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Nutritional Interventions in Depression and Perinatal Depression

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Depression is the leading cause of mental disability worldwide. Women who are depressed during pregnancy are at a higher risk for preterm delivery, preeclampsia, birth difficulties, and postpartum depression. The treatment of depression in conventional medicine has focused on physiological factors that lead to impaired neurotransmitter function and treatments to improve neurotransmitter function. Pharmaceutical substances pose risks for pregnant and lactating women, and lower risk options are preferred. Micronutrients, including certain B vitamins, folate, and docosahexaenoic acid (DHA†), play a role in the synthesis and absorption of neurotransmitters. Experimental studies suggest that supplementation with specific micronutrients may alleviate depressive symptoms and improve birth outcomes in patients with perinatal depression. Alternative treatments for depression, including nutritional supplements, are an important treatment option for depressive symptoms while limiting potential side effects and treatment costs. This article explores the biological basis of perinatal depression and reviews the potential benefits of non-pharmacological interventions.

INTRODUCTION

Depression is the leading cause of mental disability worldwide, according to the World Health Organization (WHO) [1]. Depression affects about 121 million people globally; less than 25 percent of those affected have access to effective treatment [2]. The burden of mental disability from depression falls disproportionately on women, who have two to three times greater risk than men [3]. The WHO predicts that by the year 2020, depression will be the second largest contributor to the

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†Abbreviations: IOM, Institute of Medicine; WHO, World Health Organization; DHA, Docosahexaenoic acid; MDD, Major Depressive Disorder; SSRIs, Selective Serotonin Reuptake Inhibitors; FDA, Food and Drug Administration; SAMe, S-adenosylmethionine; AA, Arachidonic acid; EPA, eicosapentaenoic acid; HDRS, Hamilton Depression Rating Scale; HPA, Hypothalamic-pituitary-adrenal; 5'-MTHF, 5'-methyltetrahydrofolic acid; ALA, Alphalinolenic acid; LA, Linoleic acid.

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global disability-adjusted life years (DALY) for all ages and both sexes [4]. The WHO initiative on depression in public health set a goal to close the treatment gap through the use of "cost-effective" treatments that will be available to those who currently have limited or no access to treatment [5].

Perinatal depression is a serious mental health problem. It has negative effects on women and poses risks for delivery and infant development [6]. Reducing perinatal depression may therefore be critical to ending the growing rates of depression and meeting the goals of the WHO initiative on depression in public health.

Women's risk of developing major depressive disorder (MDD) during childbearing years may be as high as 20 percent [2]; the lifetime risk of developing MDD in women is 10 percent to 25 percent [4]. Women with MDD often do not seek prenatal care during pregnancy and are more likely to engage in activities that may harm the fetus, such as drug and alcohol use [7]. Inadequate prenatal care and/or drug and alcohol use during pregnancy can lead to failure to thrive, poor development, both social and physical, abnormal brain development, and reduced motor tone and activity in the newborn [7]. As many as 20 percent of pregnant women demonstrate depressive symptoms, and the prevalence decreases slightly from 12 percent to 16 percent postpartum [6].

Postpartum depression ranges from maternity blues to psychosis [8]. Women with prenatal depression have increased risk of pregnancy complications including preeclampsia, birth difficulties for mother and child, [6] and postpartum depression [9]. Infants of mothers with major depressive disorder are at risk for below average physical growth, malnutrition, and chronic illnesses [10]. Beyond these physical ailments, perinatal depression can have negative effects on care giving, which in turn affects cognitive and social development, including language development [11]. One recent study revealed that perinatal depression is linked to the development of depression in adolescent offspring. Children at 16 years of age born to women with depression during pregnancy were nearly five times more likely to develop depression than were adolescents born to women without depression [12].

Depression may also affect the incidence of infectious diseases. Depressed mothers may be less likely to seek proper medical treatment and adhere to treatment regimens. One study found that depression was linked to the perception that an HIV diagnosis would decrease a woman's access to health services as a result of discrimination [13]. HIV-positive mothers with depression may not seek appropriate perinatal care and as a result may be at increased risk of mother-to-child transmission of HIV [13].

