Update on the treatment of depression during pregnancy

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Approximately one in four women will experience depressive symptoms during pregnancy. Untreated depression is associated with diminished prenatal care and can adversely affect the course of pregnancy, the developing fetus and birth outcomes. There is a pressing need therefore for safe, well tolerated, efficacious treatments. Risk–benefit decisions are best made on an individual case basis by an informed patient in consultation with her family and healthcare provider(s). Illness severity, course of illness, stage of pregnancy and patient preferences shape the decision-making process. This review summarizes recent literature on the course and impact of major depression and dysthymia during pregnancy, as well as providing an update on treatment strategies including complementary/alternative medicine, psychoeducation, psychotherapy and pharmacotherapy.

Being pregnant is a momentous time in a woman's life. However, the view that pregnancy is a period of wellbeing and protection against psychiatric disorders is disappearing with accumulating evidence that, for some women, the peripartum can be laden with mood disorders, in particular, depression. Investigators have shown that prevalence rates of depression are similar in pregnant and nonpregnant women [1]. As research evidence increasingly reveals detrimental effects of depression on both mother and fetus/infant, there is a pressing need for efficacious treatments.

In general, the treatment of depression in pregnancy is approached in a way similar manner to the treatment of depression in nonpregnant women, that is, by using psychotherapy for mild depression and combining medication and psychotherapy for more severe cases. Ultimately, treatment decisions will likely be made on a combination of clinical judgment and patient preferences.

Nonpharmacologic therapies, ranging from interpersonal therapy to acupuncture and light therapy, have been met with varying degrees of success and are useful for treating mild depression in pregnancy, or in more severe cases, as an adjunct to medication. Over the past year in particular, increasing evidence has shown that pharmacologic therapies for depression in pregnancy appear relatively safe, although debate continues on when to administer treatment and whether to taper in late pregnancy.

In the wake of recent advice and precaution from federal health authorities in Canada [101] and the USA [102] on the use of selective serotonin re-uptake inhibitors (SSRIs) and other newer antidepressants during the third trimester of pregnancy, there is an increased interest in the development of empirically evaluated, nonpharmacologic interventions for the treatment of depression in pregnancy.

This paper will review current literature on the impact of maternal depression, and will also update psychotherapeutic and psychopharmacologic strategies for the treatment of depression during pregnancy.

Prevalence & course of depression during pregnancy

Major depression

It is estimated that 25 to 35% of women experience depressive symptoms during pregnancy, and that 9 to 18% of women meet criteria for major depression [2–4]. Symptoms include low self-esteem, hopelessness, poor concentration, blunted affect, loss of interest and sleep or appetite disturbances. While the prevalence of postpartum depression (PPD) ranges between 4 and 20% [2,5–7], investigators have shown that the rate of depression is somewhat higher in pregnancy and declines across the postpartum period [2,4]. For example, Felice and colleagues found that the point prevalence of depression was 15.5% upon initial visit, 11.1% in the third trimester, 8.7% immediately postpartum and 3.9% at 8 weeks postpartum [2].

During pregnancy, investigators have found that depressive symptoms peak in the first trimester, improve during the second trimester and subsequently increase during the third trimester [1,8,9]. Overall, the course of depression during pregnancy remains relatively stable when compared with the decline of depression during

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the transition to the postpartum [10,11]. Factors associated with antepartum depression include marital disharmony, unemployment, lack of social support and a high frequency of stressful life events [4,12,13].

Untreated depression is associated with diminished prenatal care and can adversely affect the course of pregnancy, the developing fetus and the entire family. As a means to cope, some pregnant women will resort to the use of illicit drugs, smoking and drinking. Alcohol consumption is positively and linearly correlated with antenatal depression [14,15]. A recent study with a diverse ethnic sample found that approximately 15% of 169 women reported alcohol use during pregnancy [16].

Antepartum and PPD can occur independently of each other [17]; notwithstanding, there is evidence that the onset of some 'postpartum' mood disorders begin during pregnancy [18]. Most importantly, the occurrence of antepartum depression can increase the risk of developing PPD [10,19,20].

