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When She Says "No" to Medication: Psychotherapy for Antepartum Depression

Anna R. Brandon · Marlene P. Freeman

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Abstract Many women suffering from major depressive disorder during pregnancy are hesitant to initiate or continue antidepressant treatment during preconception planning, conception, pregnancy, and lactation (perinatal period). Over the past few decades, various psychotherapeutic approaches have been found to be efficacious for depression in general population research. Several observational and quasi-experimental studies also suggest that psychotherapy can be a safe first-line treatment for perinatal women with mild to moderate depression. This article summarizes findings to date regarding the use of psychotherapy for depression occurring during pregnancy and describes the adaptations made to tailor the treatment to the unique needs of women in the perinatal period.

Keywords Pregnancy · Antenatal · Perinatal · Mood disorders · Major depressive disorder · Depression · Psychotherapy · Interpersonal psychotherapy · Cognitive-behavioral psychotherapy · Psychosocial intervention

A. R. Brandon (✉)
Department of Psychiatry,
University of North Carolina at Chapel Hill School of Medicine,
Campus Box 7160, Chapel Hill, NC 27599-7160, USA
e-mail: anna_brandon@med.unc.edu

M. P. Freeman
Perinatal and Reproductive Psychiatry Program,
Harvard University Medical School,
185 Cambridge Street, 2nd Floor,
Boston, MA 02114, USA
e-mail: mfreeman@partners.org

Introduction

Current epidemiologic research has established that pregnancy does not put mental illness "on hold"; on the contrary, women with a history of unipolar or bipolar depression, anxiety disorders, eating disorders, substance dependence, or schizophrenia are particularly vulnerable to relapse in the perinatal period. Depression alone affects 8% to 20% of antenatal women, overshadowing the other most common obstetric illnesses (eg, gestational diabetes mellitus, with a prevalence of 2%–10% of US pregnancies annually, and hypertension, with a prevalence estimated at 6%–8%) [1–3].

Just as gestational diabetes and hypertension have clear associations with pregnancy outcomes, mental illness does as well. Newborns of depressed mothers mirror the same disrupted biochemistry of their mothers, reflecting abnormal serum levels of cortisol, dopamine, and serotonin [4]. Depression-exposed neonates also display less than optimal habituation, orientation, motor activity, and autonomic stability [5]; greater arousal and less attentiveness [6, 7]; less mature physiologic development [8, 9]; and increased irritability [10]. Along with other psychiatric illnesses, depression during pregnancy is associated with higher rates of prematurity [5, 11] and increased neonate admission to intensive care units [12, 13]. Alongside the negative fetal effects of depression are significant maternal sequelae. Increased maternal tobacco and substance abuse [14–17], lower health-related quality of life [18], increases in operative deliveries, use of epidural anesthesia [13], risk of preeclampsia [19], general illness during pregnancy [20], and poorer health outcomes in general across populations internationally are associated with antenatal depression [21]. The National Violent Death Reporting System

estimates suicide rates at 2 per 100,000 pregnancies, more than double the rate of death from preeclampsia and eclampsia [22, 23•, 24]. These sobering statistics emphasize the marked human and economic burden that antenatal depression places upon families and society, as well as the necessity for efficacious treatment.

Assessment

Because the characteristics of major depressive disorder (MDD) and pregnancy overlap, particularly the somatic symptoms, assessment of mood can be challenging. The most often used quick self-report screening measure for perinatal women is the Edinburgh Postnatal Depression Scale (EPDS) [25], although the General Health Questionnaire, the nine-item Patient Health Questionnaire, and the Beck Depression Inventory all have been used during pregnancy [26••, 27]. Widely accessible on the Internet in many languages, free of charge, and validated in diverse subpopulations of perinatal women, the ten questions of the EPDS report mood and anxiety symptoms over the past 7 days. The threshold score of 12/13 is the most widely used to identify women who should receive a clinical interview to establish or rule out MDD [26••].

Because depression during pregnancy is one of the most robust risk factors for depression in the postpartum period, vigilant monitoring throughout treatment is important [28]. When possible, additional administrations of the EPDS (or other symptom scale) allow continual evaluation of intervention response to inform treatment planning. Nonresponse to a first-line approach should be speedily addressed by recommending to the patient alternative or supplemental treatment options.

Current Treatment Recommendations for Perinatal Depression

Treatment algorithms for mood disorders occurring during pregnancy and the postpartum period based on case reports, pregnancy registry analyses, observational research, and peer consultations have been widely disseminated [26••, 29••]. The ensuing discussion, however, is limited by the dearth of research conducted according to the gold standard: the randomized controlled trial (RCT) [30•]. Appropriate concern for fetal effects of treatment, even nonpharmacologic treatment, has resulted in widespread reticence on the part of regulatory agencies, funding agencies, and pharmaceutical corporations to design, sponsor, or approve protocols that include pregnant participants. An unfortunate byproduct of this state of affairs is the virtually automatic exclusion of pregnant women from anything other than registries or observational studies, limiting the confidence in perinatal treatment safety and efficacy enjoyed by women outside the context of pregnancy.

