Treatment of Postpartum Depression, Part 1: A Critical Review of Biological Interventions

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Background: While postpartum depression is a major health issue for many women from diverse cultures, this affective condition often remains undiagnosed and untreated. The objective of this article is to critically review the literature to determine the current state of scientific knowledge related to the treatment of postpartum depression from a biological perspective.

Method: Databases searched for this review included MEDLINE, PubMed, CINAHL, PsycINFO, EMBASE, ProQuest, the Cochrane Library, and the WHO Reproductive Health Library from 1966 to 2003. The search terms used were *postpartum/postnatal depression* and *randomized controlled/clinical trials* in various combinations. Published peer-reviewed articles in English from 1990 to 2003 were chosen for review, although select earlier studies were also included based on good methodological quality and/or the absence of more recent work. The criteria used to evaluate the interventions were based on the standardized methodology developed by the U.S. Preventive Services Task Force and the Canadian Task Force on Preventive Health Care.

Results: Nine studies that met study criteria were examined. The interventions studied included antidepressant medication, estrogen therapy, critically timed sleep deprivation, and bright light therapy. Although some of these interventions have been better studied for depression unrelated to childbirth, methodological limitations render their efficacy equivocal for postpartum depression with limited strong evidence available to guide practice or policy recommendations.

Conclusions: Despite the recent upsurge of interest in this area, many questions remain unanswered, resulting in diverse research implications. In view of the lack of randomized controlled trials, psychiatrists who are experts in the treatment of postpartum mood disorders have developed consensus guidelines. These guidelines will require regular updating as better and stronger evidence emerges.

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Depression is a major public health problem that is twice as common in women as in men between puberty and middle age.[1] Although the overall prevalence of depression is no greater in women after delivery than during pregnancy, or other times during reproductive life, the impact of depression on the woman, her infant, and her family can be profound.[2] Moreover, the risks of severe major depression or depression with psychotic factors that require admission to the hospital are greater in the postpartum period than any other time in a woman's life.[3,4] Postpartum mood disorders represent the most frequent form of maternal morbidity following delivery.[5] These affective disorders range in severity from the early maternity blues to postpartum psychosis, a serious illness affecting approximately 1% of mothers.[6] Among these disorders is postpartum depression, a condition often meeting DSM-IV criteria for major depressive episodes and exhibiting the disabling symptoms of dysphoria, emotional lability, tearfulness, insomnia, confusion, anxiety, guilt, somatic symptoms, and suicidal ideation. While postpartum depression is a major health issue for many women from diverse cultures[7] and there are well-documented public health consequences associated with the disorder, this affective condition often remains undiagnosed and untreated. The objective of this review is to critically appraise the literature to determine the current state of scientific knowledge related to the treatment of postpartum depression using pharmacologic, hormonal, and other biological approaches. Other nonbiological approaches will be reviewed in a later article in this issue.

METHOD

Search Strategy

Databases searched for this review included MEDLINE, PubMed, CINAHL, PsycINFO, EMBASE, ProQuest, the Cochrane Library, and the WHO Reproductive Health Library from 1966 to 2003. As part of the quality assessment process and to measure the capture rate of relevant references, tables of contents for key journals were hand-searched for the previous 2 years (2001–2003), reference lists of included studies and relevant reviews were examined, graduate theses abstracts were scanned, and key postpartum depression researchers were contacted via e-mail. Finally, all abstracts related to

the combination of the keywords *postpartum/postnatal depression* and *randomized controlled/clinical trials* were reviewed to ensure all potentially significant interventions were obtained. In total, approximately 50 abstracts were examined for inclusion suitability.

Inclusion/Exclusion Criteria

The literature review involved systematically searching for published peer-reviewed articles available in English from 1990 to 2003, although select earlier studies were included based on good methodological quality and/or the absence of more recent work. Research studies that focused on postpartum depression were reviewed; other childbirth-related mental health disorders (i.e., pregnancy or postpartum anxiety, maternity blues, puerperal psychosis) were not appraised. For the purpose of this review, a generous time interval of 1 year postpartum was allowed to account for differing methodologies in the literature.

