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Complementary and Alternative Medicine Therapies for Perinatal Depression

Kristina M. Deligiannidis, M.D.^a and Marlene P. Freeman, M.D.^b

^aAssistant Professor of Psychiatry and Obstetrics & Gynecology, University of Massachusetts Medical School; Director, Depression Specialty Clinic, Psychiatrist, Women's Mental Health Specialty Clinic, UMass Memorial Medical Center, Worcester, Massachusetts, USA

^bAssociate Professor of Psychiatry, Harvard Medical School; Director of Clinical Services, Perinatal and Reproductive Psychiatry Program and Medical Director, Clinical Trials Network and Institute, Massachusetts General Hospital, Boston, Massachusetts, USA

Abstract

Complementary and Alternative Medicine (CAM) therapies are increasingly sought out by patients with psychiatric disorders. This article provides a review of the evidence for several commonly utilized CAM therapies (i.e. omega-3 fatty acids, folate, S-adenosyl-methionine (SAME), St. John's Wort, bright light therapy, exercise, massage, and acupuncture) in the treatment of perinatal depression. A number of these treatments may be reasonable to consider for women during pregnancy or the postpartum, but the safety and efficacy of these relative to standard treatments must still be systematically determined. Evidence based use of CAM treatments for perinatal depression is discussed. Adequately powered systematic studies are necessary to determine the role of CAM in the treatment of perinatal depression.

Keywords

complementary; alternative; treatment; S-adenosyl-methionine; omega-3 fatty acids; St. John's Wort; bright light therapy; acupuncture; exercise; massage; perinatal depression

The lifetime prevalence of major depressive disorder (MDD) is about twice as high in women as compared to men [1]. Approximately 18-19% of women suffer from perinatal depression [2]. Untreated depression during pregnancy poses risks to the mother and baby, including obstetrical and neonatal complications [3-8]. Depression during pregnancy is a major risk factor for postnatal depression [9]. Postnatal depression has been associated with a broad negative impact upon child development, including difficult infant and childhood

Corresponding author: Kristina M. Deligiannidis, M.D., University of Massachusetts Medical School, Center for Psychopharmacologic Research & Treatment, 55 Lake Avenue, North, Worcester, MA 01655, USA, Phone: 508.334.7262, Fax: 508.856.4854, kristina.deligiannidis@umassmemorial.org.

Co-author: Marlene P. Freeman, M.D., Harvard Medical School, Perinatal and Reproductive Psychiatry Program, Massachusetts General Hospital, 185 Cambridge Street, 2nd Floor, Boston, MA 02114, USA, Tel: 617.643.6403, Fax: 617.643.3080, mfreeman@partners.org

CONFLICT OF INTEREST

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temperament [10] attachment insecurity [11], and increased risk of developmental delay and lower IQ scores [12]. There is also a substantial rate of suicide in the postpartum, as maternal suicide accounts for up to 20% of postnatal deaths in depressed women [13].

Despite the risks of untreated perinatal depression, women often discontinue antidepressant treatment during attempts to conceive or during pregnancy. Safety and risk profiles of antidepressant use during pregnancy and lactation are increasingly being studied; however women often seek treatment other than standard medications during pregnancy or while breastfeeding. In a recent UK study, more than a quarter of women reported use of a CAM during pregnancy [14]. Therefore, an understanding of complementary and alternative medicine (CAM) therapies is important, as many women may seek CAM treatments for perinatal depression.

COMPLIMENTARY & ALTERNATIVE MEDICINE

CAM refers to a diverse range of healthcare practices used for health promotion, disease prevention and illness treatment that are not considered standard or established practices in Western medicine. In general, women use CAM treatments more frequently than men, and are also more likely to suffer from disorders such as MDD and anxiety disorders, for which CAM treatments are commonly pursued [15]. Despite the growing prevalence of CAM use, the number of adequately powered, well-designed randomized clinical trials of CAM treatments is limited. Since CAM therapies include a large number of diverse modalities that have varying amounts of study, we have reviewed the following seven CAM therapies based on their prevalence of use and the availability of randomized, placebo controlled data, with considerations for their use in women with unipolar depression during the perinatal period: omega-3 fatty acids, folate, S-adenosyl-methionine, St. John's Wort, bright light therapy, exercise, massage and acupuncture.

