Perinatal Depression: An Evidence-Based Review of Integrative Treatment

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Many women choose to avoid standard treatment for perinatal depression, and instead prefer integrative treatments that incorporate complementary and alternative therapies. This article reviews the evidence base for these treatments.

Perinatal depression is a significant problem with long-term negative consequences for women, their children, and society. Although most of the registry data for modern antidepressants are reassuring, there are still a great many unknowns regarding their use in pregnancy and lactation. In addition, many patients experience disappointing results from current standard treatments (both psychopharmacology and psychotherapy).

In the face of the current uncertainty about long-term safety, as well as frequently limited effectiveness, many women choose to avoid standard treatment, and instead prefer integrative treatments that incorporate complementary and alternative therapies. This article reviews the evidence base for these treatments (Table).

Exercise
Depression is generally less common in active women, but these results are variable, and treatment data have been limited and inconclusive.

Exercise has been shown to be comparable to both psychotherapeutic and pharmacologic treatments for depression. Even vigorous exercise is generally considered safe during pregnancy, with certain caveats such as avoidance of scuba diving and sports with a high risk of abdominal trauma, as well as taking into account any medical or obstetrical complications and the woman’s general level of fitness. Although there are insufficient data for conclusions on prevention, significant improvements in antenatal depression have been seen with exercise. Most of these studies used a yoga-based exercise program, which is reviewed in detail below. For now, standard exercise recommendations in pregnancy are prudent and may assist in alleviating depressive symptoms.

Massage
Pregnancy massage is an inexpensive, well-accepted treatment that can be delivered in the home after initial training. Partner-provided massage for depressed pregnant women improves depression, relationship measures, and neonatal outcomes, and results in fewer prenatal complications. Mothers who used baby massage had less postpartum depression and better parenting outcomes. Massage, either given or received, appears to be a low-risk and potentially beneficial addition to treatment for perinatal depression.

Combining group interpersonal psychotherapy with massage can be helpful for both depression and anxiety. Interpersonal psychotherapy was also helpful, albeit to a lesser degree.

Group visits
Support programs, including both professional- and peer-led programs such as support groups, may reduce postpartum depression. Centering Pregnancy is a group model that provides patient-centered prenatal care. In these groups, 8 to 10 women are followed up using the recommended schedule of 10 prenatal visits. Each visit is 90 minutes to 2 hours long and includes both private time with the woman’s provider, as well as group support and education about such topics as nutrition, common discomforts, stress management, labor and delivery, breastfeeding, and infant care.

Significant benefits were seen in high-stress mothers who had depression and conflict—both during pregnancy and postpartum—with far less depression and social conflict at 1 year postpartum. Positive outcomes such as appropriate weight gain during pregnancy, compliance with prenatal care appointments, breastfeeding outcomes, and contraceptive use postpartum as well as lowered risk of postpartum depression were also observed.
However, results have been mixed. The Thinking Healthy Programme is a 16-session cognitive behavioral therapy–based program that consists of 5 modules: preparing for the baby; the baby’s arrival; and early, mid, and late infancy. It begins at about 30 weeks’ gestation and continues to 10 months postpartum. This program was successfully used across varying cultures, although the results for depression and anxiety were mixed.\textsuperscript{10,11} A Cochrane review of group prenatal visits noted no differences in levels of stress and depression.\textsuperscript{12}

The data for group programs in pregnancy are positive overall. Such programs are reasonable to recommend, although the evidence for perinatal depression is still mixed.

**Yoga**

The term “yoga” encompasses a broad and ever-growing collection of physical, mental, and spiritual practices strictly or loosely based on ancient Indian philosophy. The heterogeneity of these practices makes scientific interpretation difficult.

In a meta-analysis, a 12-week yoga program significantly reduced depression scores in pregnant women.\textsuperscript{13} Symptoms were reduced in both depressed and non-depressed women. Physical exercise–based yoga showed non-significant improvement and was inferior to integrated yoga (eg, pranayama, meditation, or deep relaxation), which demonstrated significant improvement. Some control subjects received social support or massage instead of yoga, so yoga may be even more effective than reported. A 2016 systematic review of 13 studies found that “yoga interventions are generally effective in reducing depression and anxiety in pregnant women.”\textsuperscript{14}

Yoga is well-tolerated and improves a wide variety of pregnancy outcomes. The literature supports its use in perinatal depression. Significant benefits are documented for yoga practice that includes pranayama, meditation, or deep relaxation.