There is currently debate about whether antidepressants, specifically selective serotonin reuptake inhibitors (SSRIs) and other serotonergic/noradrenergic antidepressants, are safe during pregnancy [14]. The American Academy of Pediatrics recommends using the lowest effective dose of psychotropic drugs in pregnant patients who require pharmacologic interventions [15]. The Food and Drug Administration (FDA) classifies SSRIs and other serotonergic/noradrenergic antidepressants as pregnancy category C or D [16]. Pregnancy category C indicates that studies in animals demonstrate adverse effects on the fetus or that studies in women or animals are not available [16]. When studies are not available, the drug should only be given if the potential benefit justifies the potential risk to the fetus [16]. Pregnancy category D indicates that there is positive evidence of risk to a human fetus, but that the benefit in an emergent situation may be acceptable despite the risk [16]. Antidepressants have been associated with major fetal malformation, persistent pulmonary hypertension of the newborn, self-limiting neonatal behavioral syndrome, and possibly the occurrence of miscarriage [14].

Nutritional interventions have the potential to serve as both preventive measures and treatment measures for depression. Since depression awareness is on the rise, prophylactic use of nutritional measures may reduce the incidence of perinatal depression. In addition, nutritional measures may serve as a primary solution for mild depression and as an adjunctive measure in se-

vere cases of depression. Since antidepressants pose risks to the fetus, providing a safe intervention that may reduce the necessary dose of an antidepressant may decrease the risk to the fetus while providing the same level of therapy to the mother.

It is important to find a way to treat depression in pregnant and lactating women without harming infants. Nutritional interventions may be a safe and cost-effective way of alleviating depression during pregnancy. The importance of nutritional status as a factor in perinatal depression merits further investigation. There is limited research available in the area of perinatal depression and nutrition. Much of the available research on the impact of nutrition on depression suggests that there is a promising link between the two; however, this hypothesis has not yet been adequately tested.

NUTRITION AND BRAIN FUNCTION

Nutrition is essential for normal brain functioning, including the proper functioning of neurotransmitters, which may be a key element of the connection between nutrition and depression [17]. Nutritional status, particularly fatty acids, folate, and B12, have been shown to affect depression. Low omega-3 fatty acid status has been linked to an increased incidence of depression [18]. Membrane phospholipids mediate the entrance of neurotransmitters into the cell. If the cell has an inadequate amount of membrane phospholipids, the ability of neurotransmitters to pass through cell membranes may be impaired. Several studies have shown that providing folic acid supplements in conjunction with selective serotonin reuptake inhibitors led to a 50 percent decrease in depression scores [19]. Low levels of serotonin, dopamine, and norepinephrine may affect the formation of S-adenosylmethionine (SAMe), a universal methyl donor that takes part in the formation of membrane phospholipids and synthesis of neurotransmitters.

In order to explore how non-pharmacological interventions may affect depressive symptoms, it is important to first examine the physiology of depression. The next sections will review the basic physiology of perinatal depression and the impact that nutritional interventions may have on depressive symptoms.

PHYSIOLOGY OF PERINATAL DEPRESSION

Three different physiological causes of depression have been identified: low serotonin, dopamine, and norepinephrine levels in the brain; altered neuromembranes and the impact of polyunsaturated fatty acids on these membranes; and hormones, especially hormonal changes that occur during and after pregnancy [8,20,21]. Each of these pathways is affected by specific nutrients and may be altered by nutritional approaches.

Patients with depression have altered levels of monoamine neurotransmitters [21]. Research has shown that monoamine neurotransmitters that fail to cross the blood brain barrier may result in depression. Early investigation of the relationship between monoamine neurotransmitters and depression initially focused on serotonin. However, studies that deplete serotonin in human subjects concluded that not all individuals with depression responded with similar levels of mood changes to depletion [22]. For example, in a study by Ruhe et al., adult patients ingested a tryptophan-deficient amino acid mixture that decreased serotonin levels in the brain. This study showed that previously depressed patients would experience a brief relapse of symptoms, while individuals without a history of depression tended not to exhibit any mood changes [23].

The tryptophan-serotonin pathway, whereby tryptophan crosses the blood-brain barrier and converts to serotonin, has also been linked to depression [24]. Failure to process sufficient amounts of tetrahydrobiopterin, a cofactor in the biosynthesis of monoamine neurotransmitters, will lead to a slower production of neurotransmitters [23]. The dopaminergic system has currently become of interest as a potential pathway involved in depression. Studies suggest that

dopamine may be the primary neurotransmitter responsible for depression.