OMEGA-3 FATTY ACIDS

Omega-3 fatty acids are among the most commonly used CAM treatments in the United States (U.S.) [16]. Omega-3 fatty acids are essential fatty acids with well-established health benefits and particular benefits for obstetrical outcomes and infant development [17,18]. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are two important omega-3 fatty acids found in fish. The American Heart Association recommends eating fish, especially fatty fish, at least 2 times weekly. To optimize pregnancy outcomes and foetal health, consensus guidelines have recommended that pregnant women consume at least 200 mg of DHA per day [19]. The United Kingdom (U.K.) government recommends that adults consume 2 portions of fish per week which corresponds to approximately 450 mg EPA plus DHA daily [20]. Recommendations for pregnant women include 1 or 2 portions of oily fish weekly [20] or 200 mg DHA per day [21]. The European Food Safety Authority recommends 250 mg EPA plus DHA daily for adults, with an additional 100–200 mg DHA a day during pregnancy [22]. Despite increased demand for omega-3 fatty acids during pregnancy, dietary intake by perinatal women in the U.S. and U.K. has been noted as deficient, with dietary intake during pregnancy even more diminished in the U.S. after U.S.

Food and Drug Administration issuances of mercury advisories regarding fish intake during pregnancy.

Omega-3 fatty acids have received the most rigorous study to date in randomized controlled trials for adjunctive treatment of MDD. Meta-analyses of randomized controlled trials demonstrate a statistically significant antidepressant benefit of omega-3 fatty acids in mood disorders overall, but there has been noted heterogeneity in study designs and results, and they are best studied as an augmentation treatment [23-25] rather than monotherapy [26]. The Omega-3 Fatty Acids Subcommittee, assembled by the American Psychiatric Association, recommends that patients with a mood disorder should consume 1 gram EPA + DHA daily. Current evidence may support the use of 1-9 g supplement of EPA + DHA daily for patients with mood disorders, though use of greater than 3 g daily should be monitored by a physician due to the risk of bleeding [27].

Studies investigating the relationship between seafood intake and perinatal depressive symptoms have been mixed, with some demonstrating an inverse relationship between the two [28] and others reporting no such relationship [29]. In a large Danish prospective cohort study of more than 54,000 women, participants who were in the lowest quartile of self-reported fish intake during pregnancy were at increased risk of being treated for depression with an antidepressant up to one-year postnatally [30]. While relatively low omega-3 fatty acid intake was associated with higher rates of treatment with an antidepressant, the investigators found that fish intake was also strongly associated with sociodemographic characteristics.

Although several studies have shown an inverse relationship between antenatal fish intake and perinatal depressive symptoms, several randomized placebo-controlled trials assessing the effectiveness of omega-3 fatty acid supplementation compared to placebo have not demonstrated a benefit in acute treatment or prevention of perinatal depression [31-33]. In by far the largest double-blind, multicentre, randomized controlled trial in which 2399 pregnant women during the last half of pregnancy were randomized to supplementation with fish oil (800mg/d DHA and 100mg/d EPA) or vegetable oil (placebo), depressive symptoms, measured by the Edinburgh Postnatal Depression Scale (EPDS) at 6 weeks and 6 months postnatally did not differ between groups, nor did neurodevelopmental outcomes of their offspring differ at 18 months age [34]. There were fewer very preterm births (<34 weeks' gestation) in the DHA group compared with the control group but more post-term births requiring obstetric intervention in the DHA group compared with the control group.