Dysthymia

Dysthymia, or dysthymic disorder, is a mild, chronic, depressive condition defined as a course of depressive symptoms lasting for at least 2 years with symptom-free periods that last for no more than 2 consecutive months. Dysthymia symptoms are similar to those of major depression; however, the frequency of vegetative symptoms (i.e., sleep or appetite disturbances) is far less common than observed in major depression. The prevalence of dysthymia in the general population is approximately 6% [21]. Currently, there are no published studies investigating, or at least identifying, women with dysthymia during the peripartum period. The majority of studies use dysthymia as an exclusion factor when studying chronic depression in the peripartum.

Maternal depression & birth outcomes

Although the impact of antepartum depression is not fully understood, two recent studies have shown a significant association between the symptoms of depression during pregnancy and preterm delivery (i.e., <37 weeks gestation). In a community sample of 1399 low-income African–American women, investigators found that 12.7% of women with 'high' depression scale scores in pregnancy (Center for Epidemiologic Studies Short Depression scale [CES-D] > 33) had spontaneous preterm births compared with 8% of women who had 'low' (CES-D < 33) depression scores. The authors reported an adjusted odds ratio of 1.96 (95% confidence interval [CI]: 1.04–3.72) for an elevated CES-D score associated with spontaneous preterm birth [22]. Drewett and colleagues found that in a British cohort of over 10,000 women, those with preterm births were significantly more likely to have been depressed early in pregnancy – they had Edinburgh Postnatal Depression Scale (EPDS) scores of less than 12 at 18 weeks and 32 weeks gestation [23].

A recent prospective study in rural Pakistan compared growth and illness status in infants of women who were depressed with those who were psychologically well in the third trimester of pregnancy. Results showed that compared with controls, at 6 months of age infants of depressed mothers had a relative risk (RR) for being underweight of 4.0 (95% CI: 2.1–7.7) and 4.4 for stunted growth (95% CI: 1.7–11.4). Maternal depression had a RR of (2.4; 95% CI: 1.7–3.3) for five or more episodes of diarrhea/year. Poorer growth and an increased risk of illness were also found in infants of probands at the 12-month postnatal assessment. Chronic depression carried a greater risk for poor outcome than episodic depression [24].

Although research has shown that maternal depression is associated with a negative effect in the infant and socioemotional disturbances in children up to 5 years of age at home and in school [25,26], it is unclear whether adverse effects are related to antepartum or PPD. Huot and colleagues followed 123 women from pregnancy to approximately 6 months postpartum and found that depression during the first two trimesters, but not the third trimester or postpartum, was associated with a negative effect in the infants [27]. Studies of animal models have shown hypothalamic–pituitary–adrenal axis hyperresponsivity in offspring of depressed mothers [28]. Huot and colleagues also found that antenatal depression was associated with heightened infant cortisol levels in response to a stressor. Further, a stress response in infants at 6 months of age was predictive of negative affect up to 7 years of age.

Treatment decision making & options

Risk–benefit decisions are best made on a case-by-case basis by an informed patient in consultation with her family and healthcare provider(s). Illness severity, course of illness, stage of pregnancy and patient preferences shape the decision-making process [29]. Any risk associated

with the use of antidepressant medication during pregnancy must be weighed against the known risks associated with untreated depression [30]. In general, psychopharmacologic treatment is pursued when alternative therapeutic strategies are not sufficient or when it is felt that the risks associated with psychiatric illness during pregnancy outweigh the risks of fetal exposure to a particular medication.

Expectant women who present with depressive symptoms should be encouraged to make lifestyle modifications to enhance their wellbeing. For example, increased rest and sleep, regular meals, asking for help with household chores, talking to their spouse/partner, family and friends about how they are feeling, reducing their workload, taking short walks, postponing major life changes (e.g., moving house) and joining a support group for women with depression.

