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REVIEW

Treatment of postpartum depression: clinical, psychological and pharmacological options

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Abstract: Postpartum depression (PPD) is a common complication of childbearing, and has increasingly been identified as a major public health problem. Untreated maternal depression has multiple potential negative effects on maternal-infant attachment and child development. Screening for depression in the perinatal period is feasible in multiple primary care or obstetric settings, and can help identify depressed mothers earlier. However, there are multiple barriers to appropriate treatment, including concerns about medication effects in breastfeeding infants. This article reviews the literature and recommendations for the treatment of postpartum depression, with a focus on the range of pharmacological, psychotherapeutic, and other nonpharmacologic interventions.

Keywords: postpartum depression, postnatal depression, lactation, antidepressant, hormone therapy, psychotherapy, bright light therapy, omega-3

Introduction

Epidemiology of postpartum depression

Estimates of prevalence of PPD in the US, UK and Australia range from 7%–20%, with most studies suggesting rates between 10%–15%.[6,7] Significant risk factors for PPD include a history of depression prior to or during pregnancy, anxiety during pregnancy, experiencing stressful life events during pregnancy or the early puerperium, low levels of social support[8] or partner support,[9] low socioeconomic status, and obstetric complications.[7] Although mental health often is not prioritized as a problem in poorer countries where access to basic nutrition and health care are not consistent, the evidence suggests that postnatal depression may be both more common and more grave for women and their children in low-income countries. The limited data from resource-constrained countries suggests that rates of depression in mothers of young infants exceeds 25%,[10] and in some settings may be as high as 60%.[11] The intersection of cultural, interpersonal and socioeconomic factors may also confer significant risk of PPD: in one study in Goa, India, risk for depression after delivery increased with economic deprivation, marital violence, and female gender of the infant.[12]

Negative effects of maternal depression

Untreated maternal depression is associated with serious morbidity for the mother, the infant, and the family system. Perinatal depression causes significant suffering in women at a time when personal or societal notions of motherhood as a uniquely joyful,

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if tiring, experience may be incongruous with the depressed woman's ability to feel gratification in the mothering role,[13] connect with her infant, or carry out the often overwhelming tasks of caring for a new baby.[14] Such a disconnect can reinforce the disabling sense of isolation, guilt, helplessness and hopelessness that frequently characterize the depressed state. Women with PPD are at higher risk for smoking,[15] alcohol or illicit substance abuse,[16] and are more likely than nondepressed mothers to experience current or recent physical, emotional, or sexual abuse. Although rates of suicide for women during pregnancy and the puerperum are lower than the general population, suicide is an important cause of maternal mortality.[17] Self-inflicted injury is the leading cause of one-year maternal mortality in the United Kingdom.[18] A recent World Health Organization report on women's health identifies self-inflicted injury as the second leading cause of maternal mortality in high-income countries; suicide remains an important cause of maternal deaths in moderate and low-income countries.[19] Intrusive thoughts of accidental or intentional harm to the baby are common in the early postpartum time.[20] These thoughts are more frequent and distressing in women with postpartum depression;[21] however, nonpsychotic depressed women are unlikely to commit infanticide.[22]

The adverse impact of maternal depression on infant outcomes has also been studied. Depression has significant negative effects on a mother's ability to interact appropriately with her child.[13] Depressed women have been found to have poorer responsiveness to infant cues[23] and more negative, hostile or disengaged parenting behaviors.[24] These disruptions in maternal-infant interactions have been associated with lower cognitive functioning and adverse emotional development in children, and they appear to be universal across cultural and economic divides.[25,26] Other parenting behaviors are also affected, including problematic sleep habits, lower preventative health care utilization and undesirable safety practices.[26] Chronic depression in mothers places children at higher risk for behavioral problems[27] and later psychopathology, including anxiety, disruptive, and affective disorders; conversely, remission of depression in mothers is associated with reduction or remission in the children's psychiatric diagnoses.[28] Maternal depression also increases the risk for negative infant feeding outcomes, including lower rates of initiating or maintaining breastfeeding, lower levels of breastfeeding self-efficacy, and more difficulties while breastfeeding.[29] In low-income countries, maternal depression has been associated with both malnutrition and higher rates of diarrheal illness in children.[30]

Diagnosis of postpartum depression

The diagnostic criteria for a Major Depressive Episode (MDE) as defined by the Diagnostic and Statistical Manual (DSM-IV) do not differ in the postpartum period as compared to other times, and include at least 2 weeks of persistent low mood or anhedonia, as well as at least four of the following: increased or decreased appetite, sleep disturbance, psychomotor agitation or retardation, low energy, feelings of worthlessness, low concentration, and suicidal ideation.[31] A MDE may be classified as having a postpartum onset if the depressive symptoms begin within the first 4 weeks after delivery. However, studies suggest that depressive episodes are significantly more common in women in the first three months after delivery,[32] and an increased vulnerability to psychiatric illness may persist for a year or more.[33] It is important to differentiate PPD from other psychiatric and nonpsychiatric diagnoses. The "postpartum blues" or "baby blues" is a transient mood disturbance that affects up to 75% of new mothers in the 10 days following delivery, and consists of crying, irritability, fatigue, anxiety, and emotional lability. Symptoms are generally mild and self-limited, and do not involve total loss of pleasure or interest, persistent low mood, or suicidal ideation.[34] On the other extreme, postpartum psychosis is a psychiatric emergency that requires immediate intervention, and is characterized by the rapid onset of severe mood swings, a waxing and waning sensorium, delusions, hallucinations or disorganized behaviors, and a relatively high incidence of suicidal ideation or homicidal ideation toward the infant.[35] Women presenting with a depressive episode, mood elevation, or psychotic symptoms should be screened for any prior history of mania or hypomania to rule out previously undiagnosed bipolar disorder.[36] Anxiety disorders are common in perinatal women, and women may have depression comorbid with obsessive-compulsive symptoms, generalized anxiety disorder, panic disorder or post-traumatic stress disorder.[37] Substance use and medical causes of psychiatric symptoms, such as thyroid disorders, should also be considered.