Despite several hypotheses about the specific role that monoamine neurotransmitters play in depression, research has yet to identify an exact malfunction in the monoamine system that is consistently associated with depression [25]. Most likely, several neurotransmitters are related to depression. Nutritional interventions, particularly folate supplementation, may aid in maintaining healthy levels of monoamine neurotransmitters in the brain [26].

Polyunsaturated fatty acid availability determines the structure and properties of phospholipid membranes, especially in the brain [18]. These fatty acids play a key role in receptor function, neurotransmitter uptake, and signal transmission [17]. Docosahexaenoic acid (DHA) concentrations are highest in the brain. High concentrations of DHA are essential to proper serotonin receptor sensitivity in the brain [27]. Dietary profiles of polyunsaturated fatty acids, including DHA, have changed dramatically in the last 30 years [27]. These changes may have affected brain chemistry.

Depressed patients have reduced concentrations of n-3 fatty acids, which alter the ratio between arachidonic acid (AA) and eicosapentaenoic acid (EPA) in cell membranes [28]. A study of 34 patients with major depressive disorder and 14 normal volunteers found a deficiency of n-3 fatty acids and a resulting increase in monounsaturated fatty acids in depressed patients [29]. Another study reported that patients with a higher plasma ratio of AA to EPA had more severe depressive symptoms [30]. Polyunsaturated fatty acid deficiency, especially n-3 fatty acids, alters the fatty acid composition of neural membranes in the brain, which changes membrane fluidity and structure. Such changes can interfere with serotonin, norepinephrine, and dopamine metabolism and signaling [30]. In a placebo-controlled trial of EPA as an add-on therapy for major depressive disorder, patients who received 1g/day of EPA were more likely than controls to show a 50 percent reduction in the Hamilton Depression Rating Scale (HDRS) [31].

Hormones including progesterone, estradiol, prolactin, thyroid-stimulating hormone, and thyroxine are hypothesized to have a role in the physiology of maternal depression [32]. Hormones change drastically during pregnancy. For example, estradiol levels increase 50 times during pregnancy [8]. Research on nutrients and their role in the biosynthesis and function of hormones is just beginning. Additional work is needed to fully understand the relationship between nutrition and hormone function.

Hormonal depression may be caused by low production of serum estrogen or changes in gonadal hormones. These may block neurotransmitters, causing depressive symptoms. Several hormone-related mechanisms have been investigated as contributors to perinatal depression, including the hypothalamic-pituitary-adrenal (HPA) axis and cortisol and pregnancy-related hormones including estrogen, progesterone, testosterone, and oxytocin. Studies investigating the involvement of the HPA axis and cortisol have had mixed results. Some studies have found that adrenocorticotropic hormone and cortisol levels are unrelated to depression; others have shown that higher adrenocorticotropic hormone and lower cortisol levels are associated with perinatal depression [33,34,35,36].

A study by Pedersen and colleagues examined the relationship between thyroid status in late pregnancy and perinatal depression scores, both prenatal and postpartum, in 31 women with normal range thyroid hormone levels. Thyroid measures and mood assessments were taken at 32 to 35, 36, and 37 weeks of pregnancy. Patients also rated their mood every other week between postpartum weeks 2 through 24. Mood ratings were measured on the Edinburgh Postnatal Depression Scale and the Beck Depression Inventory. Results showed that thyroxine concentrations and free thyroxine indices were correlated significantly and negatively with depression scores postpartum [37]. However, a review by Bloch, Daly, and Rubinow showed that the link between postpartum depression and a particular hormonal deficiency are uncertain [38].

During pregnancy, estradiol increases 50 times and progesterone increases 10

times by the third trimester [39]. Abrupt hormone withdrawal postpartum is hypothesized to lead to the development of depression, though whether it is a particular hormone or several is unknown [39].

Women who had a major depressive disorder prior to pregnancy are more likely to develop postpartum depression than women who had no symptoms of depression prior to pregnancy [40], suggesting that these pathways likely contribute to perinatal depression. Understanding the interaction of pregnancy-related hormones and neurotransmitters may be essential to understanding the neurobiology of perinatal depression. Epidemiological evidence has linked B-6 to hormone-related depression in women [32]. Although B-6 alone may not be an effective treatment of depression, B-6 supplementation may be a valuable adjunctive therapy in the treatment of depression [32].