For women who present with a new onset of minor depressive symptoms, nonpharmacologic treatment strategies, such as counseling or psychotherapy should be explored first [31]. In women with ongoing milder depression, it may be appropriate to consider discontinuation of pharmacologic therapy under medical supervision during pregnancy. Close monitoring during pregnancy is essential, even if all medications are discontinued and there is no apparent need for medication. Women with histories of mood disorders who discontinue antidepressant treatment are at a high risk for relapse and early detection and treatment of recurrent illness in pregnancy is essential [32].

For women with more severe and recurrent depressive illness, the patient and clinician together may decide that the safest option to enhance the likelihood of sustaining euthymia is to continue pharmacologic treatment through delivery. This may necessitate switching from one psychotropic agent to another with an enhanced reproductive safety profile. Close monitoring of the patient's condition and adequate dosage of medication should be used. Combination treatment of medication and psychotherapy is recommended as the treatment of choice [31]. Screening tests and a level II ultrasound should be performed at 16 to 18 weeks of gestation to exclude possible major malformations [33].

Expecting women with severe depression, psychosis and suicide ideation require hospitalization. Electroconvulsive therapy, an effective treatment that was found to be safe in pregnancy, should also be considered [31,34].

Nonpharmacologic treatments

Complementary & alternative medicine

There have been a number of recent studies using complementary/alternative medicine approaches for treating depression in pregnancy. These strategies include light and massage therapy, acupuncture and sleep deprivation, with some promising early results. While these studies offer insight into the use of alternative approaches, the findings should be viewed with caution as all of the studies require further replication and several have very small sample sizes.

In an open trial of light therapy, 16 pregnant women (23 weeks) with major depression were exposed to an ultraviolet-screened diffused white florescent light source for 3 to 5 weeks, 60 min daily, within 10 min upon awakening [35]. The findings showed a significant decrease in Hamilton Depression Rating Scale (HRDS) scores. In a subsequent double-blind, placebo-controlled trial (n = 10), the active treatment group showed little change in mood after 5 weeks of treatment (7000 lux) compared with placebo (500 lux), although a clear treatment effect was seen after an additional 5 weeks of light therapy (i.e., 10 weeks of treatment in total) [36]. Bright light therapy was well tolerated by subjects. One instance of hypomania was reported that resolved in 2 days with shortened exposure duration.

A study of massage therapy has also shown positive results. A total of 84 depressed pregnant women (18–24 weeks) were randomly assigned to massage therapy (by their significant other), individual muscle relaxation or standard prenatal care [37]. The women in the massage and muscle relaxation groups had two 20-min sessions/week for 16 weeks. At study end, there was a significant decrease in depression scores on the Profile of Mood States (POMS) and the CES-D for the massage group, less leg and back pain, as well as a lower level of cortisol compared with the muscle relaxation and standard care groups.

In a randomized, controlled pilot study, 61 antepartum women with major depression (11–28 weeks) were assigned to acupuncture tailored for depressive symptoms, nonspecific acupuncture or massage [38]. All participants received 12 sessions of 25 to 30 min each, over 8 weeks. There was a 69% RR in the group receiving acupuncture specific for depression (i.e., HDRS score < 14) and a minimum of 50% reduction of score from baseline. Acupuncture appeared to be well tolerated and no side effects were reported. Individuals in the massage group

showed a significantly lower RR (32%) than those in the specific acupuncture group. Unlike the previous study on massage therapy, this study utilized massage as a control condition and was not designed to test for efficacy.

Parry and colleagues examined the use of partial sleep deprivation in a pilot study of early (slept 3:00–7:00am) or late (9:00pm–1:00am) sleep deprivation, followed by an evening of sleep recovery (10:30pm–6:30am) for the treatment of perinatal depression [39]. Response was measured by a 50% reduction in scores on the Beck and Hamilton Depression scales from baseline. Of the three pregnant subjects, two responded to early sleep deprivation and one of these remained well for the duration of pregnancy, the outcome of the other subject is unknown. Depression symptoms in the third subject did not improve with late sleep deprivation. However, sleep deprivation as a treatment strategy for depression in general, remains controversial [40], and the results of this very small sample should be interpreted with caution.