Data Abstraction

In the initial stage of the search process, peer-reviewed publications were identified, and potentially relevant abstracts that met the predetermined eligibility criteria were subsequently extracted for further examination. Research articles were then selected and assessed in a more rigorous manner to determine inclusion suitability. These articles were either included or excluded and further subgrouped. The critical review process consisted of assessing the disorder definition (i.e., diagnostic/screening criteria used), population sampled (i.e., inclusion/exclusion criteria, recruitment process, sample size, participant characteristics), research design (i.e., control for potential bias, method and timing of assessment, statistical analysis, outcome measures, length of follow-up), level and quality of evidence, and critical analysis of variations between findings of pertinent studies.

Methodology for Synthesis

Interventions included in our study were evaluated according to the published criteria used by the U.S. Preventive Services Task Force (http://www.ahrq.gov/clinic/uspstfix.htm) and the Canadian Task Force on Preventive Health Care.[8] Specifically, each preventive and treatment approach was evaluated and given a research design rating using the following scheme: I = evidence from randomized controlled trial(s); II-1 = evidence from controlled trial(s) without randomization; II-2 = evidence from cohort or case-control analytic studies, preferably from more than 1 center or research group; II-3 = evidence from comparisons between times or places with or without the intervention; dramatic results in uncontrolled experiments could be included here; and III = opinion of respected authorities based on clinical experience, descriptive studies, or reports of expert committees. Following this rating, studies were given a quality (internal validity) rating using the following scheme: good = a study (including meta-analyses or systematic reviews) that meets all design-specific criteria well, fair = a study (including meta-analyses or systematic reviews) that does not meet (or it is not clear that it meets) at least 1 design-specific criterion but has no known "fatal flaw," and poor = a study (including meta-analyses or systematic reviews) that has at least 1 design-specific "fatal flaw," or an accumulation of lesser flaws to the extent that the results of the study are not deemed able to inform recommendation.

After the quality of evidence assessment was complete, each strategy was further classified to determine clinical practice recommendations based on the following grading scheme: A = there is good evidence to recommend this approach; B = there is fair evidence to recommend this approach; C = the existing evidence is conflicting and does not allow making a recommendation for or against use of this approach; however, other factors may influence decision-making; D = there is fair evidence to recommend against this approach; E = there is good evidence to recommend against this approach; and I = there is insufficient evidence (in quantity and/or quality) to make a recommendation; however, other factors may influence decision-making.

RESULTS

For this critical review, 9 treatment studies that met our criteria were identified. Study summaries and limitations are presented in Table 1, while clinical practice recommendations based on the U.S. and Canadian Task Force methodology are outlined in Table 2.

Pharmacologic Interventions

Antidepressant medication. There are over 20 antidepressant medications commercially available in North America today, with this number expected to increase in upcoming years.[9] While tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), and other antidepressant drugs have been shown to be effective in randomized controlled trials for the treatment of depression in men and in women of childbearing age, there is a dearth of good studies among postpartum women. For the last decade, SSRIs have been recommended by several researchers as the initial choice of treatment for postpartum depression,[10–12] and the literature on the use of these drugs in new mothers, especially those breastfeeding, has rapidly expanded in recent years. However, only 4 studies have been found evaluating the effect of antidepressant medication specifically on postpartum depression, with 3 incorporating the use of SSRIs. Of these studies, only 1[13] was included in a Cochrane systematic review evaluating the effect of antidepressant drug treatment for postpartum depression.[14] The purpose of this randomized controlled

