limited discussion about postpartum blues and postpartum psychosis.

PPD

Postpartum blues

Postpartum blues have been reported to occur in 15–85% of women within the first 10 days after giving birth, with a peak incidence at the fifth day.[1] Common symptoms include mood swings, mild elation, irritability, tearfulness, fatigue, and confusion.[1,2] Antenatal depression, previous depression not related to pregnancy, and previous premenstrual dysphoria have been identified as risk factors.[1] No clear biologic measure has been identified to be causative or predictive of postpartum blues. Although postpartum blues is a common and transient

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postpartum occurrence and generally does not require intervention, its recognition is important because postpartum blues is a risk factor for subsequent PPD.[3]

PPD: diagnosis and epidemiologic factors

PPD is defined strictly in the psychiatric nomenclature as a major depressive disorder (MDD) with a specifier of postpartum onset within 1 month after childbirth.[4] However, depression in women during the postpartum period may start during pregnancy or may have onset beyond the first postpartum month.[5] To meet criteria for MDD, depressed mood or loss of interest or pleasure in activities must be present for at least 2 weeks. In addition, symptoms of sleep disturbance, appetite disturbance, loss of energy, feelings of worthlessness or guilt, diminished concentration, and thoughts of suicide may be present.[4] The diagnosis of PPD is challenging because of changes in sleep patterns, changes in appetite, and excessive fatigue being routine for women after delivery.[6]

The optimal time to screen for PPD is between 2 weeks and 6 months after delivery.[6] Several self-report measures that are available to screen for PPD include the Edinburgh Postnatal Depression Scale,[7] which is a validated and widely used 10-item questionnaire. An Edinburgh Postnatal Depression Scale score of ≥12 is indicative of probable PPD.[7] The Postpartum Depression Screening Scale[8] is another self-report screening measure that is popular with clinicians because of its construct validity and emphasis on clinical domains; however, because of high false-positive rates for PPD, it has been reported to be less accurate than the Edinburgh Postnatal Depression Scale.[9]

A systematic review of studies that diagnosed depression by clinical structured interview reported that the point prevalence of MDD and minor depression ranged from 6.5–12.9% through the first 6 postpartum months, peaking at 2 and 6 months after delivery.[5] A large cohort study that was conducted in Denmark reported that the first 90 days after delivery represented a time of increased risk of new-onset psychiatric disorder (mostly PPD) in new primiparous mothers, but not in new fathers.[10] Other recent studies document an increased risk of MDD during the postpartum period.[11,12] The prevalence of PPD varies in non-Western countries from 0.5–60%; cultural factors can influence the development and reporting of PPD.[13]

Psychosocial risk factors for PPD include MDD during pregnancy, anxiety during pregnancy, previous nonpuerperal MDD, previous premenstrual dysphoria, stressful life events during pregnancy or the early puerperium, poor social support, marital conflict, low income, immigrant status, and young maternal age.[14,15] A recent study identified previous depression, current depression and anxiety, and low partner support as key risk factors.[16]

PPD may be related to a differential sensitivity to hormonal fluctuations. Euthymic women with previous PPD experienced dysphoria after both the addition and withdrawal of supraphysiologic doses of estradiol and progesterone, compared with healthy control subjects.[17] In addition to sensitivity to estrogen and progesterone fluctuations, biologic theories have included fluctuations of other gonadal hormone and neuroactive steroid levels after delivery, altered cytokines and HPA axis hormones, and altered fatty acid, oxytocin, and arginine vasopressin levels.[18,19] Involvement of the serotonin system has been suggested by reports of altered platelet serotonin transporter binding[20] and decreased postsynaptic serotonin-1A receptor binding in the anterior cingulate and mesiotemporal cortices.[21] A recent study that used a functional magnetic resonance imaging (fMRI) neuropsychologic activation paradigm suggested altered neural processing in women with PPD.[22]