**Acupuncture**

Although the results of a meta-analysis did not support the use of acupuncture for non-perinatal MDD, there may be benefit in perinatal MDD.\textsuperscript{15} In 2 pilot studies, both depression-specific acupuncture and control acupuncture were beneficial, but specific acupuncture did not outperform control.\textsuperscript{16,17}

Manber and colleagues\textsuperscript{18} reported a significantly better treatment response (but not remission) rate in depression-specific acupuncture (12 sessions) than either control acupuncture or combined controls (control acupuncture, massage).

Findings indicate that acupuncture is well-tolerated and safe in pregnancy, and may be beneficial in the treatment of perinatal MDD.\textsuperscript{19}

**Bright light**

Light therapy has good evidence to support its use in both seasonal and non-seasonal depression. It is low cost and can be delivered in the home. A meta-analysis noted mixed results for bright light therapy in perinatal depression, with non-significant improvements based on very small numbers but good tolerability.\textsuperscript{20} Overall, research results have been mixed: some studies showed significant improvements, while others were unable to replicate the benefits.\textsuperscript{21} While the safety profile is encouraging, the efficacy and feasibility of light therapy in this population are still unclear.

**St John’s wort**

St John’s wort (SJW, *Hypericum perforatum*) is an herb with a strong evidence base to support its use in mild to moderate depression in the general population.\textsuperscript{22} Overall safety data for SJW in pregnancy show no clear pattern of adverse pregnancy outcomes, malformations, or later problems in either animal or human studies.\textsuperscript{23,24}

Outcomes for the use of SJW during lactation are reassuring, with no serious adverse effects noted, despite the herb being detectable in breast milk.\textsuperscript{25} Unfortunately, no studies have yet examined the efficacy of SJW for the treatment of perinatal depression, so no recommendations can be made.

**Omega-3 fatty acids**

The clinical utility of omega-3 fatty acids (omega-3) for non-perinatal mood disorders is widely recognized. In the most recent meta-analysis, omega-3 was found to be effective (especially as adjunctive therapy) for MDD and for depressive symptoms with no MDD diagnosis but not for perinatal depression.\textsuperscript{26} Only one study from 1993 found that omega-3 (3.4 g daily) reduced postpartum depression and anxiety symptoms significantly compared with placebo.\textsuperscript{27}

Omega-3 supplementation is recognized as safe and benefits overall health and improves obstetric outcomes.\textsuperscript{28,29} Based on animal data and the benefits of omega-3 in non-perinatal MDD, it is reasonable to consider adjunctive omega-3 supplementation for perinatal women with MDD or who are at risk for MDD.
Folate
In non-perinatal MDD, depression risk and treatment response are inversely correlated with folate levels. Adjunctive folate supplementation has been found in some studies to improve antidepressant treatment outcomes.\(^30,31\) Folate supplementation is recommended during pregnancy to reduce the risk of neural tube defects.\(^32\)

Data do not support associations between perinatal MDD and dietary folate, vitamin B\(_6\), or vitamin B\(_12\) intake or serum levels of folate or homocysteine.\(^33-35\) One study found increased risk of antenatal (but not postnatal) depression in those with reduced folate levels.\(^36\) The literature does not support folate augmentation for perinatal MDD at doses beyond those already recommended during pregnancy.

S-adenosyl methionine
S-adenosyl methionine (SAMe) is a naturally occurring methyl donor whose production by the one-carbon cycle requires vitamin B\(_12\) and folate. SAMe supports serotonin production and has antioxidant, anti-inflammatory, and neuroprotective properties. The literature supports the efficacy of SAMe (adjunctive or monotherapy) in the treatment of non-perinatal MDD.\(^37,38\) Although SAMe has been found to be safe for the treatment of intrahepatic cholestasis of pregnancy, there are no studies of SAMe for antenatal depression.\(^39,40\) The only perinatal treatment study reported reduced anxiety and depression symptoms in postpartum women treated with SAMe (1600 mg daily) versus placebo.\(^41\)

SAMe cannot be recommended for perinatal MDD without further investigation into safety and efficacy.

Mindfulness training
Mindfulness interventions are skill-building training programs that have been shown to improve a variety of physical and mental health conditions. Ten pregnant women with MDD completed 8 weeks of mindfulness-based cognitive therapy (MBCT). Significant improvements were seen in stress, depression, and anxiety scores, which persisted at 6 weeks postdelivery compared with controls.\(^42\) This confirmed the results of 2 earlier pilot studies that also found improvements in anxiety, affect, and mindfulness.\(^43,44\) These findings suggest that mindfulness training could be incorporated into routine childbirth classes.