A small (N=36) randomized, double-blind placebo-controlled trial did find a significant benefit of omega-3 fatty acids compared with placebo in the treatment of antenatal depression [35]. Other studies have provided promising preliminary data regarding feasibility, tolerability, and efficacy in perinatal depression [36,37]. Omega-3 fatty acid supplements have been well tolerated by perinatal women and appear free of significant levels of mercury or other contaminants. Based on positive findings from RCTs and meta-analyses in non-perinatal depression, we recommend perinatal patients with depression should consume 1 gram EPA + DHA daily. At this time, considering that the studies to date

have been small and with inconsistent findings in regard to efficacy in MDD, it is reasonable to augment other treatments with omega-3 fatty acids.

FOLATE

Folate, available as folic acid, folinic acid and 5-methyltetrahydrofolate (5-MTHF) or L-methylfolate, functions as a coenzyme or co-substrate in single-carbon transfers in the synthesis of nucleic acids and amino acid metabolism. An important folate-dependent reaction is the conversion of homocysteine to methionine in the synthesis of S-adenosyl-methionine. Folate undergoes transformation to L-methylfolate, a biologically active form of folate which crosses the blood-brain barrier; 5-MTHF is biologically active. Folic acid and folinic acid are synthetic forms of dietary folate which require the enzyme methylenetetrahydrofolate reductase (MTHFR) for conversion into bioactive forms; however this enzyme is affected by a polymorphism common in patients with depression which impairs transformation to L-methylfolate and is associated with MDD. Some patients with depression may exhibit relatively low folate levels and experience impaired methylation and monoamine neurotransmitter metabolism. Most, but not all, studies report an association of low folate levels and an increased risk of depression [38-40]. Low blood folate has been associated with a poorer response to treatment with antidepressants in MDD [41] and higher folate levels at baseline appear associated with a better response [42].

Folate has been studied in a placebo-controlled trial an adjunctive treatment to fluoxetine, with significantly greater improvement in the folate group, a difference most pronounced in women [43]. 94% of women who received fluoxetine with the addition of folate 500 mcg per day were treatment responders, compared to 61% of those who received fluoxetine and placebo. More recently, results were mixed from two multicentre placebo-controlled RCTs examining the use of L-methylfolate with on-going antidepressant therapy for MDD; improvement was found with 15mg per day but not the 7.5 mg per day dose [44].

It is recommended that women of reproductive age consume 0.4-1mg folic acid daily to reduce the risk of neural tube birth defects: in a large U.K. prospective cohort study of non-pregnant women, less than 6% of women who became pregnant during the observation period reported daily folic acid supplementation of 0.4mg/day [45]. For women with a family history of neural tube defect or who take antiepileptic medications, the recommendation is to take 5mg folic acid daily before and during pregnancy [46]. High rates of unplanned pregnancy make folate supplementation important in women of reproductive age, regardless of plans to conceive. There have been no studies published on the efficacy of folate monotherapy or augmentation therapy for perinatal depression. Epidemiological data do not demonstrate that higher folate intake during pregnancy mitigates against the development of postnatal depression [47]. Considering the potential decrease in birth defects and RCT data that modestly support an antidepressant effect of augmentation with folate (i.e. folic acid 0.4-5mg/day or folinic acid 15-30mg/day), we recommend folate as an important adjunctive strategy for perinatal unipolar depression that carries little risk and may be particularly effective in those women with low serum folate levels.

S-ADENOSYL L-METHIONINE (SAME)

S-adenosyl-methionine (SAME) naturally occurs in the humans, including in the brain. SAME is produced from the amino acid L-methionine through the one-carbon cycle, a metabolic pathway that requires adequate concentrations of folate and vitamin B-12. SAME's antidepressant effect may be via methyl donation in neurotransmitter synthesis or effects on anti-oxidative, anti-inflammatory and neuroprotective processes having important biological roles in depression.

Several placebo-controlled RCTs and two meta-analyses found SAME, studied in doses of 200-1600mg per day, significantly more efficacious than placebo and equivalent to tricyclic antidepressants, in the treatment of depression, while a couple of studies report it equivalent to placebo [48-50]. More recently, studies assessing adjunctive SAME with a serotonin reuptake inhibitor have also been positive [51] with one study indicating that adjunctive SAME improves memory-related cognitive symptoms in depressed patients [52]. SAME is generally well tolerated, with infrequently reported side effects that include mild gastrointestinal symptoms, sweating, dizziness, irritability and anxiety.