Table 1. Summary of Postpartum Depression Treatment Studies

Study	Design	Participants	Intervention
Antidepressant medication			
Appleby et al (1997)[13]	Randomized controlled trial Random allocation by computer-generated numbers Double-blind Intent-to-treat	87 women from the United Kingdom with major PPD at 6 to 8 wk postpartum	4 treatment groups: (1) fluoxetine and 1 CBT session, (2) fluoxetine and 6 CBT sessions, (3) placebo and 1 CBT session, or (4) placebo and 6 CBT sessions Sessions derived for health visitors after brief training but provided by a psychologist with no previous clinical experience over 12 wk
Stowe et al (1995)[17]	Open-label Single group	26 US women with major depression that developed within 24 wk postpartum	8 wk of sertraline using an initial dose of 50 mg/d, adjusted according to side effects and depression severity, to a maximum dose of 200 mg/d
Suri et al (2001)[19]	Open-label Single group	6 US women with major PPD onset within the first 8 wk postpartum Identified using the EPDS and HAM-D	Fluvoxamine treatment, 50 mg/d titrated to 150 mg/d over 2 wk
Cohen et al (2001)[20]	Open-label Single group	15 US women who met DSM-III-R criteria for major depressive disorder with onset within the first 12 wk postpartum	8 wk of venlafaxine (immediate release; mean dose = 162.5 mg/d)
Estrogen therapy			
Gregoire et al (1996)[40]	Randomized controlled trial Double-blind	61 women from the United Kingdom with major depression, which began within 12 wk postpartum and persisted for up to 18 mo Identified using EPDS and clinical interview Intervention group = 34 mothers Control group = 27 mothers	12 wk of transdermal 17beta-estradiol 200 µg/d alone, then 12 wk with added cyclical dydrogesterone, 10 mg/d for 12 d each month
Ahokas et al (2001)[42]	Open-label Single group	23 Finnish women fulfilling ICD-10 criteria for major depression with postpartum onset	8 wk of sublingual 17beta-estradiol
Bright light therapy			
Parry et al (2000)[48]	Single group	9 US women with DSM-IV criteria for major mood disorder	A trial of either early-night partial sleep deprivation (slept from 3 am to 7 am) or late-night sleep deprivation (slept from 9 pm to 1 am) Each night of sleep was followed by a night of recovery sleep
Corral et al (2000)[49]	Case report	2 Canadian women with severe postpartum depression Identified using HAM-D	Daily phototherapy by means of a 10,000-lux light box for 30 min for 4 wk
Oren et al (2002)[50]	Single group	16 pregnant US women with diagnosis of major depression	Ultraviolet-screened diffuse white fluorescent light source incorporating a 100,000-lux box, tilted downward at home for 60 min/d beginning within 10 min of awakening for at least 3 wk

Abbreviations: BDI = Beck Depression Inventory, CBT = cognitive-behavioral therapy, EPDS = Edinburgh Postnatal Depression Scale, SCID = Structured Clinical Interview for DSM-III-R, SIGH-D = Structured Interview Guide for the Hamilton Depression Rating Scale-Depression.

trial was to assess the clinical efficacy of fluoxetine, combined with at least 1 session of counseling in postpartum women, and included 4 treatment cells: fluoxetine or placebo plus 1 or 6 sessions of counseling.[13] The 30-minute to 1-hour counseling sessions were derived from cognitive-behavioral therapy principles and designed to be delivered by nonspecialists after brief training. Eighty-seven women who satisfied Research Diagnostic Criteria for major (N = 51) and minor (N = 36) depression at 6 to 8 weeks postpartum participated, with 61 (70%) completing the 12 weeks of treatment. Depressive symptomatology was assessed at 1, 4, and 12 weeks of treatment using the Edinburgh Postnatal Depression Scale (EPDS),[15] the Hamilton Rating Scale for Depression (HAM-D),[16] and a revised clinical interview. While improvements were seen in all 4 treatment groups, the progress in participants receiving fluoxetine was significantly greater than in those receiving the placebo, and 6 counseling sessions had a significantly greater effect than 1 session. These differences were evident after 1 week, and improvement in all groups was complete after 4 weeks. The interaction between counseling and fluoxetine was not statistically significant. While it appears that both fluoxetine and cognitive behavioral counseling are effective treatments, it should be noted that of the 188 confirmed cases of postpartum depression, 101 women refused trial partici-