Screening for postpartum depression

To try to mitigate these serious adverse outcomes of PPD, there has been increasing focus on the importance of early and accurate detection and treatment of depression after or during pregnancy.[38] Identification of depression in the postpartum period may be complicated by some of the normal physical and emotional demands of new motherhood, including changes in energy and appetite, sleep deprivation, and heightened concern for the infant. Experts

have recommended screening for PPD at the first postnatal obstetrical visit (usually 4–6 weeks after delivery),[39] or in the family practice[40] or pediatric setting,[41] as these are the most widespread points of interaction with the health care system for new mothers within the first three months of delivery. The most commonly used screening tool for PPD is the Edinburgh Postnatal Depression Scale (EPDS),[42] a 10-item self-report that emphasizes emotional and functional factors rather than somatic symptoms. Although variability in sensitivity and specificity occurs across languages and cultures,[11,43] a reasonable cutoff for a positive screen on the EPDS is ≥13 (out of a possible 30), though special note should be made of any positive responses to Item 10 assessing suicidal ideation.[39,43] Other commonly used screening tools with evidence of validity in the puerperium include the Postpartum Depression Screening Scale (PDSS),[44] as well as the 9-item Physician's Health Questionnaire (PHQ-9).[45] It should be emphasized that these instruments are screening tools which will generate a certain number of false-positives; diagnosis of depression must be confirmed by clinical interview.

Discusssion

Pharmacological treatments for postpartum depression

Antidepressant medication

A small but growing literature suggests that postpartum depression can be thought of as a variant of major depression that responds similarly to antidepressant medication.[46,47] Concerns unique to pharmacologic treatment of PPD include metabolic changes in the postpartum period, exposure of the infant to medication in breast milk, the effect of depression and treatment on the ability of the depressed mother to care for a new baby, and the perceived stigma of being seen as a "bad mother" for requiring medication.[48–50] These factors, as well as the woman's level of distress, access to care, and experience with past treatment may influence the decision of the patient and her caregiver regarding the choice of pharmacologic and nonpharmacologic treatments for PPD. Data comparing the effectiveness of medication against other treatment modalities for PPD are scarce, though do suggest that medications are at least as effective as most psychological interventions based on effect size.[51] To date, four randomized controlled studies on the treatment of PPD with antidepressant medications have been published, along with several open trials. Additionally, two randomized studies have looked at the prevention of PPD with antidepressant medication.

In a study of 87 women with major or minor depression in the postpartum period, subjects were randomized to one of four groups receiving either fluoxetine or placebo plus one or six cognitive behavioral therapy (CBT) based counseling sessions.[52] Breastfeeding mothers were excluded from the study. Improvement was seen in all groups, with greater reduction in depression severity in the fluoxetine group compared to the placebo medication, and greater improvement with six counseling sessions compared to one session. Women receiving both fluoxetine and counseling did not differ significantly in outcome compared to women who received fluoxetine alone. Because the mean baseline level of depressive symptoms based on rating scales was mild, the findings are not easily generalized to a population with more severe postpartum depression.

A subsequent study randomized 35 women with postpartum depression and comorbid anxiety to receive paroxetine or paroxetine plus CBT for 12 weeks.[53] Both groups showed significant improvement in depressive and anxiety symptoms (response rates 87.5% in the paroxetine group and 78.9% in the combined group) without significant differences between groups. The study did not include a placebo arm, making analysis of the specific effects of either intervention difficult. A third study compared paroxetine to placebo in an 8-week randomized controlled trial.[54] The attrition rate in this study was high, with only 31 of 70 participants completing the study (17 in the paroxetine arm and 14 in the placebo arm), but the authors found lower mean severity scores and a higher remission rate after 8 weeks of treatment with paroxetine compared to placebo.

Very few studies have compared different classes of medications used in postpartum depression. One comparative study found treatment with nortriptyline to yield similar outcomes as treatment with sertraline.[55] After 8 weeks of treatment in this large, randomized, double-blind trial, both groups showed improvement, and response rates (nortriptyline 69%, sertraline 56%), remission rates (nortriptyline 48%, sertraline 46%) and side effect burden were similar between groups at week 4, 8 and 24, though side effect profiles differed. There was no placebo arm. The response rate could be predicted earlier in the group receiving sertraline, but the overall response rates were equivalent. Sub-analyses of this study revealed an improvement in maternal role function[56] and sexual function[57] that was equivalent in both groups.