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Normal fluctuations in hormonal levels during pregnancy and after delivery result in changes in sleep patterns. Declining levels of progesterone in the early postpartum period promote insomnia.[23] In the first postpartum month, decreased sleep efficiency and increased slow wave sleep have been reported.[23,24] The changes in hormones and sleep during the early postpartum period may contribute major vulnerability to the onset of PPD. A recent study identified difficulty falling asleep in the first 3 months after delivery as a possible risk factor for PPD.[25] In addition, infant sleep disturbance may be both a risk factor for and an outcome of PPD in the early postpartum period.[26,27] Studies have suggested that persistent infant and child sleep problems are related to maternal depression.[28,29] Despite the consistent findings of a relationship between maternal depression and infant and child sleep problems, a causal pathway has not been determined, and few studies have measured infant sleep objectively.

Role of obstetricians and pediatricians

Numerous studies have reported on the low rates of screening, diagnosis, and treatment of perinatal depression in medical settings. Clinician discomfort with psychiatric disorders, time constraints, low belief in maternal mental health having an important effect on child development, and lack of knowledge about resources are some of the barriers to clinician screening for psychiatric disorders in medical settings.[30–32] However, the postpartum obstetric visit and pediatric well-baby visits are opportunities for the clinician to assess the mother's clinical status.[31,33] Although women with PPD are often hesitant to divulge their mood and anxiety symptoms to their clinician because of guilt about having symptoms when motherhood is expected to be joyful, there may be indicators that further evaluation is needed. For example, PPD may lead to negative maternal perceptions of infant temperament and behavioral patterns; such complaints should be addressed in the context of the infant's behavior and how well the mother is coping with these difficulties.[34] PPD has been associated with frequent nonroutine visits to the pediatrician; such visits and telephone contacts may be warranted but could also be an indicator for further assessment of maternal mood and family functioning.[35] Follow-up with the woman who is referred for treatment within the practice or to a mental health clinician reinforces the importance of treatment recommendations.

Risks to children of not treating PPD

There is a well-established relationship between untreated maternal depression and impaired child development.[36,37] Infant and child outcomes that are associated with PPD include a higher incidence of excessive infant crying or colic, sleep problems, and temperamental difficulties.[34,38] Infant crying and sleeping problems may increase the risk for new onset PPD but may also be reported more frequently by women with PPD. In a study of > 600 infants, objective evidence of infant regulation difficulties were found as early as 1 month after delivery, with infants of mothers with PPD having poorer self-regulation, more stress signs, and heightened arousal compared with infants of mothers without PPD.[39] PPD is associated with negative mother-infant interactions that include maternal withdrawal, disengagement, intrusion, and hostility.[40,41] Women with PPD may be less likely to initiate or maintain breastfeeding; depressive symptoms commonly precede the early cessation of breastfeeding.[42,43]

PPD is linked to poor cognitive functioning, behavioral inhibition, and emotional maladjustment in infants and children.[44–46] Persistent untreated maternal depression is associated with violent behavior and externalizing disorders (eg, conduct disorders)[47–49] and with psychiatric and medical disorders in adolescence.[50] The complex relationship between maternal depression and child behavioral-emotional development is not yet understood but is likely to be a multidimensional progression that may onset during pregnancy. Women

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with PPD often have been depressed during pregnancy,[5] which is a potential source of exposure or influence on the fetus. The few published studies on the effects of antenatal depression on fetal outcomes have not always used a diagnosis of MDD but have shown that higher levels of self-reported depressive symptoms during pregnancy were related to heightened fetal behavioral and physiologic reactivity.[51] Alterations in fetal neurobehavioral development are likely to influence infant outcomes. The serious negative effects of PPD on the mother, the infant, and the other family members have made the recognition, prevention, and treatment of PPD a current area of noted public health significance. Recent evidence suggests that successful treatment of PPD may not be sufficient to improve attachment, temperament, and cognitive development in infants and toddlers,[52,53] which indicates that efforts toward the prevention and treatment of depression during pregnancy and after delivery are critical. Additional focus on mother-infant attachment and the needs of the family are also indicated.

