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Bipolar disorder in the postpartum period: Management strategies and future directions

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Bipolar disorder in the postpartum period: management strategies and future directions

Bipolar I and II disorder are chronic and severe psychiatric illnesses that affect many women. Furthermore, women are at increased risk for mood episodes during the postpartum period compared with non-postpartum periods. Unfortunately, identification of clinically significant depressive or (hypo)manic episodes can be challenging. Delays in detection, as well as misdiagnosis, put women at risk of many negative consequences, such as symptom exacerbation and treatment refractoriness. Early and accurate detection of bipolar I or II disorder in the postpartum period is critical to improve prognosis. At this time, limited recommendations can be made due to a paucity of research. Further research on postpartum bipolar I or II disorder focusing on its identification, consequences and treatment is urgently needed to allow for empirically informed clinical decision-making.

Keywords: bipolar disorder • breastfeeding • diagnosis • mood episodes • pharmacological treatment • postpartum • psychosocial treatment

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Bipolar I and II disorder are chronic and severe psychiatric disorders that have an early age of onset and potentially devastating consequences if improperly managed. It is a disorder resulting from an interaction between complex environmental and genetic factors [1] that are not entirely understood. Reproductive events and hormonal therapies also affect the course of bipolar spectrum disorder (bipolar I or II, and subthreshold bipolar disorder) in women [2]. Individuals with bipolar spectrum disorder experience unusual shifts in mood, energy, cognition and activity. The clinical course of bipolar spectrum disorder in general is characterized by hypomanic, manic, mixed and depressive episodes. A diagnosis of bipolar I disorder requires at least one episode of mania while bipolar II disorder requires an episode of both depression and hypomania. Bipolar I or II disorder results in a high economic burden on healthcare resources, as well as a significant loss of productivity [3]. A recent international study suggests that worldwide bipolar spectrum disorder affects an estimated 2.4% of individuals [4]. In addition, for both men and women bipolar disorder is ranked as the ninth leading cause of years of 'healthy' life lost resulting from disability and premature mortality [5]. The average age of onset for bipolar I disorder is late teens and for bipolar II disorders it is mid-20s, although it can surface in adolescents [6].

For females between the ages of 15 and 44 years old bipolar disorder is the seventh leading cause of years of 'healthy' life lost resulting from disability and premature mortality [5]. Thus, bipolar disorder can greatly affect the lives of women during the childbearing years making bipolar disorder (especially type I and II) in women of childbearing potential an essential public health concern [7]. More striking is that the postpartum period has been found to be a period when women are at high risk for experiencing episodes of severe mental illness, such as bipolar I or II disorder [8–11] and women with a history of bipolar I or II disorder have a 25–40% risk of developing mood symptoms in the postpartum period [12–14]. Diagnosis

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of mood symptoms in the postpartum period can be challenging for a number of reasons, and until recently hypomania was not recognized by the Diagnostic and Statistical Manual of Mental Disorders (DSM) as part of the postpartum specifier [6,15]. The DSM-5 bipolar specifier 'with peripartum onset' now recognizes mood symptoms (depression, mania, or hypomania) with onset during pregnancy or the first 4-weeks postpartum, which will hopefully improve the recognition and care of perinatal mood disorders. However, as the onset specifier of the first 4-weeks postpartum is argued to be too restrictive, women should be monitored for symptoms even after the first month of the postpartum period [16].

This article discusses the presentation, clinical course, and management of bipolar I and II disorder during the postpartum period. The consequences of the disorder, particularly as they relate to the postpartum period, are emphasized throughout. Finally, as our current understanding of the causes and treatment of bipolar spectrum disorder during the postpartum period is limited, areas in need of further empirical inquiry are highlighted.

Identification, prevalence & illness course

Episodes of bipolar spectrum disorder can arise in the postpartum period for the first time or as a recurrence of an existing disorder. However, recognition of episodes during the postpartum period can be particularly challenging for a number of reasons. First, women may not report symptoms. For many women, especially those who have never had a mood episode, it may be difficult to recognize symptoms of depression and/or hypomania. Instead, new mothers may attribute the symptoms (e.g., tearfulness, sleep disruption or changes in energy) to normal physiological changes following childbirth. As a result there can be a delay in the recognition of bipolar spectrum disorder with postpartum onset, especially hypomanic or depressive episodes.