Complementary/alternative medicine is an area that needs further exploration. At this point there is a paucity of studies that address the efficacy of such approaches. The studies that have been reviewed tend to have low sample sizes, issues associated with power in analyses and can only provide suggestive results at best. However, the importance of these studies is in extending treatments that have been used for other forms of depression/mood disturbance into the area of depression during pregnancy.

Psychoeducation approaches

Psychoeducation approaches combine education within a supportive framework such as one-on-one or group sessions with a facilitator (i.e., nurse, midwife or physician), in order to enhance women's psychosocial health through education and support. Hillier and Slade found that antepartum educational initiatives were beneficial in reducing anxiety and promoting a perception of benefit in participating women [41].

To date, six published studies have examined the effectiveness of psychoeducation sessions during pregnancy in preventing PPD [42–47]. In all but one of the studies [41], the participating women were considered to be at-risk due to identified vulnerability factors (i.e., current or previous depressed mood, familial history of depression or poor social support). Hayes and colleagues excluded women who were considered at-risk, as they were interested in preventing PPD in first-time mothers who had no identifiable risk factors [44]. These studies were reviewed for clues as to whether psychoeducation approaches might help depressed pregnant women.

In a British study, women attended five antenatal monthly group meetings and six postnatal monthly meetings or standard prenatal care. The women had all been identified as being vulnerable to PPD due to current depressive mood, previous history of depression and/or psychosocial factors, as assessed by the Leverton Questionnaire and the Crown–Crisp Experiential Index. Primiparous women attended sessions entitled *Preparation for Parenthood* and second-time mothers attended *Surviving Parenthood*. Both types of sessions focused on providing women with information on adaptation to motherhood, challenges in mothering and PPD. All women were assessed throughout the postpartum period. While second-time mothers showed no benefits from the treatment, first-time mothers in treatment group showed fewer depressive symptoms during the postpartum period than those in the control group [45].

Another study demonstrated a reduction in depressive symptoms postpartum for both treatment and control groups when expectant women were provided with an information package about PPD or standard prenatal care [44]. A midwife guided the women through the information package which included a booklet concerning mood changes during pregnancy that detailed when assistance was necessary and how help could be obtained as well as information concerning how partners and family could be supportive. Women also received an audiotape that described one women's experience of PPD. The information package intervention had no significant treatment effect. Similarly, in the four remaining studies, there were no differences in measures of postpartum mood between the treatment and control groups [42,43,46,47].

Taken together, there is limited evidence that psychoeducation approaches may be helpful in reducing PPD and the effect on antepartum mood remains unclear.

In a review of parenting program studies, Barlow and colleagues found that parent education programs were effective in improving mothers' psychosocial health, including reducing depression [48]. However, these studies have focused on mothers with toddlers and older

children. Future studies might examine how psychoeducation approaches can be combined with other interventions to benefit pregnant women with symptoms of depression.

Psychotherapeutics

Interpersonal psychotherapy (IPT) has been studied in the treatment of depression in pregnancy. The effectiveness of IPT in acute treatment and maintenance therapy of mild-to-moderate depression has been well demonstrated and it is highly acceptable to recipients [49]. IPT is especially well suited for use in pregnant women where a change in role (e.g., transition to motherhood) is a significant issue. IPT has been modified to meet the needs of expectant women (IPT-P) [50], including pregnancy complications [51] or HIV-positive status [52].

In a controlled clinical trial comparing IPT-P with a parenting education program, 50 pregnant women with major depression were randomly assigned to either individual IPT or parenting education for 45 min sessions, weekly, for 16 weeks [53]. Women in the IPT group (21/25 completers) showed significantly greater reductions in depression and global impression measures compared with the education group (17/25 completers). Since improvement was noted by the 12th week of treatment, a shorter period of IPT-P has been suggested for use in future trials.