There are several nutrient changes that develop during pregnancy. These nutrient changes may compound underlying physiological changes that develop with depressive symptoms. Pregnant women may be at a higher risk of depression because of concurrent nutrient deficiencies that develop during pregnancy. As a result, it is important to account for increased nutritional demands during pregnancy.

NUTRIENT CHANGES DURING PREGNANCY

Pregnant women are at an increased risk of nutrient deficiencies because nutrient requirements are higher during pregnancy [41]. The WHO recommends that pregnant women consume three times more vitamin B-12 (0.4 mcg/day non-pregnant to 1.4 mcg/day pregnant) in order to compensate for changes in B-12 metabolism during pregnancy [42]. Additionally, pregnant women require 70 percent more folate compared with non-pregnant and non-lactating women [41].

The high nutrient demands of pregnancy coupled with an inadequate intake of nutrients before pregnancy can lead to nutrient depletion by the end of gestation. These nutrients do not easily recover postpartum [17]. For example, DHA is essential to brain growth and development in the fetus. As a result, maternal requirements for n-3 fatty acids are high. Maternal DHA status begins to decline in the second trimester and is ultimately depleted by the end of most pregnancies. DHA status does not return to its original level until over 6 months postpartum [43]. As a result, women who do not supplement their diets with n-3 fatty acids are likely to develop DHA deficiency, which is associated with major depressive disorders.

Folate, vitamin B-12, and vitamin B-6 are critical factors in homocysteine metabolism, and homocysteine is a necessary precursor in the biosynthesis of the monoamine neurotransmitters serotonin, dopamine, and norepinephrine. Folate likely influences the rate of synthesis of tetrahydrobiopterin, which is a cofactor in the hydroxylation of tryptophan and is involved in the biosynthesis of dopamine, norepinephrine, and serotonin. All of these neurotransmitters are implicated in the pathogensis of depression [44]. Essential fatty acids make up 45 percent of the fatty acids in synaptic membranes; as a result, they are necessary for normal neuronal membrane function [45].

The following sections will elucidate the specific roles of homocysteine metabolism, polyunsaturated fatty acids, and vitamin B-12 in the development of depression and review the available literature addressing the potential effects of non-pharmacological interventions on these pathways.

HOMOCYSTEINE METABOLISM AND DEPRESSION

Homocysteine is a non-protein-forming sulfur amino acid. Homocysteine is a key component of two major metabolic pathways: remethylation to methionine (requiring folate and vitamin B-12) and transsulfuration to cystathionine (requiring pyridoxal-5-phosphate, the RBC plasma form of vitamin B-6). These pathways are coordinated by SAMe [46]. The first of these pathways, remethylation to methionine, is vitamin B-12 dependent [47]. Once

methionine is formed, the majority of it is activated to form SAMe in a folate-dependent reaction, which serves as a methyl donor in neurological reactions such as the synthesis of neurotransmitters, the formation of membrane phospholipids, and the metabolism of nucleic acids [48]. Folate and vitamin B-12 are needed for the synthesis and metabolism of serotonin and other monoamine neurotransmitters [49].

High homocysteine levels and folate deficiency are not only risk factors for perinatal depression, but also for several placenta-mediated diseases: low birth weight, preeclampsia, spontaneous abortion, and placental abruption [50,51]. Folate supplementation prevents neural tube defects and decreases incidence of low birth weight [51]. Folate deficiency may lead to perinatal depression and poor birth outcomes or poor birth outcomes alone in two ways: Folate deficiency may lead to perinatal depression as well as poor birth outcomes, which could in turn cause depression in women. In either case, folate supplementation may reduce the risk of poor birth outcomes by preventing placenta-mediated diseases and lowering incidences of perinatal depression.

Several studies have shown that plasma and red cell folate levels are low in major depression; this may be related to poor response to antidepressants [48]. In a placebo-controlled study by Coppen and Bailey, 127 patients with major depression based on DSM-III-R criteria were randomly assigned to receive either 500 ug/d of folic acid or an identical looking placebo in addition to 20 mg/d of fluoxetine, both for 10 weeks. Ten weeks showed significantly lower Hamilton rating scale scores in those receiving placebo and fluoxetine. Interestingly, this result was confined to women, who had a baseline Hamilton Rating Scale score of 11.7 (SD 6.7) and a 10-week score of 6.8 (SD 4.1) [48]. Similarly, in a study by Reyonds and colleagues, of 101 patients with depressive disease, patients with low folate levels had significantly higher depressive scores based on a self-rating depression inventory [52]. Another study found that in depressed patients 60 years or older, the effectiveness of a selective serotonin reuptake inhibitor (sertraline), as well as that of a tricyclic antidepressant (nortriptyline), depended on folate levels [53].