Several open studies have found sertraline,[58] venlafaxine,[59] nefazodone,[60] fluvoxamine,[61] and bupropion[62] to be effective in the treatment of postpartum depression. These studies have been small, with 4–15 participants, lacked control groups, and in several cases were sponsored by the pharmaceutical companies manufacturing the studied drug. Though there is

little data comparing medications to placebo in the perinatal population, taken together, data from both the controlled and open studies suggest that antidepressants typically used to treat major depression are equally effective in postpartum depression, without clear differences between medications in efficacy and side effect burden. Therefore, some experts recommend that if a patient has responded to a specific antidepressant in the past, that medication should be among the first to be considered in treating her depression in the postpartum.[63]

Two placebo-controlled studies have looked at the role of medication in preventing recurrent PPD. In one small randomized placebo controlled pilot study, sertraline initiated shortly after birth for nondepressed women with at least one prior episode of PPD was found to prevent recurrence and prolong time to relapse.[64] However, in another study, no difference was found in rates of recurrence or time to relapse between patients receiving nortriptyline and patients receiving placebo: one out of four women in both groups suffered a relapse within the 20-week study period.[65] Further research is needed to conclude whether initiation of antidepressants after childbirth in a select group of high risk women is preventative against postpartum depression.

Breastfeeding considerations

The benefits of breastfeeding have been well described[66–73] and have led the World Health Organization, the American Academy of Pediatrics and the American Academy of Family Practitioners to recommend breastfeeding for at least the first 6 months for most women.[66,67,73] Potential effects of antidepressant medication on breastfeeding are of concern to many mothers and clinicians.[49,74] Neonates and young infants are especially vulnerable to potential drug effects due to their immature hepatic and renal systems, immature blood–brain barriers, and developing neurological systems.[75,76] Because relatively little is known about the effects of antidepressant medication in breast milk, some experts have recommended nonpharmacologic treatment modalities when possible, particularly for mild to moderate depression.[76] However, nonpharmacologic treatments are not effective for some women, and may not be accessible for many women.

Information about the effects on infants of exposure to antidepressants through breast milk is limited to case reports and small studies, with little prospective data.[77,78] Several reviews of the pooled available data on antidepressant medication and breastfeeding have concluded that among the serotonergic reuptake inhibitors (SSRIs), sertraline and paroxetine are least likely to be detectable in infant plasma, and have been associated with rare, if any, adverse events in infants, whereas fluoxetine and citalopram appear to have higher passage through breast milk.[75,79–81] Individual cases of suspected adverse effects that have been reported in infants of breastfeeding mothers on antidepressant medications have ranged from mild to more serious, and include sleep changes, gastrointestinal problems, respiratory problems, and seizure. In most cases, reported effects have been mild and resolved with cessation of the medication or breastfeeding. These adverse events have been reported in the context of mothers taking citalopram, escitalopram, fluoxetine, doxepin and bupropion,[79–81] though rates and causality are difficult to assess from case reports, and other studies have reported no adverse effects with the same medications. Given the lower infant blood levels and fewer adverse reports, paroxetine or sertraline may be the most prudent choice for a patient who is naïve to antidepressant medication prior to the postpartum episode. However, adverse events have not been definitively linked to elevated plasma levels in infants; conversely, there is little data to suggest that undetectable levels of antidepressant medication ensure infant safety in the long term. In an effort to determine whether even low-level SSRI exposure through breast milk has central effects in infants, Epperson and colleagues found in separate studies that while sertraline and fluoxetine had the expected significant effects on the platelet 5-HT transporter of mothers taking the medication, their breastfed infants did not experience a significant change in 5-HT platelet transporters.[82,83] Whether the lack of effect on peripheral transporters can be extrapolated to predict no effects in the central nervous system of infants remains unclear, though the results are encouraging. Among tricyclic antidepressants, nortriptyline has the most data supporting safety during breastfeeding, whereas doxepin is considered relatively contraindicated.[80,82] Information on the newer antidepressant medications is sparse, but few adverse effects have been reported.[80]

The long-term risks of low-level exposure to antidepressant medication in breast milk are largely unknown. The risks of untreated maternal depression are well-known and significant. Some experts recommend that if medication treatment is indicated, clinical factors such as the patient's prior response or nonresponse to an individual medication rather than data on blood levels should take precedence in the choice of first-line agent.[75,84] Decisions about initiating antidepressant medication during breastfeeding and the choice of agent must be made on a case-by-case basis, and should involve a discussion of clinical factors, including severity of the depressive symptoms and prior response to medications and/or psychotherapy, known and unknown risks of the

medication, the known risks of under- or untreated depression, and the patient's preferences.[85] Regardless of which antidepressant medication a breastfeeding mother takes, the infant's pediatrician should be made aware of the possible exposure, and the infant should be monitored for changes in feeding patterns, sleeping patterns, sedation, irritability and other signs of drug toxicity. As blood levels have not been correlated with adverse effects, routine laboratory testing of infant blood levels is not currently recommended.