A second US study found that an adaptation of interpersonal therapy for pregnant women (n = 37) who reported at least one risk factor for PPD (i.e., current depressive symptoms or poor social support), was effective in preventing PPD [54]. Subjects were randomly assigned to receive either four 'IPT-oriented' group sessions or to treatment-as-usual. Each IPT-oriented session had a specific focus. The first session provided a rationale for the program and psychoeducation on mood disturbance (blues and PPD) while the second session focused on role transitions associated with new motherhood. The third session dealt with goal setting, developing support networks and identifying potential interpersonal conflicts arising after birth. The final sessions focused on teaching interpersonal skills for resolving conflicts and reviewing the main ideas from the previous sessions. Women in the treatment group had significantly lower depression-scale scores than the control group and none developed PPD in the first 3 months postpartum.

A briefer version of IPT with depressed pregnant women, delivered in an obstetrics clinic setting, was found to be effective in treating depression [55]. Participants (n = 12), recruited from a public care obstetrics clinic and with an EPDS score of more than 10, received eight (as opposed to 16) sessions of IPT. Participants were compensated for childcare and travel expenses and session scheduling was flexible (including phone sessions). In total, nine of the 12 subjects completed the sessions and depressive symptoms were alleviated in all participants. Only one subject subsequently developed PPD. Notwithstanding the small sample size, this pilot study demonstrated the effectiveness of brief IPT for treating depression in pregnancy, in a culturally sensitive manner among low-income, predominantly African–American women, in a normative setting. This pilot study of IPT suggests that more if its kind are necessary.

There is limited information available on cognitive behavior therapy (CBT) and depression in pregnancy. A Swiss pilot study examined the use of group CBT by having participants attend 12 group sessions and one couple session [56]. They found that group CBT was effective in decreasing depressive symptoms in expectant women and mothers of children up to preschool age. A recent Italian study found that group CBT was effective in reducing psychologic uneasiness in couples waiting for assisted reproduction procedures [57]. Appleby and colleagues found cognitive-behavioral counseling delivered by trained health visitors was a cost-effective approach for treating PPD [58].

Conversely, Zayas and colleagues found that CBT failed to reduce antenatal and PPD symptoms in a group of low-income minority women who were treated in urban primary-care settings [59]. The investigators reported that participant attrition, high turnover of student therapists and hurdles of the research settings negatively impacted the study. Further, Carter and colleagues found that, in a sample of 400 pregnant women, while 370 women agreed to complete an Edinburgh depression scale, most did not agree to additional contact or assessment [60]. Of the 49 women who scored more than 12, only 15 women agreed to be contacted. Only one out of three subjects randomized to CBT started treatment.

In contrast to studies that have incorporated a single modality, several authors have suggested combination or multimodal treatment for

depressed pregnant women, in particular, for women with psychosocial stressors and moderate to severe levels of depression. One group has suggested combining CBT with advocacy, psychoeducation and social support enhancement to reduce depression, expand social networks and enhance mothers' knowledge of child development [61]. A case report of a depressed pregnant adolescent describes an integrated approach using individual cognitive-oriented psychotherapy in combination with antidepressant medication [62].

Psychopharmacologic treatments

SSRIs and serotonin norepinephrine re-uptake inhibitors (SNRIs) are widely used to treat mood and anxiety disorders and a recent survey of prescribing clinicians showed that SSRIs are the first-line pharmacologic treatment preference [63]. Further, recent data indicate that women respond more favourably to SSRIs than tricyclics in the treatment of depression, although the side-effect profile is potentially larger [64].

A US survey of experts in the field of women's mental health showed that SSRIs as a class and in terms of specific medications, are preferred for the treatment of depression in pregnancy [65]. Fluoxetine, sertraline or citalopram are first-line treatments of choice; tricyclic antidepressants and paroxetine are highly rated alternatives [65,66]. If a sedative/hypnotic is deemed essential, then lorazepam or clonazepam is recommended [65].