In addition, in the postpartum period hypomania and depression can be very difficult for clinicians to accurately identify [17]. Many individuals with bipolar spectrum disorder are misdiagnosed as having another mental health issue and women appear to be at a higher risk then men for misdiagnosis. For women especially, misdiagnosis of bipolar spectrum disorder as unipolar disorder is common [18]. One study found that postpartum bipolar spectrum disorder is often misdiagnosed as unipolar disorder, even when a history of mood elevation exists [19]. Sharma and colleagues [19] found that 54% of 56 outpatients diagnosed with postpartum depression were later rediagnosed as having postpartum bipolar depression based on lifetime episode history. For 10% of the women, the referral diagnosis of postpartum depression was given regardless of the women previously receiving a diagnosis of bipolar spectrum disorder. The rest of the women had never formally been diagnosed with a bipolar spectrum disorder.

A diagnosis of bipolar I or II disorder may be overlooked or may be ruled out due to no known or actual history of clinically significant manic or hypomanic episodes. Compared with men, women with bipolar I or II disorder experience more depressive episodes [6]. In addition, a high proportion of bipolar I or II disorder, for most individuals affected, is spent in the depressive phase compared with the manic phase [20] and women in particular are more prone to experiencing both mixed features as well as rapid cycling [6]. The disproportionate amount of depressive symptoms can result in unipolar disorder appearing to be the appropriate diagnosis.

Furthermore, while bipolar I disorder appears to affect both sexes equally, some, but not all, reports suggest that bipolar II has a higher prevalence for females [4,6,21,22]. Bipolar II disorder can be particularly challenging to diagnose in the postpartum period because both depressive and hypomanic symptoms can be misconstrued as normal reactions to giving birth. In particular, while hypomanic symptoms are common following delivery [23,24] they may be viewed positively by the individual due to feelings of increased energy and productivity [1,25], and thus go unreported unless questions pertaining to hypomanic symptoms are specifically asked.

In order to assist in detecting individuals at risk for bipolar I or II disorder some research has looked into what factors differentiate bipolar I or II depression from unipolar depression. Individuals with bipolar depression have been found to have more psychotic symptoms, atypical features, mixed depression compared with those with unipolar depression [26]. Individuals with bipolar I depression appear to have more mood lability, psychotic features, psychomotor retardation and comorbid substance abuse. By contrast, those with unipolar depression reportedly have more agitation, anxiety, insomnia, somatic complaints, anorexia and weight loss [27,28]. To date, few studies have addressed the differences between postpartum bipolar depression and unipolar depression. However, one recent study reports that women experiencing their first episode of depression in the postpartum period have higher rates of bipolar disorder compared with women who experience first episode onset of depression at other time points in their lives [26]. Thus, women who have episode onset of depression following childbirth should be closely monitored for symptoms of mania and hypomania.

In addition to differences found between bipolar depression and unipolar depression, some studies have looked at the difference between bipolar symptoms experienced in the postpartum period compared with other time points. Depressive symptoms or mixed episodes appear to be more prevalent than hypomania or manic episodes in the postpartum period for women with bipolar spectrum disorder [2,29]. However, compared with pregnancy, women appear to experience more hypomanic symptoms in the immediate postpartum period [30]. In terms of symptom presentation, one study found that women who experience postpartum onset manic symptoms appear to differ on a number of symptoms from women who have nonpostpartum onset of manic symptoms. Specifically, during manic episodes postpartum women experienced more mixed features including inner tension, worrying over trifle matters, both reported and observed muscular tension, as well as symptoms of apparent sadness, lethargy, emotional response lability, perplexity and disorganization. These women also experienced significantly more depressive and anxiety symptoms than did the women with a non-postpartum manic episode [31].