Outcome Measure	Results	Limitations
PPD at 1, 4, and 12 wk of treatment Clinical interview, EPDS, HAM-D	Significant improvements seen in all 4 treatment groups. The improvement with fluoxetine was significantly greater than with placebo. Improvement after 6 sessions of counseling was significantly greater than after 1 session. Interaction between counseling and fluoxetine was not statistically significant. All group improvements were complete by 4 wk	Significant number of eligible women declined participation due to reluctance to take antidepressant medication No true control group (no treatment)
PPD posttreatment SIGH-D, EPDS, BDI	20 out of 24 women exhibited a salutary response as defined by > 50% reduction in SIGH-D baseline scores; 14 out of 21 women demonstrated complete symptom remission	Small sample size Lack of a control group Participants were not blinded to treatment Potential cointervention through the provision of support
PPD at 8 wk posttreatment HAM-D	Significant decline in HAM-D scores over time with the greatest degree of improvement occurring between wk 2 and 3	Small sample size Lack of a control group Participants were not blinded to treatment
PPD posttreatment HAM-D	12 of 15 women experienced remission of major depression (HAM-D score < 8)	Small sample size Lack of a control group Participants were not blinded to treatment
PPD every 4 wk for 24 wk (end of treatment) EPDS, clinical interview	During the first 4 wk of therapy, women receiving estrogen improved significantly more than women in the placebo group	Small sample size 47% of women in the intervention group and 37% in the control group were taking antidepressant medication at trial enrollment A high EPDS cutoff score of 14 was used to determine initial eligibility Inexplicit randomization process
PPD at 2 wk of treatment MADRS	MADRS scores were compatible with clinical recovery in 19 (82.6%) women	Small sample size Lack of a control group
PPD before and after the night of sleep deprivation and after a night of recovery sleep SCID HAM-D BDI EPDS	More participants responded to late-night sleep deprivation (9 of 11 trials: 82%) compared with early-night sleep deprivation (2 of 6 trials: 33%), and they responded more after a night of recovery sleep (9 of 11 nights: 82%) than after a night of sleep deprivation (6 of 11 nights: 55%)	Small sample size Lack of a control group Limited number of women complied with the request to complete daily mood ratings Unique sample—most had severe illnesses and family histories of bipolar or other psychiatric illness
PPD at last session at 4 wk HAM-D (29-item version)	HAM-D scores dropped from above 29 and 28 to 11 and 12, respectively	Small sample size Lack of a control group
Depression after 3 wk of treatment HAM-D	HAM-D depression rating improved moderately by 49% after 3 wk	Small sample size Lack of a control group

HAM-D = Hamilton Rating Scale for Depression, MADRS = Montgomery-Asberg Depression Rating Scale, PPD = postpartum depression,

pation primarily due to a reluctance to take antidepressant medication.

To determine the effectiveness of another SSRI, sertraline, in the treatment of women with depressive symptomatology that developed within 24 weeks postpartum, an 8-week, open-label trial was conducted.[17] Twenty-six U.S. women who fulfilled DSM-III-R criteria for major depression were treated with sertraline using an initial dose of 50 mg/day, which was adjusted according to side effects and depression severity, to a maximum dose of 200 mg/day. Biweekly assessments were conducted and included the Structured Interview Guide for the Hamilton Depression Rating Scale (SIGH-D).[18] Twenty-one women (81%) completed the 8-week study, with 20 of those exhibiting a salutary response as defined by a greater than 50% reduction in SIGH-D baseline scores; 14 women demonstrated complete symptom remission. While the results indicate that sertraline may be an efficacious treatment, limitations such as small sample size, open-label single-group design, homogeneous sample, and the possibility of a cointervention (women were concurrently provided with support) render it impossible to determine whether the findings are due to the medication, psychosocial support, or both.