Antidepressant safety issues

It has been shown that nearly all drugs that are administered during pregnancy will enter, to some degree, the circulation of the fetus via passive diffusion [67]. Based on published studies, venlafaxine appears to cross the placenta in the highest concentration, followed by fluvoxamine and sertraline [68–70]. However, further investigation is required before definitive conclusions can be established (**Table 1**).

Drug-related teratogenesis

During neonatal development, the first 12 weeks of pregnancy is the most vulnerable time for the occurrence of drug-related teratogenesis [71]. To evaluate the risk of fetal malformation due to pharmacotherapy in pregnancy, the incidence of major malformations in pregnancies exposed to drugs should be compared with nonteratogen-exposed pregnancies and to the baseline incidence in the general population, which is approximately 3%. For instance, if there is an increased incidence of a particular malformation above the baseline in a group of infants who were exposed to a drug *in utero* during the first trimester, then the drug is likely unsafe during that time. It is therefore imperative that the baseline risk of congenital malformations and the gestational week of exposure be taken into consideration when deciding on a treatment regime involving medication. A recent meta-analysis has shown that, as a group, SSRIs and SNRIs (specifically fluoxetine, fluvoxamine, paroxetine, sertraline, venlafaxine, bupropion, trazodone and nefazodone), have not shown evidence of major malformations above the baseline rate of 1 to 3% when the recommended dosages are used during pregnancy [72].

Poor neonatal adaptation

This term originally described a pattern of symptoms that included jitteriness, tachypnea, hypoglycemia, hypothermia, poor muscle tone, weak or absent cry, respiratory distress or desaturation on feeding in newborns of women who were taking fluoxetine during the third trimester [73]. With accumulating literature on the SSRIs and SNRIs lethargy, poor colou, sleep disturbance and irritability have been included in this cluster [74], as well as seizures and low Apgar score [33]. These symptoms are generally reported as being transient and self-limiting. Currently, affected infants are generally treated conservatively with observation in a special-care nursery. More severely symptomatic infants may be treated with anticonvulsant therapy (e.g., phenobarbital), fluid replacement and respiratory support. No reports of serious complications or death from poor neonatal adaptation have been published to date [74].

A recent descriptive report of the World Health Organization (WHO) database of adverse drug reactions (with at least 3,000,000 case records) noted 51 certain cases of neonatal 'withdrawal syndrome' associated with the use of paroxetine (43 cases were exposed to paroxetine only), compared with ten certain cases associated with fluoxetine, seven with sertraline, and six with citalopram [75].

What underlies poor neonatal adaptation is not yet understood. The symptoms are posited to result either from SSRI withdrawal or serotoninergic toxicity [33]. The evidence; however, is hampered by an overlap in symptoms between these two phenomena in neonates, and limited knowledge of neonatal psychopharmacology.

Table 1. Median cord to maternal serum concentration ratios of antidepressants and their metabolites.

	Rampono [68]	Hendrick [69]	Hostetter [70]
Antidepressant			
Venlafaxine	1.1		1.7
Fluvoxamine			0.71
Sertraline	0.67	0.27	0.77
Fluoxetine	0.67	0.54	
Citalopram		0.62	
Paroxetine	0.52 (mean)	0.56	
Metabolite			
O-desmethylvenlafaxine	1.0		3.24
Desmethylsertraline	0.63	0.25	0.47
Norfluoxetine	0.72	0.60	
Desmethylcitalopram		0.57	

Notwithstanding, after gestational exposure to an antidepressant, the newborn experiences abrupt discontinuation. Hence, symptoms consistent with withdrawal are biologically conceivable [33].

Further, an understanding of poor neonatal adaptation is confounded by the possible impact of maternal emotional status on fetal development and infant outcome. Investigators have found that newborns of women with high anxiety, depression or anger symptom ratings, were slower to habituate, had a lower birth weight, spent more time in deep sleep, had lower vagal tone and greater relative right frontal electroencephalograph (EEG) activation [76].

Babies of mothers taking SSRIs or SNRIs should be observed for longer than the typical 1 or 2 days postpartum, so that symptoms of poor neonatal adaptation can be recognized and if necessary, treated.