For women with a pre-existing diagnosis of bipolar I or II disorder, Di Florio and colleagues [12] found that greater than two-thirds will experience at least one mood episode during pregnancy or in the postpartum period. In addition, in this large sample of perinatal women, a diagnosis of bipolar I disorder was associated with a greater risk for perinatal mood episodes a diagnosis of bipolar II disorder or unipolar depression. Furthermore, most perinatal mood episodes had an onset in the postpartum period (versus during pregnancy). Interestingly, women with a bipolar II disorder were almost twice as likely as women with bipolar I disorder or unipolar depression to experience episode onset during pregnancy. Furthermore, in this study approximately 80% of women with bipolar I disorder and 53% of women with bipolar II disorder who experienced onset in the postpartum period did so within the first 4 weeks postpartum. In addition, for women with bipolar I disorder 20% of deliveries were found to be associated with mania or psychotic depression and the episodes usually occurred earlier in the postpartum period while 25% of women experienced nonpsychotic depression and these episodes occurred later in the postpartum period. For women with bipolar II disorder, 40% of deliveries were followed by some major mood episode and they were found to experience a later episode onset than women with bipolar I disorder [12].

Risk

Risk of mood episodes for women with a diagnosed mood disorder is much higher during the postpartum period than during pregnancy, with women with bipolar I disorder presenting the highest risk for mood episodes. In addition, women have a greater risk of postpartum mood episodes if they experienced a mood episode during pregnancy [2,14]. Of those who present with a perinatal mood episode, one in 13 women have been found to have experienced their first lifetime episode during the perinatal period [14]. There are a number of reasons why the perinatal period may be a particularly vulnerable period for the expression of mood symptoms. For instance, hormonal fluctuation, neuroimmunological changes [32–34] and alterations in sleep practices [35], as well as additional stress that can come from having to care for an infant [36], are experiences which have been implicated in the development of postpartum mood symptoms in vulnerable women.

In addition to perinatal specific changes, a number of other factors have been associated with the development of perinatal mood symptoms. Women experiencing depressive symptoms in the postpartum period are also at risk for hypo(manic) symptoms as recent research suggests that women who experience depressive symptoms during the postpartum period are more likely to endorse bipolar symptoms on the Mood Disorder Questionnaire [37] and neuroticism traits on the NEO – Five Factor Inventory [38] than are women who do not experience postpartum depressive symptoms [39]. Furthermore, women whose first ever psychiatric contact was during the first month of the postpartum period had an increased probability of receiving a later diagnosis of bipolar disorder when compared with women who experienced their first ever psychiatric contact at other time points [8]. Thus, the risk of mood symptoms during and following the postpartum period is significant, especially for women with a prior history of a mood disorder.

This risk appears to be particularly high for women with a previous diagnosis of bipolar disorder. One study found that 50% of a sample of 43 women with a pre-existing diagnosis of bipolar I or II disorder or schizoaffective disorder bipolar type had a mood episode reoccurrence following childbirth [40]. Another study reports that 52% of women with a pre-existing diagnosis of bipolar I or II disorder experienced a mood episode during the postpartum period compared with 30% of women with a pre-existing diagnosis of unipolar disorder. In terms of episode presentation, unipolar depression and dysphoric-agitated mixed states were the most common experiences for these women [14]. In addition, recent research suggests that childbirth may be a particular trigger for hypomanic episodes [6] and the postpartum period is found to be a particularly vulnerable time for women to convert from unipolar disorder to bipolar II disorder compared with other

time points [41]. Thus, a pre-existing mood disorder increases the risk for experiencing mood symptoms during the postpartum period as well as the risk of converting from unipolar to bipolar spectrum disorder. Taken together, these reports highlight the need for close monitoring of women with a history of mood disturbance for an underlying bipolar diathesis.