The effect of another SSRI, fluvoxamine, was evaluated in an 8-week, open-label U.S. trial. Six women at

Table 2. Summary of Quality of Evidence and Practice Recommendations for Treatment Interventions With a Biological Approach[a]

Intervention Strategy	Study	Research Design Rating[b]	Quality Rating[c]	Classification of Recommendation[d]
Pharmacologic				
Antidepressant medication	Appleby et al (1997)[13]	Randomized controlled trial: I	Fair	I[e]
	Stowe et al (1995)[17]	Descriptive: III	Poor	I[e]
	Suri et al (2001)[19]	Descriptive: III	Poor	I[e]
	Cohen et al (2001)[20]	Descriptive: III	Poor	I[e]
Hormonal				
Estrogen therapy	Gregoire et al (1996)[40]	Randomized controlled trial: I	Poor	I
	Ahokas et al (2001)[42]	Descriptive: III	Poor	I
Other				
Critically timed sleep deprivation	Parry et al (2000)[48]	Descriptive: III	Poor	I
Bright light therapy	Corral et al (2000)[49]	Case report: III	Poor	I
	Oren et al (2002)[50]	Case report: III	Poor	I

[a]Based on guidelines of the U.S. Preventive Services Task Force and the Canadian Task Force on Preventive Health Care.[8]
[b]I = evidence from randomized controlled trial(s); II-1 = evidence from controlled trial(s) without randomization; II-2 = evidence from cohort or case-control analytic studies, preferably from more than 1 center or research group; II-3 = evidence from comparisons between times or places with or without the intervention, dramatic results in uncontrolled experiments could be included here; III = opinion of respected authorities based on clinical experience, descriptive studies, or reports of expert committees.
[c]Good = a study (including meta-analyses or systematic reviews) that meets all design-specific criteria well; fair = a study (including meta-analyses or systematic reviews) that does not meet (or it is not clear that it meets) at least 1 design-specific criterion but has no known "fatal flaw"; poor = a study (including meta-analyses or systematic reviews) that has at least 1 design-specific "fatal flaw," or an accumulation of lesser flaws to the extent that the results of the study are not deemed able to inform recommendation.
[d]A = there is good evidence to recommend this approach; B = there is fair evidence to recommend this approach; C = the existing evidence is conflicting and does not allow making a recommendation for or against use of this approach; however, other factors may influence decision making; D = there is fair evidence to recommend against this approach; E = there is good evidence to recommend against this approach; I = there is insufficient evidence (in quantity and/or quality) to make a recommendation; however, other factors may influence decision making.
[e]There is evidence based on the depression research in nonpostpartum populations to recommend this approach.

8 weeks postpartum identified with depressive symptomatology using the EPDS and HAM-D began fluvoxamine treatment, 50 mg/day titrated to 150 mg/day, and were followed with weekly clinical interviews and administration of the HAM-D by a blinded assessor.[19] Repeated-measures analysis of variance indicated a significant decline in depression scores over time with the greatest degree of improvement occurring between the second and third week. Similarly, an 8-week, flexible-dose, open-label study of venlafaxine, a serotonin and norepinephrine reuptake inhibitor, (mean dose = 162.5 mg/day) was performed in a group of 15 U.S. women who met DSM-III-R criteria for major depression with onset within the first 12 weeks postpartum.[20] Women were assessed at baseline and every 2 weeks across the study using the 17-item HAM-D. Despite high baseline scores, treatment response was robust; 12 of the 15 women experienced remission of major depression (HAM-D score of < 8). Unfortunately, the results of these 2 studies are severely limited due to small sample sizes, an open-label single-group design, and the lack of a placebo control group. Only 1 antidepressant study[20] indicated that financial support was received from a pharmaceutical company.

While these preceding studies suggest that antidepressant medication is probably an effective treatment option for postpartum depression, it is noteworthy that Hendrick and colleagues[21] opine that women with postpartum depression may be significantly more likely than nonpostpartum women to present with anxious features, take longer to respond to pharmacotherapy, and require more antidepressant medication to obtain a therapeutic response. Furthermore, there have been concerns regarding the use of antidepressant medication in pregnant and breastfeeding mothers, as it provides a medium for direct infant exposure. While it is beyond the scope of this review to appraise the different studies assessing the effects of antidepressant medication in pregnant and breastfeeding women, several reviews have been published to provide further assistance,[10–12,22–38] and specific studies are presented in Table 3.