Suicide during the postpartum period

Completed suicide rates are lower during the postpartum period compared with nonpuerperal time periods, although rates in postpartum adolescents are higher than in older postpartum women.[54] A study of perinatal maternal deaths in the United Kingdom from 1997–1999 reported that suicide was the leading cause of maternal death, was increased in women with psychiatric and substance abuse disorders, and was more likely to be a violent death compared with the suicides of men and nonpuerperal women.[55] Suicide may also be a leading cause of maternal deaths in Australia.[56]

A study of a United States population sample reported that there was a 3 times greater risk of a suicide attempt and that inpatient psychiatric admissions were increased after fetal death or infant death in the first postpartum year.[57] In this study, labor and delivery complications, cesarean section, pre-term delivery, low birthweight, and congenital malformations were not associated with increased risk of suicide attempts. A review of studies that confirmed that suicide rates are lower during pregnancy and the postpartum period emphasized that perinatal women complete suicide by more violent and lethal means than do women who are not perinatal.[58] Assessment of suicidality in the perinatal woman should include specific inquiry about depressed mood, substance abuse, previous suicide attempts, current or previous psychiatric illness, previous trauma, current intimate partner violence, and access to firearms.[58,59]

Postpartum psychosis

Postpartum psychosis occurs in 1 of 500 mothers, with rapid onset in the first 2–4 weeks after delivery.[60] Postpartum psychosis includes confused thinking, mood swings, delusions, paranoia, disorganized behavior, poor judgment, and impaired functioning.[61] Postpartum psychosis is considered a psychiatric emergency and usually results in inpatient psychiatric hospitalization. Risk factors include a previous episode of postpartum psychosis, previous hospitalization for a manic or psychotic episode, recent discontinuation of mood stabilizers, primiparity, obstetric complications, sleep deprivation, and a family history of bipolar disorder or postpartum psychosis.[61–63] Longitudinal studies suggest that most cases of postpartum psychosis are related to bipolar disorder, not schizophrenia.[61]

Neonaticide and infanticide

Infanticide is 1 of the most serious risks of postpartum psychosis. The rate of homicide of infants up to 1 year of age is 8 per 100,000 in the United States,[64] but it is unknown how many women with postpartum psychosis commit infanticide. Symptom exacerbation, command hallucinations, and the stressor of new infant care can increase the risk of infanticide after delivery in a mother with psychosis.[65] Infanticide may also occur in the

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context of severe PPD, caused by neglect and abuse, because of the child being unwanted or as revenge against the infant's father.[65,66] Between 16% and 29% of mothers who kill their children also kill themselves.[64] *Neonaticide* is defined as killing a newborn infant within 24 hours of birth and is associated with denial of pregnancy, lack of prenatal care, dissociation, depersonalization, and intermittent amnesia of delivery.[64,67] More study is needed of risk factors for neonaticide and infanticide.[64] Intrusive thoughts of potential accidental harm occurring to a newborn infant are ubiquitous, and intrusive thoughts of intentionally harming an infant are also common.[68] It is important to reassure women that intrusive thoughts of harm to an infant or thoughts of infanticide rarely are acted upon.

Treatment of PPD

Psychotherapy

Interpersonal psychotherapy (IPT), a short-term efficacious treatment for MDD that addresses interpersonal issues (such as role change, the marital relationship, social support, and life stressors) is highly pertinent to the needs of women during the postpartum period.[69] A randomized controlled trial (RCT) reported that 12 sessions of individual IPT was superior in efficacy to a waitlist control in 120 women with PPD in reducing depression and improving social adjustment.[70] A smaller RCT in women with PPD also reported that individual IPT was superior to a wait-list condition.[71] Additionally, 2 small open studies of group IPT demonstrated significant reduction of depression in women with PPD.[72,73]