In addition to a history of mood or psychiatric disturbance, other factors have been identified as potential risk factors for postpartum bipolar episodes. Women with a younger age of illness onset are more likely to experience mood episodes during pregnancy and the postpartum period, while women who are unmarried or unemployed are also at increased risk for peripartum mood episodes, especially during pregnancy [14]. In addition, women with a history of antidepressant 'misadventures' (rapid response, loss of response, induction of (hypo)mania or depressive mixed episodes) or treatment resistance to antidepressants are also at particular risk of a bipolar spectrum disorder as are women with a history of bipolar disorder in a first-degree relative [41–44]. These findings of postpartum mood symptoms aggregating in families [44,45] support the proposal that some women may have a genetic vulnerability for experiencing mood symptoms [44]. For women with a history of bipolar I or II disorder or schizoaffective disorder bipolar type, the risk for recurrence of a mood episode is increased for those women who report that the pregnancy was unplanned, are younger in age, or who have history of more than one manic episode [40]. Taken together, women with a personal or family history of a mood disorder or who are experiencing depressive symptoms during pregnancy or in the postpartum period should be closely monitored for a bipolar diathesis, particularly the expression of hypomanic symptoms. This is especially critical for decisions regarding treatment, which will be discussed in a later section.

Comorbidity

One of the challenges in making an accurate diagnosis comes from the finding that those diagnosed with a bipolar disorder have a high risk for comorbid disorders [28]. Those diagnosed with bipolar spectrum disorder frequently are diagnosed with anxiety disorder, behavioral disorders and substance use disorders [4,6,46]. During the postpartum period in particular, comorbidity with anxiety disorders, particularly obsessive–compulsive disorder, has been found in women with a postpartum mood disorder. Furthermore, women may also present with comorbid organic conditions, such as thyroid disorder, which can also result in mood dysregulation [19]. Thus, in many cases comorbid conditions can confound the identification of a bipolar spectrum disorder and can further complicate treatment plans, especially in cases where first-line treatment for comorbid conditions is contraindicated for individuals with bipolar spectrum disorder (e.g., antidepressant monotherapy). For this reason it is important that clinicians carefully screen for bipolar disorder in women presenting with other psychiatric disorders as it has serious implications for management of the bipolar spectrum disorder as well as the comorbid conditions.

Parity

Research tells us that women who experience a mood episode after a first pregnancy have an increased probability of experiencing a mood episode following subsequent deliveries [2]. Conversely, primiparious women have also been reported to be at increased risk for postpartum depression compared with multiparious women. For instance, one study found that primiparous women have a greater risk of experiencing a postpartum mental disorder compared with women on their second live birth. Furthermore, although the rate is reduced compared with the first birth, women on their second live birth are still at increased risk compared with those on their third live birth, while women on their third live birth were not found to have an elevated risk of a mood episode following child birth [47]. Another study found that women who had four or more pregnancies had a reduced risk for mood disorder episodes. The authors speculate that this finding might reflect self-selection against many pregnancies by women who experience complications of the mood disorder during pregnancy or the postpartum period, or women who are more resistant to treatment (i.e., respond poorly to treatment) [14]. Taken together, the findings of these studies suggest that women who experience postpartum depression following a first or second birth may be less inclined to have further pregnancies.

With regard to episode presentation, a recent study found that primiparity was associated with psychosis/manic episodes but not nonpsychotic depression following childbirth in women with bipolar I disorder. The investigators found no association between parity and postpartum episodes experienced by women with bipolar II disorder. Interestingly, and in contrast to the women with bipolar I disorder, an association between nonpsychotic postpartum depression and primiparity was found in women with a diagnosis of recurrent unipolar disorder [48].

In spite of this research, the exact relationship between parity and postpartum mood episodes is still unclear. However, as Viguera and colleagues [14] suggest, the difference in risk for a mood episode based on parity may reflect decisions made to have more

children based on women's personal experience of mood symptoms following childbirth. However, other psychosocial and environmental factors may also play a role. For instance, it is possible that the women do not find subsequent births as stressful or that the women learned how to better balance the challenges of their disorder with motherhood. Furthermore, as women's age increases with each subsequent delivery, age rather than parity might be partially responsible for the observed differences in risk. Thus, there are a number of factors that remain to be explored to better identify why women who have more children are at a reduced risk of postpartum mood episodes or if it is just a matter of self-selection not to have more children in women with a history of postpartum mood disorders.