To assist health professionals in optimizing treatment plans for childbearing women, a risk-benefit decision-making model was suggested by Wisner et al.[39] This model not only directs physicians to structure the problem through diagnostic formulation and assists in the identification of pharmacologic treatment options, but also provides structure to a process that is frequently stressful for both women and physicians and ensures that the critical aspects of the risk-benefit decision are included in the provision of care.

Hormonal Interventions

Estrogen therapy. To evaluate the effect of estrogen on postpartum depression, a double-blind, placebo-controlled trial was conducted. Sixty-one women from the United Kingdom with major depression, which began within 12 weeks postpartum and persisted up to 18 months, were randomly allocated to either an active treatment (12 weeks of transdermal 17beta-estradiol, 200 µg daily alone, then 12 weeks with added cyclical dydrogesterone, 10 mg daily

Table 3. Study References Related to Antidepressant Use During Pregnancy or Breastfeeding

Category	Medication	Study Reference
Tricyclic antidepressants	Amitriptyline	60–63
	Clomipramine	64
	Desipramine	65, 66
	Doxepin	67, 68
	Imipramine	69, 70
	Nortriptyline	62, 71–74
Selective serotonin reuptake inhibitors	Citalopram	75–78
	Fluoxetine	79–91
	Fluvoxamine	92–99
	Paroxetine	92, 96, 100–106
	Sertraline	17, 30, 71, 92, 96, 107–114
Monoamine oxidase inhibitors	Moclobemide	115–118
	Phenelzine	119
	Terbutaline	120–122
Others	Amoxapine	123
	Bupropion	124
	Nefazodone	125, 126
	Trazodone	127
	Venlafaxine	128–130
	St John's wort	131

for 12 days each month; N = 34) or a placebo (placebo patches and tablets according to the same regimen; N = 27) group.[40] All participants were assessed monthly using the EPDS and a clinical psychiatric interview (Schedule for Affective Disorders and Schizophrenia). On EPDS baseline assessments, women in both groups were in the severely depressed range (intervention group mean = 21.8, SD = 3.0 vs. placebo group mean = 21.3, SD = 2.9), and, notably, 47% (N = 16) of women in the intervention group and 37% (N = 10) in the control group were taking antidepressant medication. During the first 4 weeks of therapy, women receiving estrogen (mean EPDS score = 13.3, SD = 5.7) improved significantly more than those in the placebo group (mean EPDS score = 16.5, SD = 5.3). The estimated overall treatment effect of estrogen on the EPDS was 4.38 points (95% CI = 1.89 to 6.87), and no other factors (e.g., age; psychiatric, obstetric, and gynecological history; severity and duration of current episode of depression; and concurrent antidepressant medication) influenced the response to estrogen. This study suggests that transdermal estrogen may be an effective treatment or augmentation option. However, further research is required to establish the minimum effective dose and duration of treatment as well as the possible synergy between antidepressant medication and estrogen. The appropriateness of transdermal estrogen also needs to be assessed in less severely depressed women and in those women not receiving antidepressant medication.

Building upon a previous case study,[41] Ahokas and colleagues performed an open-label study of physiologic 17beta-estradiol to further evaluate the treatment effect of estradiol.[42] Twenty-three Finnish women fulfilling ICD-10 criteria for major depression with postpartum onset were consecutively recruited from a psychiatric emergency unit. Serum estradiol concentrations were measured at baseline and weekly during the 8 weeks of treatment with sublingual 17beta-estradiol; the treatment effect was assessed using the Montgomery-Asberg Depression Rating Scale (MADRS). At baseline, all women were severely depressed (MADRS mean total score = 40.7; range, 35–45) and had a low serum estradiol concentration (mean = 79.8 pmol/L; range, 23–140 pmol/L); in 16 (70%) women, the concentration was lower than the threshold value for gonadal failure. During the first week of treatment, depressive symptoms diminished significantly, resulting in a mean MADRS score of 11.0 ($z = -4.20$, $p < .001$), and serum estradiol concentrations approached those of the follicular phase (mean ± SD = 342 ± 141 pmol/L). At the end of the second treatment week, the MADRS scores were compatible with clinical recovery in 19 women (82.6%). This initial study illustrates that depressive symptomatology may be rapidly reduced through treatment with 17beta-estradiol in women who have documented low estradiol levels. However, estradiol levels are physiologically low in all postpartum and breastfeeding women, and further research is required to determine the significance of estradiol in the pathophysiology of postpartum depression.