Beyond its potential as a supplement to pharmaceutical interventions, folic acid itself may have antidepressant effects. A study by Godfrey and colleagues included 123 patients with a diagnosis of major depression or schizophrenia. Forty-one of these patients had a folate deficiency and took part in a double-blind, placebo-controlled trial of methylfolate. These patients took 15 mg of methylfolate daily for 6 months in addition to their standard psychiatric treatment. Among both the depressed and schizophrenic patients, supplementation with methylfolate significantly improved clinical and social recovery [54]. In a study by Passeri and colleagues, 96 patients with dementia and a score of >18 on the HDRS participated in a double-blind multicenter study. Of these patients, 47 received 50 mg/d of 5'-methyltetrahydrofolic acid (5'-MTHF), the active form of folic acid, and 49 received 100 mg/d of trazodone, a tetracyclic antidepressant, both for 8 weeks. After 4 weeks of treatment, HDRS score dropped from 23 +/-5 to 20 +/-6 in the 5'-MTHF group and from 23+/-3 to 21 +/-4 in the trazodone group [55].

SAMe has been evaluated as a supplement and has an antidepressant effect similar to tricyclic antidepressants [56,57,58]. In a study by Pancheri, Scapicchio, and Delle Chiaie, 147 patients received 150 mg/d of oral imipramine and 146 patients received 400 mg/d of SAMe, both for four weeks. All patients had a diagnosis of major depressive disorder and scores of >18 on the HDRS. The study found that the efficacy of SAMe is not significantly different from imipramine, but was better tolerated by patients [56]. In a review by Papakostas, Alpert, and Fava, the authors indicate that the literature supports the antidepressant efficacy of SAMe, specifically that parenteral SAMe is more effective than placebo and at least as effective as standard antidepressants. Further supplementation with SAMe may enhance the treatment response of standard antidepressants [57,58,59,60,61].

High homocysteine levels may influence depressive symptoms through decreased production of SAMe, combined with the increased production of S-adenosylhomocysteine (SAH), leading to impaired synthesis of neurotrasmitters and membrane phospholipids [57].

POLYUNSATURATED FATTY ACIDS AND DEPRESSION

Polyunsaturated fatty acids are classified into two main groups: n-3, in which the parent essential fatty acid is alphalinolenic acid (ALA), and n-6, in which the parent essential fatty acid is linoleic acid (LA). n-3 and n-6 fatty acids must be obtained through diet [62]. Major sources of ALA are fish, canola oil, soybean oil, and walnuts; major sources of LA are vegetable oils, margarine, lean meats, organ meats, and eggs [62].

n-3 fatty acids may influence depression through their effects on membrane fluidity. Deficiency of n-3 fatty acids alters the fatty acid composition of organ membranes, including the brain; this results in a change in membrane viscosity. Changes in membrane viscosity influence the metabolism of serotonin 5-hydroxytryptamine, a neurotransmitter associated with the pathophysiology of depression [28]. Depressed patients have reduced concentrations of n-3 fatty acids, especially DHA, in red blood cell membranes and an increased AA:EPA ratio. This alteration is generally attributed to low dietary intake of n-3 fatty acids [28].

EPA and DHA are the primary n-3 derived long-chain fatty acids. n-3 fatty acids accumulate in membrane phospholipids of neural tissue primarily as DHA, which is required for brain function. EPA and DHA control membrane fluidity, enzymatic activities, binding between molecules and receptors, biochemical interactions, and movement of nutrients [63]. Both observational and experimental studies suggest an association between n-3 fatty acids and depression [64].

AA is an n-6 fatty acid that is derived from LA. AA competes with EPA and DHA for membrane space and conversion to biologically potent eicosanoids. When there is an abundance of AA, excessive production of eicosanoids results. The over-production of eicosanoids affects function of the immune, cardiovascular, renal, bone, and central nervous systems [30]. AA has pro-inflammatory effects, while EPA has anti-inflammatory effects. When there is an equal distribution of n-6 and n-3 fatty acids, EPA is able to mediate the inflammatory effects of AA [65]. It is important to have an even distribution of n-6 and n-3 fatty acids so that the effects of each are kept in check.