Consequences

Bipolar disorder, especially type I and II, has significant repercussions for the mother, her infant and her family, especially if the disorder is not well managed or goes untreated. Interpersonal conflict and marital difficulties may be an unfortunate consequence experienced by many individuals with bipolar disorder [18]. This is of concern especially for women with bipolar I or II disorder who experience these difficulties during the postpartum period, as strong social support systems can be very helpful with regard to symptom management [49–51]. In addition to marital and intimate relationship difficulties, bipolar disorder may also have adverse consequences on the mother's relationship with her children [18] and may impair the mother–infant interaction [29]. Furthermore, children of mothers with a history of unipolar or bipolar disorder are at increased risk for intellectual disability [52]. Moreover, maternal depression may also put the child at risk for developing psychosocial and emotional or behavioral disturbances [53].

There are also more serious consequences associated with bipolar disorder, particularly type I and II. The strongest predictor for developing severe manic and psychotic episodes during the postpartum period, both of which are considered psychiatric emergencies, is a history of bipolar I or II disorder [44,54]. Furthermore, women with a bipolar disorder are 23-fold more likely to be admitted to hospital during the first postpartum month than during pregnancy [47]. Moreover, puerperal psychosis following childbirth is much more common for women with a diagnosed bipolar disorder, especially bipolar I disorder, than it is for women in the general population [6]. Puerperal psychosis can present as hallucinations and delusions and/or as symptoms of fluctuating confusion or catatonic features [55] and can result in devastating consequences for the mother and infant as well as the rest of the family [31] as it often leads to hospitalization and substantial functional impairment [56]. One study found that psychosis occurred following 26% of births to women with bipolar I disorder or schizoaffective disorder bipolar type [44]. This rate is substantially higher that the estimated rate of 1–2 in every 1000 deliveries in the general population [6], which illustrates that there is a strong association between bipolar disorder and postpartum psychosis. In addition, a close association between bipolar spectrum disorder and the experience of postpartum psychosis following delivery has been reported, further substantiating the view that bipolar disorder is a high risk factor for episodes of postpartum psychosis. Furthermore, women with bipolar disorder who also have a first-degree relative who experienced postpartum psychosis have an elevated risk compared with women who have no such family history (73 and 30%, respectively) [44].

Individuals with bipolar disorder are also at an estimated 15-fold increased risk of suicide compared with the general population and the life-time prevalence rate for attempted suicide is estimated to be 32.4% for bipolar I disorder and 36.2% for bipolar II disorder. The risk is even greater for those individuals with a history of past attempts [6]. As maternal suicide is a leading cause of death in the postpartum period, particularly for women experiencing a depressive episode [57], those with bipolar I or II disorder are likely at increased risk. Furthermore, a recent report shows that women with a history of mood disorders experienced postpartum suicidal and self-harm ideation at a rate of 6.16 and 16.70%, respectively [58]. In addition to increased risk of suicide, abuse or neglect, and infanticide are other possible serious and tragic consequence of postpartum psychosis or bipolar depression [59,60].

Management

Psychopharmacology

Psychopharmacological treatment is currently the mainstay treatment for bipolar I or II disorder; however, treatment with pharmaceutical agents presents with unique problems during the postpartum period particularly with regard to breastfeeding. The WHO [61] recommends exclusive breastfeeding for at least the first 6 months postpartum. After 6 months postpartum they further recommend that breastfeeding be continued in conjunction with complementary foods for 2 years postpartum or more. Specific health benefits for the infant include enhanced cognitive development, protection against some infections, and reduced risk of sudden infant death syndrome [62,63]. Long-term maternal benefits include protection against both breast and ovarian cancer [62]. Thus, the inherent benefits of breastfeeding, as well as the risk of psychopharmacologic agents being transferred to the infant

through breast milk must be carefully considered when deciding on psychopharmacological treatment for bipolar I or II disorder during the postpartum period.

In some circumstances, due to concerns about infant exposure to pharmacological treatment or as a result of stress or sleep deprivation related to breastfeeding, some women may choose to forgo breastfeeding and formula feed instead. In such instances these women can follow standard treatment guidelines for the pharmacological treatment of bipolar I or II disorder. However, if the woman is breastfeeding, even partially, special considerations must be taken balancing treatment benefits with the risks to the infant, as all psychopharmacologic agents pass into breast milk [64].