There are no studies to date which have evaluated the efficacy of SAME in antenatal depression. However, there is a precedent of using SAME in pregnancy, as it has been studied as a treatment for cholestasis in pregnancy. In five trials of SAME for cholestasis of pregnancy, there were an absence of adverse events or side effects for mothers or for their infants [50]. In one placebo-controlled study of SAME for postnatal depressive symptoms, significant decreases in depressive symptoms with SAME compared to placebo were reported [53]. Further studies should be done before SAME can be recommended for use in the perinatal period given the lack of efficacy and safety data during pregnancy.

ST. JOHN'S WORT (HYPERICUM PERFORATUM)

Hypericum perforatum, from the plant St. John's Wort, has been used for its medicinal properties since ancient times. Several of its bioactive substances, including hypericin, hyperforin and flavonoids, have affinity for neurotransmitter systems known to be important to the pathophysiology and pharmacotherapy of MDD, including activity at γ -aminobutyric acid (GABA), N-methyl-D-aspartic acid (NMDA) and serotonin receptors.

Two meta-analyses have compared the efficacy of St. John's Wort to placebo or standard antidepressants in the treatment of depressive symptoms or MDD [54,55]. Results from the individual studies were mixed with a more robust effect seen in patients with mild to moderate depressive symptoms and less evidence of effectiveness in severe MDD. St. John's Wort, at a daily dosage of 300-1200mg, had an advantage over placebo and efficacy similar to tricyclic or SSRI antidepressants, with better efficacy than the standard antidepressant in a subgroup of patients with mild to moderate depression [55].

St. John's Wort contains high concentrations of the bioactive component hyperforin which induces the cytochrome P450 system (CYP3A4) and inhibits a membrane-bound transporter that facilitates transport across the intestinal lumen and the blood-brain barrier. St. John's Wort may interact with medications including oral contraceptives, reducing oestrogen

plasma concentration and effectiveness. Studies have not been done to advise whether women should be on higher doses of oestrogen oral contraceptives so clinicians should be aware of the herb-drug interaction.

Few studies have investigated the safety of St. John's Wort during the perinatal period, and no published RCTs have evaluated efficacy or safety in perinatal depression. Safety data based on animal studies are mixed with some studies raising concerns regarding exposure to hypericum and hypericin [56-58]. Limited data in 54 human pregnancies indicated no increased risk of major malformations or prematurity rate for infants born to women taking St. John's Wort during pregnancy and matched controls [59]. It appears to be excreted into breast milk at undetectable to low levels, comparable to other antidepressants and its bioactive components at or below the limit of quantification in infant plasma [60]. In one small prospective observational study women who were (N=33) treated with hypericum while breastfeeding their infants, increased rates of adverse events in infants were reported, such as colic, drowsiness, and lethargy, compared to infants of matched depressed and non-depressed controls [61]. Further studies should be done before St. John's Wort can be recommended for use in the perinatal period, given reported infant side effects during lactation and a limited evidence base for efficacy.

BRIGHT LIGHT THERAPY

Most, but not all [62], studies demonstrate that bright light therapy is an efficacious, first-line treatment for both seasonal and non-seasonal MDD [63,64]. Bright light therapy is generally well tolerated, although there is a risk of induction of mania in individuals with bipolar disorder [64,65]. In studies of seasonal depression, predictors of beneficial response included patients of younger age and with symptoms of hypersomnia and increased eating. Three studies that assessed bright light therapy in antenatal depression suggest efficacy. In a small open study, pregnant women (N=16) received one hour of morning bright light therapy [66]. In participants who received at least three weeks of bright light therapy, depression scores improved by a mean of 49%; among participants who completed at least five weeks, scores improved by 59%. No significant side effects were reported, except treatment-related nausea. In a small double-blind study, pregnant women (N=10) were randomized to bright light therapy (7,000 lux) or a dim light (500 lux) placebo condition for five weeks followed by a five-week extension phase [67]. Bright light therapy produced a significantly greater antidepressant response than dim light, with significant differences at the end of the extension phase. One participant who received bright light therapy experienced hypomania, which resolved upon reduction of the duration of daily light exposure. In a larger randomized control trial of 27 pregnant women randomized to 7,000 lux bright (active) light or 70 lux dim red (placebo) light upon awakening for 60 minutes over five weeks, bright light was associated with a greater reduction of depressive symptoms, with 81.3% of women receiving bright light experiencing 50% reduction in symptoms as compared to 45.5% who received placebo dim light. The treatment was tolerated well, without adverse effects reported [68].