Hormone therapy

There is a dramatic drop in maternal levels of estrogen and progesterone at the time of delivery, and this shift has been proposed as one trigger for the onset of PPD in some women. Effects of estrogen in the brain include the promotion of neuronal growth and survival, enhancement of neurotransmitter activity, mitigation of oxidative stress and modulation of the hypophyseal-pituitary axis.[86] A study designed to replicate the hormonal changes experienced around the time of birth found that women with a prior history of postpartum depression experienced mood symptoms when exposed to a drop in estradiol and progesterone, whereas women without a history of PPD did not.[87] This finding suggests vulnerability to hormone shifts in a subset of the population, and raises the possibility of hormonal intervention as a treatment or preventative intervention for PPD.

In a double-blind placebo-controlled study by Gregoire et al 61 women with postpartum depression were randomized to receive estrogen or placebo patches.[88] Breastfeeding women were excluded. Over the first month of treatment, women receiving estrogen showed greater and more rapid improvement in their symptoms as measured on the Edinburgh Postnatal Depression Scale and in clinical interviews. Women in the placebo group also improved, but maintained depression scores above the screening threshold. Neither group had complete remission of symptoms. The authors did not control for women receiving concomitant antidepressant medication, which was more common in the estrogen treatment group, making interpretation of the study results difficult. Additionally, women were included in the study up to 18 months postpartum, by which time the effects the postpartum drop in estrogen would likely have resolved.[86]

Although an early naturalistic study suggested progesterone as a promising preventative therapy against recurrent postpartum depression,[89,90] the results of that study were contradicted by a subsequent double-blind, placebo-controlled trial that found an increase in depressive symptoms in women treated with norethisterone enanthate, a synthetic progestogen.[91] In this study, 180 women were randomized to receive one depot injection of norethisterone enanthate or one injection of saline placebo within 48 hours after delivery and were followed for three months. The investigators found that women who received the synthetic progestogen were more likely to develop depressive symptoms, more likely to have bleeding, and more likely to complain of exhaustion. A recent review of the above studies concluded that while the research on estrogen is promising but preliminary, there is no role for synthetic progestogens in the treatment of PPD, and that given the increased risk for depressive symptoms their use as contraception in this population is questionable.[92]

Other studies without control groups support an effect of estrogen in the treatment of postpartum depression. A small prevention study found that when a slow taper of estrogen therapy was administered immediately after birth to 11 women with a history of postpartum psychosis or depression only one woman suffered a relapse episode.[93] Another small study treated 23 women with severe postpartum depression with sublingual 17-beta estradiol over 8 weeks, and found remission of symptoms in 19 of the women, which the authors correlated with increased serum estrogen levels in the subjects.[94] Both studies should be interpreted with caution, given the lack of a comparison group.

Although initial results for the use of estrogen in the treatment of postpartum depression are promising, additional methodologically sound studies are needed.[86] Furthermore, estrogen therapy should not be used in women with an increased risk of thromboembolism. Treatment with gonadal steroids can interfere with lactation, which should be discussed with women prior to initiating therapy. Long-term use of estrogen therapy can cause endometrial hyperplasia and slightly elevates the risk of endometrial cancer; although this risk can be mitigated by co-administration of progesterone,[86] the increase in depressive symptoms with progestogen seen in the Lawrie study complicates the implementation of this strategy.

Psychological and psychosocial treatments for postpartum depression

Many mothers with postpartum depression are hesitant to take antidepressants due to concerns about infant exposure to medication through breast milk or concerns about potential side effects,[95] and therefore often prefer psychological treatments.[49,50,96] Although relatively few studies have systematically investigated nonpharmacologic treatments for PPD, existing research supports the use of both psychological treatments (specifically interpersonal therapy, cognitive-behavioral therapy, and psychodynamic

psychotherapy), as well as psychosocial interventions, such as nondirective counseling. A Cochrane meta-analysis of ten randomized controlled trials of psychosocial and psychological treatments for postpartum depression concluded that both psychosocial and psychological interventions are effective in decreasing depression and are viable treatment options for postpartum depression.[97]

Interpersonal therapy (IPT)

Interpersonal therapy (IPT) is a time-limited treatment for major depression based on addressing the connection between interpersonal problems and mood,[98] which frames depression as a medical illness occurring in a social context.[99] In IPT, the patient and clinician select one of four interpersonal problem areas (role transition, role dispute, grief, or interpersonal deficits) as a treatment focus. Over the course of the therapy (typically 12–20 weeks), strategies are pursued to assist patients in modifying problematic approaches to relationships and in building better social supports. IPT has been adapted to address problem areas relevant to postpartum depression such as the relationship between mother and infant, mother and partner, and transition back to work.[100] The fact that IPT is both time-limited and problem-focused fits well with the demands of the postpartum mother.

Several studies, including one large-scale randomized controlled trial, have supported the effectiveness of IPT for treating postpartum depression. O'Hara and colleagues randomized 120 women with postpartum depression to receive 12 weekly 60-minute individual sessions of manualized IPT by a trained therapist versus control condition of a wait-list.[101] The women who received IPT had a significant decrease in their depressive symptomatology (measured by Hamilton Depression Rating Scale and Beck Depression Inventory) as compared to the wait-list group, as well as significant improvement in social adjustment scores. In another study by Clark et al 35 women with postpartum depression were assigned to individual IPT (12 sessions) versus mother–infant group therapy versus a wait-list condition.[102] Both IPT and mother–infant group therapy were associated with greater reduction in depressive symptoms as compared to the wait-list conditions. Both studies support the effectiveness of IPT as a treatment for PPD, though there is not enough data to suggest a specific benefit to IPT compared with other therapeutic modalities.