While no specific guidelines exist regarding the pharmaceutical management of bipolar I or II disorder during the postpartum period, the American College of Obstetricians and Gynecologists has classified a number of psychopharmaceuticals in terms of lactation risk. Valproate, carbamazepine and olanzapine have been classified as 'safer'; lamotrigine, risperidone, aripiprazole and clozapine as 'moderately safe'; and quetiapine and ziprasidone as 'possibly hazardous' [65]. Other reports suggest that lamotrigine should be used cautiously due to reports of higher-than-expected drug levels in the infant after exposure through breastfeeding [66]. Lithium may be considered contraindicated with breastfeeding because of concerns that it is secreted it high levels into the breast milk and that infants may be unable to clear it effectively [24,67]. However, while high infant serum lithium concentrations have been associated with congenital complications, to date there are no reported adverse clinical or behavioral effects reported in infants of mothers taking lithium during lactation [10,68]. As a result, lithium may be considered in carefully selected women for the treatment of postpartum bipolar disorder. It is also important to consider that renal lithium clearance during pregnancy is nearly double what it is in the postpartum period, and doses may need to be altered in the postpartum period to reflect changing clearance rates and avoid lithium toxicity, which requires close monitoring of serum lithium concentrations [69]. When mothers are being treated with lithium, pediatricians should closely monitor infant lithium levels, as well as thyroid and renal functioning, while the infant is receiving breast milk. Viguera and colleagues recommend that laboratory monitoring include assays of infant serum lithium, TSH, blood urea nitrogen and creatinine [10]. In addition, pediatricians and prescribing clinicians should also advise the mother to monitor the infant for signs of dehydration, such as vomiting and diarrhea, as this can lower the ideal threshold of serum lithium concentrations [70].

Comorbid disorders must also be addressed, although currently no guidelines exist for the pharmaceutical management of postpartum bipolar I or II disorder with comorbid disorders. For the present time, treatment approaches for nonperipartum individuals with comorbid bipolar I or II disorder should be consulted with considerations made for breastfeeding status. However, many individuals with comorbid conditions are excluded from trials on bipolar I or II disorder treatment resulting in a paucity of information being available [71]. Two of the most common comorbid disorders with bipolar spectrum disorder are anxiety and substance use disorder. For comorbid anxiety, antidepressant monotherapy should be avoided due to the potential for exasperating bipolar symptoms. Alternatively, quetiapine or olanzapine monotherapy, or olanzapine combined with fluoxetine, may be considered as first-line treatment. As there is currently a paucity of research on other atypical antipsychotic medication for the treatment of bipolar I or II disorder during the postpartum period, more research is needed before specific recommendations can be made for this population with regard to other atypical antipsychotic. For comorbid substance abuse requiring pharmaceutical treatment, valproate may be considered alone or in combination with lithium (see [71] for a review). Once again, there is limited research for the pharmaceutical treatment of bipolar spectrum disorders with comorbid conditions and none of the studies focused on the postpartum period, necessitating careful monitoring with these treatment strategies.

While the prospect of taking psychotropic drugs while breastfeeding may not be a desirable treatment option in the eyes of many mothers or clinicians, the benefits of psychopharmaceutical treatment may outweigh the risks of infant exposure. Following childbirth, women with bipolar I or II disorder are at high risk for episode recurrence and as a result many experts recommend prophylactic treatment in the postpartum period with mood stabilizers [64,72]. Unfortunately few studies report on the safety and efficacy of prophylactic treatment for the prevention of postpartum mood symptoms in women with a history of bipolar I or II disorder. However, there is some evidence that prophylactic treatment with mood stabilizers through delivery and into the early postpartum period significantly reduced mood episode recurrence rates [73] and lithium discontinuation during pregnancy is associated with increased risk for postpartum mood episodes compared with women who remained on lithium therapy through pregnancy and into the postpartum ([74]; also see [75]). Olanzapine prophylactic treatment also has preliminary evidence of being effective in preventing mood symptoms in the postpartum period in women

with bipolar I or II disorder, including for women with a previous history of postpartum mood episodes [76]. On the other hand, divalproex sodium as prophylactic treatment administered in the immediate postpartum period was not found to be more beneficial than clinical monitoring without drug treatment [75].