In a small randomized trial of women with postnatal depression (N=15), participants were assigned to 30 minutes of 10,000 lux bright light or a 600 lux dim light placebo condition

for a duration of six weeks [69]. Both groups experienced significant improvement from baseline, without differences in response. Light therapy may be an attractive option for some perinatal women as ultraviolet screened light boxes with 10,000 lux illumination are available commercially. Based on a growing evidence base, we recommend initial dosing of 30 minutes beginning within ten minutes of awakening. Considering the high prevalence of mood episodes during pregnancy and the postpartum in the course of bipolar disorder, even if not previously diagnosed, patients should be monitored carefully for emergent symptoms of hypomania or mania, sleep disturbance, and agitation when bright light therapy is initiated.

EXERCISE

Exercise is integral to optimal health in pregnancy, as well as in the prevention of heart disease, obesity and diabetes, comorbid conditions that those with MDD are more likely than the general population to develop. Mechanisms underlying the potential antidepressant effects of exercise are not yet clearly delineated, but exercise may impact neuroendocrine function and neurotransmission. Several trials have demonstrated that aerobic exercise reduces depressive symptoms [70,71]; epidemiological data suggest that regular exercise is associated with decreased risk of depressive symptoms [72], although not all trials have consistently demonstrated benefit [73]. Treatment research is difficult with exercise, as adequate “dosing” (e.g. type, intensity and duration), study control conditions and maintenance to treatment assignment pose challenges in study design [74].

According to recommendations from both the American College of Obstetricians and Gynecologists and the Royal College of Obstetricians and Gynaecologists, pregnant women without medical contraindications should engage in regular aerobic and strength-conditioning exercise during the perinatal period [75,76]. Studies of both antenatal aerobic exercise [77] and general physical activity [78] in women without MDD, have shown that exercise or physical activity was associated with fewer depressive symptoms in pregnancy. No studies to date assess exercise for perinatal MDD, although there is a small amount of data for impact upon depressive symptoms in women without MDD. In one study, investigators evaluated if antenatal exercise consisting of aerobic and strengthening exercises prevented postnatal depressive symptoms. They did not find that antenatal exercise was associated with a lower prevalence of postnatal depressive symptoms as measured by the EPDS [79]. An 8-week “Mother and Baby” program, including exercise, was associated with lower EPDS scores in the intervention group at study end, but between-group significance was lost at follow up one month later [80].

Few controlled studies have evaluated the effectiveness of exercise as a treatment for postnatal depression. Two RCTs comparing a 12-week intervention of exercise to a control situation in postnatal women with an EPDS score of 10 or greater (suggestive of postnatal depression, but in itself not diagnostic) demonstrated significantly greater reduction in EPDS during the study with exercise than the control situation [81,82] and one study indicated that exercise can reduce physical fatigue in postnatal depressed women [83]. Based on a limited evidence base for exercise in the treatment of perinatal depression, we recommend, for general health, 30 minutes a day of exercise most days of the week in the

absence of either medical or obstetric complications and after consultation with an obstetrician.

MASSAGE

Massage therapy has been studied broadly for health benefits, including in conditions such as depression, migraine headache, asthma, chronic fatigue, pain and stress. Massage includes the practice of different techniques including Swedish, Shiatsu and traditional Chinese massage, among others. Massage therapy is postulated to act upon modulation of the hypothalamic pituitary adrenal axis and neurotransmission. Support for its neuroendocrine effects include demonstration of massage to decrease salivary and urinary cortisol levels and increase urinary serotonin and dopamine levels over the therapy period [84].