Although antidepressant medication may be appropriate treatment for some women during pregnancy, and antidepressant discontinuation is associated with a high risk of depressive relapse, many women wish to discontinue or avoid antidepressants during pregnancy. Those who do use medications during pregnancy may also wish to maximize nonpharmacologic treatments as well, often to avoid higher doses or augmentation with other medications. While antidepressants (particularly selective serotonin reuptake inhibitors) have a large body of reproductive safety data, complications have been reported, although not consistently. Adverse effects of medication that have been reported include birth defects such as cardiovascular malformations, persistent pulmonary hypertension of the newborn, and neonatal symptoms [29••]. Although the data do not support consistent patterns of malformations that would signal that antidepressants are teratogens, an efficacious nonmedication treatment is ideal for the avoidance of medication exposure and use of minimal doses during pregnancy.

Nonpharmacologic approaches for mild to moderate MDD during pregnancy reported in case studies and small observational studies include acupuncture [31], massage [31], omega fatty acid supplementation [32], and light therapy [33]. For severe or treatment-resistant depression, repetitive transcranial magnetic stimulation [34] and electroconvulsive therapy have demonstrated safety for the fetus and have ameliorated maternal depression [35]. However, the prevailing attitude is that psychotherapy is a reasonable first-line approach to mild and moderate perinatal depression and an important augmentation to medication for severe depression [26••]. In addition to a large evidence base for the efficacy of psychotherapy in the general population [36], a small cohort of clinical investigators across almost three decades of research has provided strong evidence that psychotherapy is a safe first-line recommendation during the perinatal period for women with mild to moderate depression [26••, 37–39]. The aim of this report is to identify and describe psychotherapy approaches that have been tested in samples of antenatal women, and to summarize findings.

Psychotherapeutic Interventions

Based on current guidelines for the primary care population, problem-solving therapy, interpersonal psychotherapy (IPT), and cognitive-behavioral therapy (CBT) have demonstrated efficacy in the treatment of depression, with CBT

and IPT reducing symptoms as efficaciously as pharmacology [40, 41]. Psychotherapy is also a valuable augmentation strategy for treatment-resistant or chronic MDD, with polytherapy often superior to medication alone [42, 43]. The most robust moderator characteristics associated with better medication response to depression—shorter history of illness (<4 years), no family history of depression, and social support—are also associated with better response to psychotherapy [44–46]. To date, few treatments have been fully reported upon in antepartum treatment research [38].

General indicators for psychotherapeutic treatment identified over the history of psychotherapy research are patient motivation to participate in therapy, willingness to explore new solutions to problems, ability to form an alliance with the therapist, capacity to integrate affect and experience constructively, previous history of successful psychotherapy treatment, and available resources to attend weekly sessions. Contraindications for standalone psychotherapy intervention are high risk of suicide (history of suicide attempt and/or endorsing plan and means), substance use/abuse, and florid psychosis [47]. Personality disorders do not necessarily contraindicate psychotherapy, but an individual with severe impairment is probably not a candidate for any brief treatment.

Interpersonal Psychotherapy

IPT is the first documented intervention specifically adapted for perinatal depression and the only randomized psychotherapy study in an antenatal population reported in the literature [47–51]. Originally developed by Klerman and Weismann in the 1980s [52], the brief (12–16 sessions) guided approach of IPT can be delivered by a range of mental health professionals, including nurses, social workers, chaplains, physicians, and counselors. IPT targets at least one of the known risk factors for perinatal depression—poor social support [28, 53]—and focuses on one or more of four core experiences that are both common to the onset of depression and particularly relevant for women during childbearing and early parenthood (interpersonal conflicts or disputes, grief and loss, role transitions, and interpersonal sensitivity) [54]. During the initial phase (two to four sessions), an interpersonal history is gathered, formulating the manner in which the patient relates to the important others in her world and how she asks for help when needed, and identifying who populates her interpersonal world. Depression is framed as an illness much like any other, necessitating treatment and time for healing. The middle phase (five to seven sessions) of IPT addresses the problem area or focus of treatment by means of communication analysis, problem solving, and role playing. The final phase (three or four sessions) entails processing the impending disruption of the therapeutic relationship, summarizing the improvements made over the course of therapy, exploring strategies for maintaining improvement, and reviewing warning signals of potential relapse. The therapist may frame termination as an "adjournment," leaving the door open for the patient to return in the future if symptoms return.