Abrupt discontinuation

Confusion and/or misinformation in addition to fear of teratogenicity can lead women to abruptly discontinue their antidepressant medication after a pregnancy has been confirmed [77]. Sudden discontinuation of antidepressants has been associated with a relapse of depression [78]. Einarson and colleagues interviewed 36 pregnant women 1 month after they received counseling regarding the safety of antidepressant use in pregnancy [79]. They found that 34 subjects discontinued their medication abruptly and 28 on the advice of their healthcare providers. Of the 34 subjects, 26 (70.3%) reported deteriorating physical and psychologic health, 11 reported suicidal ideation and four were admitted to hospital.

Abrupt discontinuation of antidepressants with shorter half-lives, for example, paroxetine, venlafaxine and fluvoxamine, may be associated with withdrawal side effects (also known as discontinuation syndrome), including somatic (dizziness and light-headedness; nausea and vomiting; fatigue, lethargy, myalgia, chills and other flu-like symptoms; as well as sensory and sleep disturbances) or psychologic (anxiety and/or agitation, crying spells and irritability) symptoms [78]. A closely monitored, taper-phase regimen will dramatically reduce discontinuation of side effects.

Postpartum depression

Women with depressive symptoms during pregnancy are at risk for PPD [19]. In addition, a recent prospective study of women who were euthymic during pregnancy but had had a previous postpartum depressive episode, showed that 21 of the 51 subjects (41%) experienced a recurrence of PPD; 90% of cases occurred in the 28 weeks following birth [80]. Thus, continuous monitoring of mood during pregnancy and the first postpartum year, in particular for women who experience depression in pregnancy or who have had a prior episode of PPD, is crucial.

Expert commentary & outlook

With increased recognition of the prevalence of depression in pregnancy, it is expected that healthcare providers of pregnant women will more routinely inquire about mood symptoms during antenatal visits. More information concerning the course of dysthymia across pregnancy is needed. Furthermore, a better understanding is needed of antidepressant medication effects on fetal development, in particular, the brain. Consequent to cautionary statements from North American federal health authorities regarding neonatal adaptation, the likelihood of future clinical trials of antidepressants including pregnant women may be slim and increased scientific study of nonpharmacologic options for the treatment of depression in pregnancy can be anticipated. National public drug information registries might be implemented to document clinical experience in situations where clinical trials are deemed inappropriate. It is expected that guidelines specific to the treatment of depression in expectant women will continue to evolve with emerging evidence.

Highlights

- It is estimated that 25 to 35% of women experience depressive symptoms during pregnancy and that 9 to 18% meet criteria for major depression.
- Depressive symptoms in pregnancy are associated with diminished prenatal care and spontaneous preterm birth. A number of depressed pregnant women may resort to using tobacco, alcohol, or other substances to cope with their symptoms.
- Risk–benefit decisions are best made on an individual case basis by an informed patient in consultation with her family and healthcare provider(s).
- Expectant women who present with depressive symptoms should be encouraged to make lifestyle modifications to enhance their wellbeing.
- Nonpharmacologic treatment strategies, such as counseling or psychotherapy should be explored first in women who present with minor or subsyndromal depression symptoms.
- Preliminary evidence shows beneficial treatment effects of massage therapy, acupuncture and light therapy, although studies of psychoeducation strategies have failed to show a clear benefit for reducing antenatal depression.
- Interpersonal psychotherapy has demonstrated efficacy for the treatment of depression in pregnancy in brief (eight sessions) or longer (16 sessions) forms and can help to prevent postpartum depression.
- Selective serotonin re-uptake inhibitors (SSRIs) as a class and in particular, fluoxetine, sertraline or citalopram, are first-line psychopharmacologic treatments for moderate-to-severe depression in pregnancy.
- Neonates of mothers taking SSRIs or serotonin norepinephrine re-uptake inhibitors during late pregnancy should be observed for longer than the typical one or two days postpartum, so that symptoms of poor neonatal adaptation can be recognized, and if necessary, treated.

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