A recent meta-analysis of 17 RCTs of massage therapy in depressed patients (perinatal studies were excluded) concluded that massage therapy is significantly associated with reduced depressive symptoms [85]. Several monotherapy studies have investigated the effects of massage on pregnant and postnatal women and their infants. Antenatal massage therapy is efficacious in reducing antenatal [86-89] and postnatal [88] depressive symptoms; decreasing urinary levels of cortisol [88]; and increasing urinary levels of serotonin and dopamine [86]. Antenatal massage has also been associated with reduced rates of prematurity and low birth weight [88]. Additionally, combining massage therapy with group interpersonal psychotherapy in women with antenatal depression has been shown to reduce depressive symptomatology and cortisol levels greater than group psychotherapy alone [90]. Given safety data and a growing literature which supports massage therapy as an effective treatment for non-perinatal and perinatal depressive symptoms, massage therapy consisting of weekly sessions of 20 minutes, may be a reasonable consideration for perinatal women with mild depression symptomatology.

ACUPUNCTURE

Acupuncture is a longstanding component of Asian medicine, in which the body is seen as composed of a balance of energy. Maintenance of this balance is considered integral for optimal health, and imbalance is associated with a blockage of vital energy and illness. Acupuncture stimulates anatomical points on the body, often with thin metallic needles (manual acupuncture), which serves to restore vital energy flow which has been blocked. Because acupuncture is often practiced in the context of other cultural practices, it is difficult to assess through the lens of Western medicine, as diagnostic and symptom assessments may not be standardized across studies and acupuncture techniques may vary across sites and studies. Additionally, establishing a truly blinded placebo condition for acupuncture research is challenging. Three types of placebo that have been utilized include nonspecific acupuncture, sham acupuncture (in which needles are placed in places not thought to affect the condition being studied) and placebo needles, which are retractable and do not penetrate the skin.

Controlled trials evaluating acupuncture as a treatment for MDD have demonstrated inconsistent results regarding efficacy [91,92]. A recent meta-analysis of 30 trials evaluated

the efficacy of manual, electrical or laser-based acupuncture vs. sham treatment in men and women with depression found insufficient evidence to recommend the use of acupuncture in the treatment of depression [93].

There are few data on the safety or efficacy of perinatal acupuncture. Some acupuncture points have been reported to hasten cervical ripening at term and advance labour and delivery [94]. Two RCTs [95,96] in which pregnant women with MDD were randomized to receive 8 weeks of treatment with active manual acupuncture, control acupuncture, or massage have reported positive results. Active acupuncture was associated with significantly greater response rates in antenatal depression compared to the control acupuncture or massage groups [95,96] and a greater proportion of postnatal women with fully remitted depression [95]. Massage therapy was better tolerated than active manual or control acupuncture. A smaller study of electroacupuncture compared to sham acupuncture for the treatment of postnatal depression demonstrated that both treatments were associated with improvement in depression symptoms, with no between-group difference in outcome measures [97]. Based on the current evidence, acupuncture may be an attractive option to consider as part of a treatment plan. At this time, it is premature to recommend acupuncture as a first line treatment for perinatal MDD.

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MULTIPLE CHOICE QUESTIONS WITH ANSWERS

Question 1

What percent of U.S. adults use CAM treatments each year?

- a. 10%
- b. 20%
- c. 30%
- d. 40%

Answer to question 1

d

Explanation to the answer to question 1

(d) CAM treatment use among US adults is common. Approximately 40% of the U.S. adult population utilizes at least one CAM treatment annually.

(a,b,c) These responses represent too low of a proportion of the U.S. population which uses CAM.

Question 2

Which of the following may decrease the efficacy of oral contraceptives?