Other Interventions

Critically timed sleep deprivation. Critically timed sleep deprivation improves mood within 1 day in most patients with a major mood disorder.[43] In many, but not all of these patients, the improvement occurs primarily after the first night of sleep deprivation. Patients tend to relapse after a night of recovery sleep or even after a nap or merely a few minutes of sleep the following day.[44] However, other studies suggest that some patients who undergo sleep deprivation interventions do not respond until they have had at least a partial night of recovery sleep.[45] Many studies of sleep deprivation suggest that 1 night of partial sleep deprivation is as effective as total sleep deprivation in the first half of the night (early-night sleep deprivation).[46,47] To evaluate the efficacy of critically timed sleep deprivation for postpartum depression, 9 women who met DSM-IV criteria for a major mood disorder with onset during pregnancy or within 1 year postpartum underwent a trial of either early-night sleep deprivation, in which they were sleep deprived in the early part of 1 night and slept from 3 a.m. to 7 a.m., or late-night sleep deprivation, in which they were deprived of sleep in the latter part of 1 night and slept from 9 p.m. to 1 a.m.[48] Mood was assessed before the night of sleep deprivation, after the night of sleep deprivation, and after a night of recovery sleep (slept from 10:30 p.m. to 6:30 a.m.), by trained clinicians, blind to treatment condition, using standardized scales including the Beck Depression Inventory and the EPDS. Of the 17 trials of early- and late-night sleep deprivation,

there were 9 responders to late-night (82%) and 2 responders to early-night (33%) sleep deprivation. Of the late-night responders, 6 (55%) met criteria for response after the night of sleep deprivation and 9 (82%) after the night of recovery sleep.

Bright light therapy. While bright light therapy has been shown to be an effective treatment for seasonal affective disorder and nonseasonal depression, 2 preliminary case report studies suggest that it may also have a beneficial effect on postpartum depression. For example, Corral et al.[49] report the cases of 2 women, suffering from postpartum depression and refusing to take antidepressant medication, who consented to a 4-week trial of phototherapy by means of a 10,000-lux light box for 30 minutes a day. Baseline HAM-D scores (29-item version) for both mothers were above 27, with each showing a 75% reduction in HAM-D scores at their last treatment session (scores were 11 and 12). While no adverse effects during the course of treatment were reported, it is unknown whether the treatment effect was maintained once the phototherapy ended. It should also be noted that 1 woman felt her poor marital relationship precipitated her depression, indicating a psychosocial etiology, and that the observed improved mood may be related to the daily social interaction received during treatment.

To further explore the use of bright light therapy, a study was conducted among 16 pregnant U.S. women with major depression.[50] Treatment consisted of ultraviolet fluorescent light incorporating a 100,000-lux box for 60 minutes daily beginning within 10 minutes of awakening for at least 3 to 5 weeks; compliance was monitored through daily answering machine reports of light use. The HAM-D was administered to assess treatment effect. After 3 weeks of treatment, mean HAM-D scores improved by 49% with benefits seen through the 5 weeks of treatment; there was no evidence of adverse effects. These data suggest that bright light therapy may have an antidepressant effect; however, placebo effects cannot be eliminated. While it is evident that additional research is required, this treatment strategy may be an option for depressed women who are not responsive to traditional approaches.

Electroconvulsive therapy. For severely depressed postpartum women, electroconvulsive therapy (ECT) has been advocated by several researchers as an effective treatment option.[51–56] ECT is most commonly used for suicidal, homicidal, or drug-resistant severe depression. The therapy also has a positive advantage in breastfeeding mothers who do not want to expose their infants to antidepressant medication. No randomized controlled trials exist on the use of ECT in postpartum women.