Two small open studies have evaluated group IPT for postpartum depression. Klier et al conducted a pilot study in which 17 depressed women in two different groups received 9 weeks of group IPT and 3 individual sessions.[103] Depression scores on two rating scales decreased significantly during the course of treatment, and gains were maintained at 6-month follow-up. However, there was a high attrition rate (6 out of 17), and the study was also limited by small sample size, lack of a control group, and lack of an independent rater. Similarly, Reay et al treated, in an open pilot trial, 18 women diagnosed with postpartum depression with 8 group IPT sessions, as well as two individual and one partner session.[104] Depressive symptoms decreased significantly, and these gains were maintained at three months. Compared to the previous study, the drop-out rate was low, and authors speculated that this might be due to childcare provided. However, two-thirds of the study participants were receiving antidepressant therapy concomitantly, limiting interpretation of the effect of this group intervention. While it is difficult to make conclusions about efficacy based on this pilot data, the study authors suggest that advantages to group over individual IPT for postpartum depression might include increased social support, normalization of problems, development of interpersonal skills in a group setting that can be translated to outside relationships, and minimization of stigma associated with PPD.

Cognitive behavioral therapy (CBT)

Cognitive behavioral therapy (CBT), a well-studied and effective treatment for major depression,[105] is based on the premise that both perceptions and behaviors are intimately linked to mood. CBT focuses on helping depressed patients to modify distorted patterns of negative thinking and to make behavioral changes that enhance coping and reduce distress.[106] There have been several trials assessing CBT alone or with other interventions for the treatment of PPD. In a randomized controlled psychotherapy-pharmacotherapy study, Appleby et al assigned 87 women with PPD to one of four conditions in a factorial design, varying based on treatment with either one or six sessions of CBT-based counseling, and treatment with fluoxetine or placebo.[52] All four treatment groups had significant improvement in depressive symptoms. Women who received six CBT sessions versus one had greater decrease in depressive symptoms. Six sessions of CBT plus placebo pill was as effective as treatment with fluoxetine plus one session of CBT, but there was no added benefit in the group receiving 6 counseling sessions in combination with fluoxetine. It should be noted that the counseling sessions were delivered by briefly trained nonspecialists, and six sessions of CBT may not be a sufficient representation of a standard course of treatment. In another combination medication-CBT study, Misri et al randomized 35 women with PPD and comorbid anxiety either to paroxetine monotherapy or paroxetine and

12 weekly manualized CBT sessions with a psychologist.[53] While both groups had significant decreases in depressive symptoms, there were no significant differences between the two groups in response rates, time to remission or dose of medication required, suggesting no measurable added benefit to the CBT treatment in combination with an SSRI over the 12 week study period, as consistent with Appleby's findings. In a randomized controlled trial looking at the effectiveness of CBT versus a control condition, Prendergast and Austin assigned 37 women with PPD either to six weekly one-hour home-based CBT sessions delivered by early childhood nurses (ECNs) or to "ideal standard care", which consisted of six weekly visits to ECNs in a clinic setting.[107] Both groups with PPD had significant mood improvement, though there was a nonsignificant trend towards CBT being more effective at six-month follow-up. Among study limitations, ECNs administering CBT were not experienced therapists, though they received CBT training prior to the study and supervision throughout. Additionally, the control group more closely resembled a supportive psychotherapy rather than no-treament. These studies support CBT interventions as helpful in the treatment of PPD, though they do not support an additional benefit to CBT in combination with pharmacotherapy and do not clarify a specific benefit of CBT for this population in comparison with other treatments. Two of these studies also suggest a role for the training of nonmental-health professionals in this modality.

Nondirective counseling

As compared with IPT or CBT, psychosocial interventions are unstructured and nonmanualized, and include nondirective counseling and peer support. Nondirective counseling (also known as "person-centered") is based on the use of empathic and nonjudgmental listening and support. In the first notable study evaluating this intervention, Holden randomized 50 women with PPD to 8 weekly nondirective counseling sessions with a health visitor or routine primary care.[108] A health visitor in the UK is a public health nurse who conducts home visits with pregnant and postpartum women. This study found that the rate of recovery from PPD for counseling (69%) was significantly greater than that of the control group (38%). In a similar study conducted in Sweden, Wickberg and Hwang randomized 31 women with PPD to receive six nondirective counseling sessions by child health clinic nurses or routine primary care.[109] As in the Holden study, a significantly greater percentage of women in the treatment group (80%) had remission of depression than in the control group (25%). Study limitations include the removal of four study participants, two in each group, for more intensive mental health services due to illness severity.

Peer and partner support

Epidemiologic data as well as some prospective studies have consistently identified inadequate social support as a risk factor for developing postpartum depression,[110–112] thus raising the possibility of interventions aimed at increasing social supports as treatment options for perinatal depression. In a prospective cohort of pregnant Chinese women, Xie et al[112] found that low support in both the prenatal and postnatal time period was associated with increased risk for postpartum depression, with the highest risk for postpartum women who had low objective or practical support. The broad applicability of this study is limited by the demographics of its cohort (limited to married Chinese primiparous women without significant obstetric complications, rates of Caesarian delivery over 70%) and the use of a rating scale most validated in the Chinese population. However, the finding suggests that tangible social support, such as assistance with caring for the newborn, may be particularly important and helpful in the treatment of postpartum depressed mothers.