Systematic reviews of treatments for PPD have suggested that individual IPT, cognitive-behavior therapy (CBT), and psychodynamic therapy may be effective psychologic treatments for PPD.[74] Overall, psychologic treatments for PPD demonstrate moderate effect sizes[75]; antidepressant medications demonstrate larger effect sizes.[76] Methodologic flaws of studies of psychosocial treatments include small sample sizes, short-term treatments, lack of control groups, poorly defined treatment interventions and outcome measures, lack of partner participation, and lack of assessment of infant outcome.[74] Although 1 study included partners as 1 component of psychologic treatments,[77] there has not been systematic study of couples therapy in women with PPD. Initial positive reports that deserve further study include telephone support, lay peer support, individual counseling in the home, nurse-led or health visitor–led support groups, and group therapy led by mental health clinicians.[74,78] Women with mild PPD may respond to treatment by nonmental health professionals or to individual or group counseling with a mental health professional, although women with more severe PPD may need IPT or CBT to be administered by trained professionals and/or antidepressant medication.[78] Women who are breastfeeding may prefer psychotherapy over medication for the treatment of PPD.[79–81] Barriers to participation in psychotherapy include perceived negative stigma, lack of availability of a trained therapist in IPT or CBT, time commitment, child-care needs, and cost.[82]

Mother-baby units

The United States has lagged behind Europe and Australia in the recognition and treatment of perinatal psychiatric disorders. The practice of joint admission of mothers and infants was prompted by concerns about disrupting the mother-infant relationship during intensive psychiatric treatment. The first joint mother-baby admission occurred in the United Kingdom 60 years ago, and joint admission now takes place routinely in the United Kingdom, Australia, France, Belgium, Germany, and the Netherlands. Parent-infant units have been established in Australia. The only known current mother-baby unit in the United States is conducted as a psychiatric partial hospital.[83] Advantages of mother-baby units include support, absence of breastfeeding disruption or cessation, multidisciplinary

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treatment of PPD, direct observation of mother-infant interaction, and the promotion and modeling of a healthy maternal-child relationship.

Antidepressant treatment

Four RCTs with antidepressant medication have been conducted in women with PPD; 2 were placebo-controlled, and 2 were active comparator studies. One placebo-controlled RCT compared immediate-release flexible-dosed paroxetine with placebo in 70 women with postpartum onset of MDD.[84] After 8 weeks of treatment, both groups improved significantly over time, but paroxetine was superior to placebo in terms of remission of depression (remission rates were 37% and 15%, respectively). Approximately 40% of the subjects in this study were breastfeeding, but the effects in infants were not described in the published study.[84] Another placebo-controlled RCT compared fluoxetine, placebo, and counseling (based loosely on CBT principles) in 87 women with PPD.[85] Women were assigned randomly to 12 weeks of fluoxetine 20 mg daily and 6 counseling sessions, fluoxetine 20 mg daily and 1 counseling session, placebo and 6 counseling sessions, or placebo and 1 counseling session. Fluoxetine was significantly superior to placebo in reducing the severity of depressive symptoms. The combination of fluoxetine and 6 sessions of counseling were not superior to either treatment alone. Women who were breastfeeding were excluded from this study; most of the women who were enrolled had mild-to-moderate severity of depressive symptoms.

A comparator RCT randomly assigned 109 women with PPD to sertraline or nortriptyline, both of which were administered in an escalating dose regimen over 8 weeks.[86] Almost one-half of the subjects remitted by week 8 on either antidepressant. No adverse effects in breastfeeding infants were reported, and infant serum levels were near or below quantifiable levels.[86] Another comparator RCT compared paroxetine with combined paroxetine/CBT in 35 women with PPD and comorbid anxiety disorders.[87] Paroxetine was flexibly dosed over 12 weeks, and CBT was provided in 12 individual sessions. Both treatments led to significant improvements on measures of depression, and there were no significant differences between treatments. Approximately one-half of the subjects were breastfeeding, but antidepressant side-effects and serum levels in infants were not reported. The anxiety comorbidity in the latter study and the lack of a placebo control in both of these comparator RCTs limits conclusions about the efficacy of these treatments for PPD. Notably, the remission rate with paroxetine was lower in the paroxetine study that included a placebo control.[84] Small open trials and case reports have also suggested efficacy of antidepressants for the treatment of PPD.[82,88]