- a. Omega-3 fatty acids
- b. S-adenosyl L-methionine
- c. St. John's Wort
- d. Melatonin

Answer to question 2

c

Explanation to the answer to question 2

(c) St. John's Wort contains high concentrations of the bioactive component hyperforin which induces the cytochrome P450 system (CYP3A4) and inhibits a membrane-bound transporter that facilitates transport across the intestinal lumen and the blood-brain barrier [98]. St. John's Wort may interact with medications including oral contraceptives [99,100]; unplanned pregnancies have been reported, due to suspected drug-herb interactions.

(a,b,d) There are no known drug-herb interactions among these CAM therapies and oral contraceptives.

Question 3

The European Food Safety Authority currently recommends which of the following?

- a. 250 mg EPA plus DHA daily for adults, with an additional 100–200 mg DHA a day during pregnancy
- b. 500mg EPA plus DHA daily for pregnant women
- c. 1000mg EPA plus DHA daily for pregnant and lactating women
- d. 100mg EPA plus DHA daily for adults, with an additional 100–200 mg DHA a day during pregnancy

Answer to question 3

a

Explanation to the answer to question 3

(a) The European Food Safety Authority recommends 250 mg EPA plus DHA daily for adults, with an additional 100–200 mg DHA a day during pregnancy [22]. Despite increased

demand for omega-3 fatty acids during pregnancy, dietary intake by perinatal women in the U.S. and U.K. has been noted as deficient, with dietary intake during pregnancy even more diminished in the U.S. after U.S. Food and Drug Administration issuances of mercury advisories regarding fish intake during pregnancy.

(b,c,d) None of the responses reflect current recommendations by the European Food Safety Authority.

Question 4

Which of the following adverse events have been reported during bright light therapy?

- a. sleep disturbance
- b. agitation
- c. hypomania or mania
- d. hepatotoxicity

Answers to question 4

a, b, c

Explanation to the answers to question 4

(a, b, c) Bright light therapy has been shown to be efficacious in the treatment of seasonal and non-seasonal MDD. It is commonly well-tolerated, however, considering the high prevalence of mood episodes during pregnancy and the postpartum in the course of bipolar disorder, even if not previously diagnosed; patients should be monitored carefully for emergent symptoms of hypomania or mania, sleep disturbance, and agitation when bright light therapy is initiated.

(d) Bright light therapy is not known to be associated with hepatotoxicity.

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SUMMARY

Perinatal depression is common and carries significant risks to mother and child. Effective, evidence-based standard psychotherapies and pharmacotherapies are available, so the pursuit of relatively unstudied therapies in lieu of standard evaluation and treatment carries the risk of prolonging the time ill. However, with appropriate consideration of risks and benefits, some of the better studied CAM therapies can expand the list of treatment options available to patients. Some patients may insist on CAM therapies: these women should receive the same education on known risks and benefits of these treatments as for other depression treatments. Treatment response should be monitored with validated repeated assessments, e.g. EPDS, so that if the CAM therapy is not efficacious, other CAM or non-CAM therapies may be considered. The popularity of many CAM therapies necessitates that clinicians inquire about CAM use. Clinicians open to working with patients who prefer CAM therapies can enhance their partnership with the patient towards the shared goal of depression remission.. At this time, further study is necessary to delineate the full efficacy and safety of specific CAM therapies in perinatal unipolar depression.

PRACTICE POINTS

- Evidence for augmentation with omega-3 fatty acids, exercise or folate with standard treatments for perinatal depression
- Bright light therapy may be reasonable therapeutic options for some individuals who prefer non-pharmacologic interventions.
- Acupuncture and massage may provide benefit in the treatment of perinatal depression at this time, but should not replace more standard therapies.

RESEARCH AGENDA

- type and prevalence of CAM use in perinatal women
- effectiveness of omega-3 fatty acids, folate and acupuncture in the treatment of perinatal depression
- investigation of possible differences in underlying circadian malsynchronization in antenatal vs. postnatal depression and predictors of response
- safety of S-adenosyl-methionine and St. John's Wort during pregnancy and in lactation
- dosing studies of exercise in perinatal depression