In a pilot study, CL Dennis[113] evaluated the effect of mother-to-mother support as delivered over the telephone on depressive symptomatology in a postpartum patient population identified as at high risk for PPD based on EPDS score >9. Standard postpartum care in addition to individualized telephone-based peer support resulted in a significant reduction in depressive symptoms at 8 weeks. More recently, in a larger randomized multisite trial, Dennis and colleagues demonstrated that high-risk postpartum women who received telephone-based peer support over 12 weeks were at lower risk for developing PPD (as defined by EPDS >12) compared to a control group receiving usual care.[114] Due in part to the telephone-based nature of the study, the investigators were unable to confirm the findings from rating scales with structured clinical interviews.

While poor partner support has been identified as an important risk factor for PPD,[9] few studies have investigated the role of the partner or other family support in recovery from PPD. In one survey study, shared activities, problem-focused information and assistance, and positive feedback from the partner decreased a mother's likelihood of having depressive symptoms at 8 weeks postpartum.[115] A qualitative study examining factors identified by women who had recovered from PPD to be most important in their recovery found that "emotional support from partner", "improved communication with partner", "practical support from

partner", and "emotional support from friends" were rated as "essential" to recovery.[116] A small, nonblinded study by Misri et al examined the impact of partner support in the treatment of PPD.[117] In this study, 29 women with PPD were randomized to receive 7 sessions of psychoeducation with (support arm) or without (control arm) their partners. Relative to the control group, women in the partner group had significant reductions in depressive symptoms, while the partners in this group may also have had protective benefit on measures of general health. These studies do not provide enough data to recommend a specific partner-based intervention, but they do suggest that including the partner in the treatment of PPD may be of benefit for some women.

Comparisons of psychological and psychosocial treatments

Cooper et al designed a large study to assess the effects of different psychological interventions on PPD.[118] A community sample of 193 women with PPD were randomized to receive from weeks 8–18 postpartum routine primary care versus one of three treatment conditions: CBT, psychodynamic psychotherapy, or nondirective counseling. All three treatments decreased depressive symptoms significantly as measured by EPDS at 4.5 months, in comparison to no treatment. Rates of remission from depression, as defined by DSM-III, were higher for those receiving psychodynamic therapy (71%) than CBT (57%) or nondirective counseling (54%). However, there were no differences among any of the groups at the 9 month assessment. Milgrom et al also undertook a study to compare different psychological interventions for PPD.[119] A community of 192 women with PPD were randomized to routine primary care or 12 weeks of group-based CBT, or group-based or individual counseling utilizing supportive therapy techniques delivered by trained therapists. All three psychological interventions were superior to routine care in reducing symptoms of PPD. While there were no significant differences between counseling and CBT, individual counseling was slightly more effective than group counseling. Finally, Morrell et al in a large, cluster randomized trial, looked at an intervention that trained health visitors to identify depressive symptoms in postnatal women and to deliver either a cognitive behavioral or nondirective "person-centered" approach involving up to eight sessions of individual counseling.[120] They compared this with usual care delivered by health visitors who did not receive this training, in conjunction with general practitioners. In this study, women who had an EPDS score ≥12 at 6 weeks postpartum were followed for 18 months. At 6 months, significantly more women in the control condition remained with elevated EPDS scores compared to both intervention groups, and the differences persisted at 12 months. There were no differences between the two counseling approaches. While the specific effective component of the intervention was unclear, this study does provide evidence that training in psychologically-informed approaches for non mental-health providers can significantly enhance the care of depressed postnatal women.

A recent meta-analysis compared psychological and psychosocial interventions for PPD, including CBT, IPT, and nondirective counseling, as well as peer support.[121] This study did not find any difference in effect size for any of these treatments, and concluded that different types of psychological interventions seem equally effective for treatment of PPD.

In summary, both psychological and psychosocial interventions for PPD have shown benefit over no treatment or "usual care" in multiple studies. Further studies are needed to discriminate between the effectiveness of various psychological and psychosocial treatments for PPD and between group-based and individual modalities.

Other nonpharmacologic treatments for postpartum depression

Many women suffering from PPD and their healthcare providers may seek alternatives or adjuncts to standard psychological or pharmacologic treatments because of their concern about the effects of pharmacological treatment on breastfeeding,[122] access to care, issues of stigma in the treatment of mental illness, limited effectiveness, or personal beliefs. In the following we have provided an overview of a variety of evidence-based nonpharmacologic treatments for postpartum depression.

Electroconvulsive therapy

As with treatment-refractory major depression in the general population, electroconvulsive therapy (ECT) is an option for depressed postpartum women who do not respond to antidepressant medication or who have severe or psychotic symptoms. Data specific to this population are very limited. One small study of 5 women receiving ECT for refractory postpartum depression reported a 100% remission rate.[123] Apart from concerns regarding anesthesia and breast feeding, the use of ECT for postpartum depression does not differ from its use in major depression.[124] Anesthetic agents used in ECT are typically rapidly metabolized, and risk of transmission in breast milk can be minimized by timing breast feeding accordingly.