Additional treatments

Studies have suggested a benefit with infant massage,[89] exercise,[90] sleep deprivation,[91] infant sleep intervention,[92] and electroconvulsive therapy.[93] Studies have reported that postpartum use of estrogen may have a role,[94,95] although the postpartum use of progesterone has not been promising.[82] A small study reported that early morning bright light therapy was not more effective than sham dim red light in the reduction of depressive symptoms.[96] Two recent RCTs failed to demonstrate superior efficacy of omega-3 supplementation, compared with placebo.[97,98]

Antidepressants and breastfeeding

The breastfeeding woman with PPD must weigh the potential efficacy of antidepressant medication for her depression, the potential risks of exposure of her infant to antidepressant medication through the breastfeeding, and the known negative effects of not treating her depression on child development. Breastfeeding has multiple benefits for a developing infant,[42] and a woman with PPD may believe that breastfeeding is an important positive

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experience that she is able to share with her infant in her depressed state. There is a growing observational database of side-effects in infants who are exposed to antidepressants through breast milk, and the choice of medication should be chosen after review of these data.[99] The Food and Drug Administration has announced that, in the future, medications will be classified by their risk summary, clinical considerations, and data in terms of lactation.[100] Measurement of infant antidepressant serum levels and breast milk analyses are not obtained routinely in clinical care,[101] and milk-to-plasma ratios may not be relevant to adverse effects.[102] When an antidepressant is started in the woman after delivery, it is recommended to start with low doses and to titrate the dose up slowly while monitoring the infant for adverse effects.[82] Possible adverse effects in the breastfeeding infants include irritability, sedation, poor weight gain, or a change in feeding patterns.[103,104] Adverse events are most likely to occur in newborn infants up to 8 weeks of age, and infants who are born prematurely or with medical problems may be at increased risk.[103] Infant exposure to antidepressant medication can be minimized by avoiding breastfeeding at the time of peak antidepressant concentration in the breast milk.[105] If adverse effects in the infant are noted, options include decreasing the dose, changing to partial or full bottlefeeding, or changing the medication. Collaboration between the pediatrician and mental health clinician is important.

Several reviews of the safety of selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), and newer antidepressants with breast-feeding have been conducted.[99,104,106,107] A pooled analysis of antidepressant levels in mother-infant dyads concluded that sertraline, paroxetine, and nortriptyline usually yield undetectable infant serum levels and that elevated infant levels are more likely with fluoxetine and citalopram.[107] Sertraline has been reported to have minimal or no effect on central serotonin transport in the infant.[108] Case reports of adverse effects in breastfeeding infants have been reported with fluoxetine, citalopram, doxepin, bupropion, and nefazodone.[82,88,101] If after delivery, a woman is euthymic with antidepressant therapy that is known to be associated potentially with mild adverse effects or high infant serum levels, it may be more advisable to monitor the infant carefully rather than to switch the antidepressant.[82,104] Even if there are no adverse effects and unquantifiable levels in infants, the long-term effects of antidepressant exposure through breast milk on child cognitive, motor, neurologic, and behavioral development are unclear.[109]