Since the early research more than a decade ago, IPT has been tested in individual and group formats [50, 55–57] for both prevention and treatment of depression throughout the antenatal and postnatal period [50, 51, 58], and for assisting women in the perinatal period who are struggling with coexisting illnesses, adverse life events, or comorbid psychiatric illnesses [49, 59–63]. In a small RCT recruiting pregnant women diagnosed by clinical interview with MDD, a bilingual study team demonstrated that 16 weeks of IPT was superior to a parenting education control program in treating depressive symptoms [50]. Although conclusions are limited by the small sample size (n=38) and a significant attrition rate (n=12; 24%), it is important to note that IPT demonstrated sensitivity to ethnic and socioeconomic diversity both in this individual treatment trial and in a subsequent uncontrolled trial of IPT in a group format [58, 64].

Viewing pregnancy as a complicated life-changing experience, the broad adaptations of IPT to the antepartum patient include highlighting her affect surrounding any personal losses sustained by moving from personal independence to motherhood, exploring expectations surrounding the "mother" role and mastering the role transition, identifying her support needs from her partner and/or family and friends, and helping resolve marital disputes [47, 54, 65, 66].

Two specific variations of IPT are described in the literature. Spinelli and Endicott [50] added a fifth problem area, complicated pregnancy, to the original set, directing attention to specific gestational problems such as unplanned/undesired pregnancy, medical problems associated with the pregnancy itself, obstetrical complications, multiple births, and congenital anomalies. Responding to the challenges long-term psychotherapy courses pose for low-income women, Grote et al. [64] reduced the number of acute sessions from 16 to 8 (brief IPT), offered up to six monthly maintenance sessions in the postpartum, and allowed some sessions to be conducted over the telephone when the participant was unable to come to the clinic. Both investigative teams are currently investigating these adaptations further in larger controlled studies.

Strong patient indicators for making IPT a first-line treatment for the treatment of depression are a relatively secure attachment style, low level of social dysfunction at intake, the ability to relate coherent narratives about interpersonal relationships and incidents, high degree of interpersonal sensitivity, a specific interpersonal focus of distress, and an available social support system [67, 68]. In addition, a qualitative study suggested that the ability to entertain multiple perspectives, awareness of others' feelings, desire to effect change, and a sense of self-

responsibility contributed to response to IPT [69]. Patients with high levels of panic, agoraphobia, or somatic anxiety, or individuals with avoidant personality characteristics may not respond fully to IPT [70].

Cognitive-Behavioral Therapy

Although the family of cognitive therapies has been extensively tested in the general population, there is not a large body of literature regarding use for depression specifically during pregnancy. Integrating behavior theory from the early 20th century [71] and cognitive therapy developed in the 1960s [72], CBT evolved from the central assumption that negative or dysfunctional cognitions cause distressing emotions, and both thoughts and emotions trigger behaviors that perpetuate a depressive feedback loop. With an exhaustive body of literature describing multiple variations of the approach (eg, problem-solving therapy, behavioral activation therapy, mindfulness-based cognitive therapy) for most psychiatric illnesses, CBT has led the field of psychotherapy testing [73]. However, in the context of pregnancy, only one RCT to date is documented in the literature [38]; McGregor developed a physician-administered 5- to 10-min CBT-based augmentation to a standard obstetrics follow-up visit in a sample of 42 women, testing it against standard obstetric care over a 6-visit period (unpublished data). Although there was a trend for improvement in anxiety symptoms, there was no statistical difference in depressive symptoms between the two groups. No specific adaptations to pregnancy are apparent in the treatment description. Limitations include the lack of a clinical interview to establish MDD (participants were chosen based on a score of ≥9 on the EPDS) and untrained physicians administering CBT (only 2 h of CBT training). Nevertheless, the trial addresses the need for more efficient ways to treat antenatal depression. Cognitive approaches to treatment also have been tested in a few trials for the prevention of perinatal depression [74–77], for smoking cessation [78–80], and for specific phobia [81]. A larger number of investigations of CBT for postpartum depression are available, but the consensus is that, similar to IPT, CBT has not been adequately investigated in perinatal samples [82, 83].

Attributing depressive symptoms to distorted or inaccurate cognitions supports an educational model of intervention in which structure and the Socratic method work to change the way a patient thinks or feels about people, situations, or life events. Prominent CBT techniques include session agendas, goal setting, problem solving, addressing negative thoughts (eg, cognitive reframing, examining the evidence), pleasant event scheduling, and assigning homework tasks [84]. In depression accompanied by anxiety, relaxation training and/or exposure are incorporated into treatment. Newer variations of CBT blend the didactic and cognitive strategies with components such as mindfulness, acceptance, and attention to emotion [73, 85].