Bright light therapy

While bright light therapy was initially introduced as a treatment for seasonal affective disorder, research has supported its effectiveness as a treatment for nonseasonal depression.[125] Light therapy presents an attractive option for the treatment of perinatal depression, as there are no known risks to the fetus or nursing infant. However, despite some encouraging preliminary data in antenatal depression,[126] there is currently insufficient data on its effectiveness in the postpartum population. In one study,[127] 15 outpatient women with PPD were randomly assigned to receive bright light (10,000 lux, n = 10) or dim red light (600 lux, n = 5) daily for six weeks. This study was unable to elicit a specific treatment effect of the light therapy due to the small sample size, though both groups showed significant improvement over time on all measures of depression. Further studies are required to clarify the effectiveness of light therapy in the treatment of postpartum depression.

Omega-3 fatty acids

Omega-3 fatty acids have received specific attention in the treatment of perinatal depression, because of the known health benefits of these compounds for pregnant and postpartum women as well as some data showing positive effects on mood in the general population.[128] Omega-3 fatty acids such as the eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) found in fish oils, are the key building blocks for the development of a baby's central nervous system while in utero,[129] and depletion of maternal omega-3 fatty acids occurs during pregnancy to facilitate this process.[130] One often-cited cross-national study[131] evaluating major depression in the general population demonstrated that per capita fish consumption was inversely related to the risk of developing major depression. Further epidemiologic data support an association between low omega-3 intake from seafood and increased risk of high levels of depressive symptoms during pregnancy.[132]

Despite these epidemiologic associations, studies examining the use of omega-3 fatty acids for treatment of perinatal depression have had mixed results. Freeman et al conducted two pilot studies of omega-3 fatty acids as an intervention for perinatal depression; one was an open-label flexible-dose trial of a combination of EPA and DHA for the treatment of MDD during pregnancy,[133] and the second trial assessed the efficacy of omega-3 fatty acids for postpartum depression in an 8-week randomized dose-ranging study.[134] The outcome of the first trial showed a 40.9% mean decrease in depressive symptoms on the Edinburgh Postnatal Depression Scale. The second study, a randomized dose-ranging trial for postpartum depression found no significant difference between control and study group. Both studies were limited by their small sample sizes (n = 15 and 16, respectively) and their lack of a placebo group. A subsequent randomized placebo-controlled study investigating the combination of omega-3 fatty acids and supportive psychotherapy for the treatment of perinatal depression[135] again demonstrated no significant difference between the omega-3 fatty acids and placebo, though participants in both groups experienced significant decreases in their depression rating scales. The benefits of supportive psychotherapy received by both groups may have limited the ability to detect a specific effect of omega-3 fatty acids. A subsequent small, randomized, double blind, placebo-controlled trial investigating omega-3 fatty acids at a dose of 3.4 g per day as monotherapy for major depression during pregnancy[136] demonstrated a benefit from this intervention. Although there was relatively high attrition in both groups, subjects receiving omega-3 fatty acids had significantly lower scores on depression rating scales as compared to the placebo group at the study end point.

In sum, omega-3 fatty acids may have therapeutic benefits for perinatal depression, but thus far most studies investigating this effect have been limited by small sample sizes. Some of these studies[135] did establish that dietary intake of omega-3 fatty acids among participants was low prior to study involvement. Omega-3 fatty acids have clear health advantages for both the mother and for the developing fetus or nursing infant. Of note, omega-3 fatty acids can increase bleeding times at high doses, but according to a recent study,[137] omega-3s at doses of 3–4 g/day produced no clinically significant increase in bleeding times or in bleeding events in patients with cardiovascular disease already treated with anti-platelet agents.

Acupuncture and massage

Acupuncture is the ancient Chinese tradition of the inserting and manipulating needles into various points on the body to treat pathologic processes and relieve pain. It has been investigated for the treatment of depression in the general population with mixed results,[138] and has been increasingly investigated as adjunctive treatment in pregnancy for nausea, pain, breech presentation and induction of labor.[139] There is no data about the use of acupuncture in postnatal depression, but one small pilot study by Manber et al compared the effectiveness of targeted acupuncture vs controls of a nontargeted acupuncture and massage in the treatment of pregnant depressed women.[140] 8 weeks of

an active acupuncture intervention targeted specifically for depression (treatments were standardized but individually tailored) significantly outperformed a massage intervention in terms of reduction of depressive symptom rating scales in depressed pregnant women. While there was no significant difference in symptom reduction between the targeted and control acupuncture treatments in this study, a more recently published larger randomized trial of acupuncture in pregnant women showed significant reduction in depressive symptoms in active treatment versus both control conditions.[141] The authors caution that the study was not designed to assess the effectiveness of massage as a treatment for perinatal depression. It is not clear what the effects of antenatal or postnatal acupuncture are on postnatal depression. It should be noted that as acupuncture may have effects on induction of labor and lactation,[138,142] women who wish to try acupuncture as a treatment or adjunctive therapy for perinatal depression should be sure the practitioner is experienced in these issues.