Other psychotropic medications and breastfeeding

Some women with PPD may be administered an adjunctive benzodiazepine for anxiety or insomnia. Sedation and poor feeding have been reported in breast-feeding infants who are exposed to benzodiazepines, and divided low doses has been advised.[101] Other psychotropic medication may be used by breastfeeding women with bipolar or psychotic illness or severe depression. Even though it was reported recently that lithium could be used during breastfeeding with careful infant serum level monitoring,[110] lithium generally has not been recommended during breastfeeding because of reports of hypothermia, hypotonia, cyanosis, T-wave inversion, and lethargy reported in infants.[61,101,111] There is a paucity of data about the safety of the newer antiepileptic drugs and atypical antipsy-chotics.[105] Valproate and carbamazepine have been used safely during breastfeeding. It was reported recently that infant serum levels of lamotrigine are variable and sometimes high after breastfeeding.[112] Preliminary data have suggested that oxcarbazepine, topiramate, gabapentin, and levetiracetam are not associated with adverse effects.[61,105,111] Sporadic adverse effects have been reported with olanzapine, clozapine, and traditional antipsychotics.[113] Infant monitoring should match the monitoring of potential adverse events that is used in adults.[105] Studies that evaluate the long-term effect on child development after breastfeeding exposure to anxiolytics, mood stabilizers, and antipsychotics are needed.

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Treatment dilemmas for women with PPD

It can be argued that the risks of exposure to PPD outweigh at least the short-term risks of infant exposure to antidepressants through breast milk, because the multiple negative effects of untreated PPD on short-term and long-term child development are well-established. In addition to the multiple known benefits for infants with breastfeeding,[42] a recent large sample study reported that prolonged and exclusive breastfeeding was associated with improved cognitive development in 6-year-old children.[114] Women who are breastfeeding may prefer psychotherapy over medication for the treatment of PPD, but it may be less effective than pharmacotherapy for severely depressed women. For these women and for women whose symptoms are unresponsive to nonpharmacologic treatments, the consideration of antidepressant medication may be necessary. All psychotropic medications pass into breast milk, and the potential for infant exposure exists with each medication. Although observational reports suggest a lack of short-term adverse effects in infants with many psychotropic medications, few studies have examined long-term effects. Discussions of the treatment options with the patient and her partner after delivery must include the patient's personal psychiatric history and previous response to treatment, the risks of no treatment, available data about the safety of medications with breastfeeding, and her individual expectations and treatment preferences.[103] Time constraints, financial restraints, and perceived cultural dissonance can lead to poor treatment adherence. Even with treatment adherence support in low-income mothers in Chile, the initial benefit of multicomponent care (including psychosocial support and medication) for PPD, compared with usual care, was attenuated after 6 months.[115]

Comment

Future efforts hopefully will improve the screening and identification of psychiatric disorders in women at their postpartum visit with the obstetrician and at well-baby visits with the pediatrician. Untreated depression and psychotropic medications for the breastfeeding woman each involve exposure of the child to potential short-term and long-term negative effects. Psychotherapy is a treatment option for women with PPD, with IPT being the most validated psychotherapy to be studied to date. Antidepressant medications are also efficacious for PPD. The critical goal of treatment is the resolution of the mother's psychiatric symptoms. Breastfeeding has multiple known benefits for infant development, and a breastfeeding woman with PPD does not need necessarily to decline pharmacotherapy. Sertraline is the first-line antidepressant used in PPD in breastfeeding women because of the paucity of adverse effects that have been reported in breastfeeding infants. Paroxetine or nortriptyline are second-line agents in women who are unable to tolerate or who do not respond to sertraline. Clinicians and patients can monitor current knowledge about breastfeeding and medications through publications[116] and websites that update and review published information frequently (such as LactMed on http://toxnet.nlm.nih.gov, www.mededppd.org, www.postpartum.net, www.womensmental-health.org, and www.motherrisk.org). Although antidepressants appear to be effective for PPD, there is a need for large placebo-controlled RCTs of antidepressants in women with PPD of a least moderate severity. Breastfeeding women must be included in pharmacotherapy trials, and potential adverse effects in infants must be assessed systematically. Future studies are needed to confirm the efficacy of psychotherapies for PPD, compare antidepressants to psychotherapy, and compare combined psychotherapy/antidepressant treatment to either treatment alone. Further studies of the factors that govern treatment selection and systematic studies of nonpharmacologic and alternative treatments are needed. Longitudinal follow-up studies that will examine the long-term effects of untreated maternal depression and exposure to psychotropic medication on infant and child cognitive, motor, behavioral, and neurologic development are critically needed to help guide women with depression during the postpartum period.

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