Although there are few trials demonstrating effectiveness, the literature does contain specific adaptations of CBT piloted in small samples. Primary aims are to alter how a mother thinks about herself, her child, and her pregnancy, provoking changes in affect that may enhance a mother's ability to be more emotionally available and responsive to her baby [86–89]. Treatment is directed at the problems identified by the mother in managing her infant [89] and combating maladaptive cognitions about motherhood, self, and the world [90]. Drawing from the postpartum treatment literature, the most specific adaptation of CBT published is the Gruen group therapy model [88, 91]. The 10-week, three-phase intervention blends the presentation of education and information about the postpartum period with stress reduction techniques, relaxation training, cognitive restructuring, and the development of support systems. Although the original model has undergone minimal testing, Ugarriza and Schmidt [92] tested a novel telecare variation of the Gruen [91] approach, simplifying the intervention into two phases over 10 weeks of 45-min telephone sessions. Less explicit but more adherent to the traditional CBT model, Austin et al. [76] summarized the components of their CBT group intervention unique to postpartum depression as education about perinatal anxiety, depression, infant needs and behavior, and direction on developing a broad social support network, including local postnatal support services. Based on the assumption that marital problems and conflicts contribute significantly to perinatal depression, Cho et al. [75] also maintained the basic CBT approach but focused on marital conflicts and behavioral techniques to improve marital relationships. Meager and Milgrom [93] constructed and tested a group intervention that appears to have blended the objectives and techniques of CBT with those of IPT.

Research examining the predictors of treatment response in the general population suggests that individuals with comorbid personality disorders and avoidant characteristics respond differentially better to CBT than IPT [94, 95]. Given the focus on cognitions, CBT would be a reasonable first-line approach with women presenting with anxious depression, particularly when specific fears or anxieties pertaining to pregnancy, childbirth, or motherhood are highlighted in clinical interviews.

Other Psychotherapy Approaches

Interventions that may not meet the general research criteria as evidence based show promising results in uncontrolled pilot studies [96]. Freeman and Davis [97] compared the efficacy

of omega fatty acids with that of placebo, in which all participants with antenatal or postpartum depression received short-term supportive psychotherapy. Both groups experienced a significant decrease in depressive symptoms from baseline to the end of the study, suggesting the psychotherapy was effective, although no control group for the psychotherapy was included. Importantly in that study, the psychotherapy was meant to require a minimal time commitment from providers and patients. Brandon et al. [98] conducted a safety and feasibility trial of partner-assisted therapy (PAT) for perinatal depression in a sample of ten couples, demonstrating that partners could be valuable members of the treatment team. Eight acute sessions and one follow-up session target depressive symptoms, engaging the partner in both assessing symptoms and exploring ways to enhance social support for the depressed woman. Expectancies of each partner regarding role responsibilities, the birth/postpartum process, and parenthood-induced lifestyle changes are highlighted in the middle phase of therapy. In the pilot, ten couples demonstrated that PAT was safe, feasible, and acceptable to the partners, with all women demonstrating treatment response.

Challenges to Psychotherapy

Practical

Time, money, child care, transportation, and access to trained psychotherapists are key challenges to psychotherapy treatment adherence for women and actual barriers to care for many low-income women and/or women living in rural areas [99]. When weighing alternatives to treatment with an antenatal patient, factors such as these that may make psychotherapy infeasible for a patient need to be taken into consideration and may ultimately indicate that pharmacotherapy is a better recommendation. If this is an unacceptable choice for the patient and depression is mild to moderate, options such as exercise, light therapy, or omega fatty acids can be suggested as self-care strategies to supplement watchful waiting. Moderate to severe depression is serious, however, compelling providers to help patients choose a safe and feasible treatment.

Nonresponse to Treatment

Psychotherapy, like any treatment, sometimes fails. Unlike pharmacologic agents with identifiable biological concentrations, steady states, and "half-lives," during a course of psychotherapy, it may be difficult to assess patient response. Self-report symptom measures can aid a clinician in quantifying presence and intensity of symptoms, but frequent checking in with the patient is important for assessing the patient's perspective about the helpfulness of treatment. Generally speaking, brief trials of psychotherapy have reported response in 6- to 8-week phases; thus, a patient who does not demonstrate minimal to moderate response within this time period may be a candidate for switching treatment or augmenting psychotherapy with another intervention.

Conclusions

Psychotherapy is a reasonable and safe first-line treatment option for mild to moderate depression occurring during pregnancy, as well as a valuable augmentation to pharmacotherapy. Treatment considerations are severity of depression, patient preferences regarding intervention alternatives, and available resources (both patient and community). Group psychotherapy is less expensive and provides social support, whereas individual psychotherapy or PAT allows for the individualization of session content to patient needs. Future research is necessary to establish psychotherapy as an evidence-based treatment for depression during pregnancy. It would be of great public health importance to determine which elements of different types of psychotherapy are most feasible and efficacious in pregnant women so that efforts can be made to increase accessibility to women who wish to pursue psychotherapy for antenatal MDD.

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- •• Of major importance

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