Massage as treatment for perinatal depression has also been examined independently, and modalities include therapeutic massage, partner-delivered massage, and instruction in infant-massage in the postpartum period. Field et al looked at the effect of 10 sessions of massage versus 10 sessions of relaxation techniques in 32 adolescent inpatients with postnatal depression, and found a significant improvement in depression ratings in the massage group after session 10 but not the relaxation group.[143] There was no longer-term follow up, so the clinical implications of this study are limited. Another study looked at the effects of infant massage, and compared the effects of 15 minutes of rocking versus 15 minutes of massage on 40 full-term infants between the ages of 1 and 3 months born to depressed mothers.[144] They found multiple benefits for the infants in the massage group, including improvements in sleep patterns, interactions, crying, weight gain, and lower cortisol levels, though there was no measure of effects on maternal depression. Onozawa et al[145] compared outcomes in mother–infant pairs who received 5 weekly sessions of infant massage classes plus a support group with mothers who were in a support group alone. Depression scores in both groups decreased without significant difference, but only the infant massage group showed statistically significant improvement in global ratings of mother–infant interactions. However, there was high drop-out in this study, and significant improvement in the massage group occurred prior to the first class, suggesting nonspecific or anticipatory benefit. A subsequent trial with a similar design[146] failed to demonstrate these same advantages in mother–infant interactions after six sessions of infant massage compared to support groups alone, and depression scores in both groups again improved similarly. A more recent study investigated maternal massage therapy administered by the woman's partner for 12 weeks[147] in depressed pregnant women and found benefit in the massage group on indices of depression during late pregnancy and immediately postpartum, as well as lower cortisol levels in mothers and neonates. However, the control condition was unspecified standard care, and as there was no longer term follow-up the impact of the intervention on PPD is unclear. In summary, massage in its various forms described above has few risks, and may have benefits for women and their infants, but its effectiveness as a treatment for PPD remains in question.

Exercise

Several studies have investigated the role that exercise can play in alleviating postpartum depressive symptoms.[148] A study by Da Costa et al looked at 88 women with PPD who were randomized to a 12-week, home-based exercise program or usual care.[149] There was a reduction in depression rating scales in the intervention group as compared to the usual care group post-treatment, though not at the 3-month follow-up. However, Ko et al[150] investigated a low-intensity exercise program that was specifically designed and administered to women with postpartum fatigue and depression. There was no significant change in depression between the treatment group and the control group. Despite the limited evidence of efficacy for treatment of PPD,[151] the UK National Institute for Health and Clinical Excellence (NICE)[152] has recommended in their antenatal and postnatal mental health guidelines that health professionals should consider exercise as a management strategy in women experiencing mild-to-moderate depression. A review of the effects of exercise on PPD defined "feasible and effective" exercise as: moderate-intensity activities for at least 30 minutes per day, five days of the week, including walking in the form of "pram pushing".[153]

Conclusion

Postpartum depression is a major international public health problem that affects at least 1 in 8 mothers and their children in the year after childbirth worldwide. PPD may be more common and may be associated with more morbidity for both mothers and children in resource-poor countries. PPD has been associated with significant negative effects not only on depressed women themselves, but on the physical, cognitive and emotional development of their children. Early detection and intervention are important in mitigating these risks.

There are validated and easily administered screening tools for PPD available in many languages, such as the Edinburgh Postnatal Depression Scale; most experts recommend screening women for PPD 4–6 weeks after delivery.

Psychopharmacologic treatment of PPD is complicated by both known and unknown risks of medication in breast milk. There have been few medication trials specifically evaluating the effectiveness of antidepressant medication or ECT for postpartum depression, but the available evidence suggests that medications typically used to treat major depression in the general population are equally effective in postpartum depression. All medications pass into breast milk, though the extent of passage varies considerably between drugs, and sertraline, paroxetine and nortriptyline currently appear to have the best safety profiles in breastfeeding. There have been case reports of adverse effects in nursing infants of antidepressant medication in breast milk, but the advantages of breastfeeding to the mother and infant may outweigh the risks of exposure. Exposed infants should be monitored for any acute behavioral changes. However, the long-term risks of medication exposure to the infant remain unknown. Most experts recommend that the choice of medication in the postpartum should be based first on known efficacy for an individual woman, and that known milk-plasma ratios should be a secondary consideration unless a patient is treatment-naïve. Some studies suggest that estrogen may be an effective agent for treatment, prevention or augmentation in depressed postpartum women; however data remains limited and there are significant health considerations with hormonal intervention.

Psychological treatments for PPD are often the treatment of choice for women, as they are effective for the treatment of depressive symptoms and do not involve the risks of exposure to medications. Research supports both psychotherapy and other psychosocial interventions as effective in mitigating symptoms of PPD. Interpersonal psychotherapy, cognitive behavioral therapy, psychodynamic psychotherapy and other supportive interventions such as telephone-based peer support, counseling by a health visitor, and partner support have also shown benefit over wait-list or usual care controls.

Other nonpharmacologic interventions that have been studied in the treatment of PPD include bright light therapy, acupuncture, massage, omega-3 fatty acid supplementation, and exercise. Data on the effectiveness of these modalities in decreasing maternal depressive symptoms is limited, but these interventions have minimal risks and may have health benefits for both mother and infant.

Disclosure

The authors report no conflicts of interest in this work.

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