Coping with Anxiety through Living Mindfully (CALM) Pregnancy is an MBCT program adapted for pregnant women. Women with generalized anxiety disorder (GAD) or significant anxiety symptoms reported significant improvements in anxiety, worry, and depression symptoms. Sixteen of 17 women who initially met criteria for GAD no longer met criteria at the end of the 8-week intervention.\(^45\)

These results are encouraging. While it would be premature to make recommendations based on the current evidence, mindfulness training is low risk and merits consideration for perinatal anxiety and depression.

Heart rate variability biofeedback
Increased heart rate variability (HRV), the degree of heart rate fluctuation around a mean value, is linked to autonomic nervous system health. Adjunctive HRV biofeedback may improve MDD treatment outcomes.\(^46\) Commercially available biofeedback devices train people to increase HRV as an antidote to stress. A pilot study of HRV biofeedback found improvement in state anxiety and well-being in 10 hospitalized women with perinatal depression.\(^47\)

This study is intriguing, but recommendations for HRV for perinatal mental health will have to await additional results.

Multinutrient formulas
Several complex multinutrient formulas have evidence to support their use in mood disorders. None of these has been formally studied in perinatal mood disorders, although many perinatal patients with depression and anxiety have used these supplements to treat their symptoms.

The manufacturer of one such formula has a large patient database, many of whom used the supplement during pregnancy, with no reported major malformations (T. Kopak, personal communication, March 22, 2016). However, these data are limited, as they were not systematically collected. This product contains doses of vitamins well above the recommended dietary allowance, while not exceeding the tolerable upper intake level, defined as likely to pose no risk of adverse health effects in almost all individuals.
While theoretical safety can be established for the individual ingredients in micronutrient formulas, safety data for the products as a whole are unlikely to be available anytime in the near future, and efficacy studies are not yet under way.

**Copper overload**

An emerging hypothesis on the etiology of postpartum depression involves the role of copper, which has a number of physiological roles, including neurotransmitter synthesis and function as well as depression. Copper levels increase steadily during a normal pregnancy and quickly return to pre-pregnancy levels after birth. However, women with a history of postpartum depression have significantly higher copper levels than depressed women without postpartum depression and normal controls, even years later. While the copper hypothesis is fascinating and has some support for possible underlying pathophysiology, more research is needed to clarify the exact physiological mechanisms and the best treatment approach to address this potential area of concern.

**Conclusion**

When applying this research to day-to-day clinical practice, the need to individualize these complex decisions for each woman—while taking into account the evidence base—is the most critical factor that affects clinical decision making.

The Harvard guidelines recommend that most pregnant women continue their pre-pregnancy regimens, rather than change or taper medications in the midst of hormonal changes. The negative biochemical, psychological, and interpersonal effects of untreated perinatal depression must be weighed in the decision process. Women who taper off their medications in the perinatal period generally struggle with recurrent symptoms that may jeopardize the health of the mother-infant dyad.

The recommendations in this article are best applied to women who are not already taking medications, or to women who would like to use adjunctive treatments to minimize their medication needs during the perinatal period. Women who are taking medications and who are planning a pregnancy a year or more in advance also have sufficient lead time to cross taper pharmaceuticals to integrative approaches. Perinatal patients offer a uniquely appropriate population for a truly integrative approach, in that utilizing complementary and alternative therapies to augment the efficacy of a patient’s current treatments can be an effective way to reduce fetal/infant exposure to a psychotropic. To our knowledge, there are no contraindications to adding any of the recommended modalities to currently available medications.

Regarding plans for breastfeeding, it is important to discuss with patients that there is much more evidence for certain antidepressants (eg, sertraline) than for any nutraceutical. Based on this evidence, careful consideration must be given to a recommendation to wean the infant from breastfeeding in order to continue an effective nutraceutical, versus switching from a nutraceutical to a well-studied medication during lactation. Again, such decisions must be individualized to each woman.

The literature supports a number of integrative treatment approaches for perinatal MDD. Exercise and yoga have good evidence to support their use, and there is encouraging research supporting mindfulness and massage as well. These stress-reducing and skill-building approaches hold particular promise because the skills acquired could enhance parenting, bonding, and childhood development. In addition, based on good evidence for improving overall pregnancy outcomes, it is worth recommending both group visits and supplementation with omega-3 fatty acids, even though the evidence for efficacy in perinatal depression is still mixed.

Further research is needed in this important arena. Research is especially critical to explore long-term safety after fetal or infant exposures to these treatments. However, equally important will be research evaluating the efficacy of these treatments so that both risks and costs can be accurately evaluated in the context of expected benefit to mother and baby.
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References:


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