There is epidemiological evidence that low dietary intake of n-3 fatty acids may be a contributing factor in major depressive disorder. There has been a substantial increase in lifetime risk for major depression in the past century. This increase corresponds to a shift in diet. Americans began eating diets richer in n-6 fatty acids and lower in n-3 fatty acids [66]. The average ratio of n-6 to n-3 fatty acids in American diets has risen from approximately 1:1 to 15:1 [67,68].

A study of fatty acids and depression found that n-3 fatty acids are significantly depleted in the red blood cell membranes of depressed patients. Depleted n-3 fatty acid levels were strongly associated with the severity of depression. Depressed subjects did not differ from non-depressed subjects in terms of absolute total energy intake or current dietary intake of n-3 fatty acids [66].

Postpartum depression is associated with alterations in fatty acid composition of serum lipids [69]. Major depressed patients who were not postpartum have lower total n-3 fatty acids in serum cholesterol esters compared to minor depressed patients or healthy controls [70]. A study of patients with postpartum depression found that post partum depression patients had reduced n-3 fatty acids and a shift in the balance of fatty acids from n-3 toward n-6 [69].

Maternal concentrations of both EPA and DHA decrease during pregnancy. It may take up to 1 year for DHA concentrations to normalize [71]. A study of 112 women at 32 weeks postpartum showed that postpartum depression was associated with lower DHA levels. The non-depressed had significantly higher DHA status than the depressed par-

ticipants did [72]. DHA is particularly important during pregnancy because it accumulates rapidly in the neural tissue of the fetus from gestation through the first year of life [28]. Studies of rats showed that restriction of n-3 fatty acids during pregnancy and lactation results in impaired neural function in offspring that cannot be reversed by later supplementation [73]. In a cross-national study in which seafood consumption, DHA content in mother's milk, and postpartum depression were compared, lower concentrations of DHA in mother's milk and lower national rates of seafood consumption were largely associated with higher rates of major postpartum depressive symptoms [74].

Rats given a DHA-deficient diet showed that, with a decreased tissue concentration of DHA, there is a 55 percent decrease in dopamine concentration in neural tissue [75]. This suggests that essential fatty acids play a role in the production of neurotransmitters. A study of the brain tissue of Flinders Sensitive Line rats, rats that model behaviors characteristic of major depression, confirmed that there is altered brain fatty acid composition in an animal model of depression. There is an increased concentration of n-6 fatty acids in the brain tissue of FSL rats (21 percent higher in the hypothalamus, 24 percent higher in the nucleus accumbens, 31 percent in the prefrontal cortex, and 23 percent in the striatum) [76].

Fatty acid supplementation also demonstrates a relationship between essential fatty acids and depression. A study conducted among healthy Japanese students found that DHA supplementation reduced aggression. Interestingly, these students had a higher baseline level of n-3 fatty acids than did average Americans [77]. A study of monkeys given a low-cholesterol diet showed that n-3 fatty acids have an effect on cholesterol and behavior. Results showed that the animals on a low-cholesterol diet had lower serum cholesterol, exhibited more violent behavior, and had a greater ratio of n-6 to n-3 fatty acids than did animals on a high-cholesterol diet [78]. Additionally, a study of the behavioral effects of n-3 fatty acids in mice showed that n-3 deficiency resulted in decreased attention, motivation, and reactivity to stimuli and rewards [79]. Several studies have shown significant negative correlations between red blood cell membrane n-3 fatty acid levels and depression [66].

CONCLUSION

Nutritional interventions may be a cost-effective way of preventing and treating depression in pregnancy. When used prophylactically, nutritional interventions may decrease the incidence or severity of perinatal depression. When used as treatment methods, nutritional interventions may reduce the utilization of or the necessary dose of psychotropic drugs. Decreasing the amount of psychotropic drugs used during pregnancy may reduce the risk of harm to the fetus, while still providing the mother with an equivalent amount of therapy. Safely reducing perinatal and postpartum depression rates may lead to more positive birth outcomes and a reduction in the depression cycle in offspring.

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