DISCUSSION

While limited research has been conducted on the efficacy of pharmacologic interventions for the specific treatment of postpartum depression, 4 small studies have shown that antidepressant medications, especially SSRIs, may have a therapeutic effect in severely depressed postpartum women. However, despite limited research demonstrating infant safety, some women find this an unattractive treatment option.[13,57] As such, high attrition of participants or lack of intervention compliance may be of concern in future studies requiring randomization to treatment conditions. Building upon the primarily descriptive studies thus far, well-designed randomized controlled trials are needed to significantly advance this postpartum depression treatment approach. However, antidepressant medication has been shown to be highly effective in the treatment of depression related to childbirth. As such, a recommendation for its use to treat postpartum depression could be made based on general depression empirical work (Table 2).

Research into the characteristics of postpartum women and their intervention choice (e.g., antidepressant medication vs. other options) would be beneficial to health professionals. Furthermore, while limited specific pharmacologic treatment guidelines are available for postpartum depression, primarily due to the lack of research, there is a tendency to treat postpartum depression with less intensity (i.e., lower dose of medication and duration of treatment) than depression at other times.[11,24,58] As such, rapidity of response to different antidepressant medications requires further investigation. Even with the potential benefits of antidepressant medication, this treatment approach primarily addresses biological aspects of depression and should be considered with other interventions to assist in altering the social conditions that often contribute to, or maintain, the depression.

Estrogen therapy has been advocated with preliminary results from 2 studies demonstrating effectiveness. Until better-controlled trials are conducted, it is unclear whether specific subgroups of women, especially those with treatment-resistant depression, derive an antidepressant benefit from supplemental estrogen. Further research is recommended to establish dose-response relations, possible synergy with antidepressant medication, and optimum treatment duration. The effects of estrogen in breastfeeding women should be examined, and further research is needed into how changes in sex-steroid concentrations may contribute to the occurrence of postpartum depression.[40]

While the sleep deprivation study is limited due to the small and heterogeneous sample size, the preliminary findings suggest that with further research, critically timed sleep deprivation interventions may benefit women with pregnancy or postpartum major mood disorders and potentially provide a viable alternative treatment modality for those women who are not candidates for pharmacologic or psychotherapeutic interventions.[48] Currently, the mechanisms for the therapeutic effects of sleep

deprivation or the differential benefit of late- versus early-night sleep deprivation are unknown. Preliminary findings with sleep electroencephalographic measures suggest that one mechanism may be the restoration of sleep quality by either altering the synchronization of underlying circadian rhythms or of homeostatic mechanisms.[59] Further research is warranted to explore these hypotheses by examining the effects of sleep deprivation on other circadian and neuroendocrine measures.[48]

For severely depressed individuals with acute suicidality or psychosis, ECT may be the treatment of choice.[11] However, data on the effectiveness of ECT for severely depressed postpartum women is limited to only case studies. Similarly, only 2 case studies[49,50] have been found exploring the effect of bright light therapy on severely depressed mothers. While these treatment approaches are not first-line options, if they are to become a component of a multifactorial treatment program, well-designed randomized controlled trials are required to ascertain whether maternal mood improvement is specific to the intervention or a placebo effect from open treatment. In view of the lack of randomized controlled trials, consensus guidelines have been developed by psychiatrists who are experts in the treatment of postpartum mood disorders.[29] These guidelines will require regular updating as new and better evidence emerges.

The second part in this 2-part series appears in this issue on pages 1252–1265.

Drug names: amitriptyline (Elavil and others), bupropion (Wellbutrin and others), citalopram (Celexa), clomipramine (Anafranil and others), desipramine (Norpramin and others), doxepin (Sinequan and others), fluoxetine (Prozac, Sarafem, and others), imipramine (Tofranil and others), nefazodone (Serzone and others), nortriptyline (Aventyl, Pamelor, and others), paroxetine (Paxil and others), phenelzine (Nardil), sertraline (Zoloft), terbutaline (Brethine and others), trazodone (Desyrel and others), venlafaxine (Effexor).

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