Moreover, for many women it may not be realistic to interrupt drug treatment during pregnancy and/or the postpartum period. In such cases steps can be taken to reduce infant exposure. In order to reduce the number of drugs the infant is exposed to, it is advised that women remain on the same psychotropic drugs in the postpartum period as they received during pregnancy whenever possible [64,72]. Thus, if at all possible, careful planning should begin prior to conception. Furthermore, careful considerations should be made with regard to dose, issuing only the minimum dose required to produce the desired therapeutic effect. Finally, limiting the number of psychotropic drugs whenever possible can also limit the number of psychopharmacologic agents the infant is exposed to.

Psychotherapy

Currently there are no studies evaluating psychotherapy for the management of bipolar spectrum disorders specifically during the postpartum period. However, over the recent years, the role of psychotherapy has gained increased empirical attention and certain forms of psychotherapy are now seen as not only an effective adjunctive treatment to drug treatment, but also as a necessary component for the management of bipolar I or II disorder. In terms of empirical support, psychoeducation, particularly targeted at families, and cognitive behavioral therapies (CBT) are the most studied psychotherapies for the treatment of bipolar I or II disorder and have produced encouraging results. The goal of psychoeducation, often provided in a family format, is to teach individuals with bipolar I or II disorder (and their family) how to adjust to having bipolar I or II disorder and to give them a better understanding of the disorder [77]. CBT often incorporates psychoeducation, but also focus on the cognitive, affective, and behavioral components of the illness [78]. More recently, interpersonal and social rhythm therapy (IPSRT) has been studied in the treatment of bipolar disorder. In addition to focusing on the resolution of interpersonal problems, IPSRT aims to stabilize daily and nightly routines such as when the individual goes to bed, wakes up and when they schedule social activities [79].

Psychoeducation, CBT, or IPSRT can be used complementary to pharmacotherapy for the treatment of bipolar spectrum disorder and for individuals who are only experiencing very mild symptoms of depression, psychotherapy alone may be considered but must be closely monitored. In such cases, psychotherapy alone may be very desirable for women who intend to breastfeed in the postpartum period, due to concerns of drugs passing through the breast milk to the infant. Psychotherapy aims to improve medication adherence when applicable, as well as patients' awareness and understanding of the disorder and ability to identify prodromal symptoms in their early manifestation. Psychotherapy can also assist patients in developing and enhancing coping skills to better manage and live with the disorder. Depending on the therapy used, benefits of psychotherapy also include increased mood stability, improved interpersonal functioning, better quality of life [77,80,81], and assistance with comorbid conditions [71].

Lifestyle considerations

There are a few aspects of lifestyle women with bipolar spectrum disorder can consider to help reduce physical and psychological stress, and potentially improve mood stability. When possible, enlisting the help of others to help care for the infant may be helpful in reducing maternal stress and maintaining mood stability. Perceived social support is inversely related to depressive recurrence in bipolar I or II disorder [48], and social support from partners, other family members, and/or friends is reported to be positively related to maternal self-efficacy and inversely related to postpartum depression [49]. In fact, having two or more friends or relatives available as part of the mother's social network is reported to be significantly related to lower depression scores compared with mothers who reported having one or no friends or relatives available [50]. Thus, efforts to strengthen social ties and utilize available supports may improve maternal mental health in the postpartum period.

In addition, the demands of attending to an infant lead to sleep disruption and can impair sleep quality. As poor sleep quality has been found to be associated with postpartum depressive symptom [82] and may play a role in the development of manic and psychotic symptoms [35], efforts to maximize sleep duration and quality provide considerable benefit. In order to minimize sleep disruption and maximize hours of sleep, allowing others to assist with feeding the infant should be considered [83]. This can be done through bottle feeding breast milk extracted via breast pump or, when necessary or appropriate, through supplementation with formula.

Expert commentary

Distinguishing between unipolar disorder and bipolar spectrum disorder is necessary as optimal management of these conditions differ, and treating bipolar spectrum disorder with antidepressant monotherapy can precipitate or exasperate mood symptoms, namely

mania and mixed episodes [84]. As well, improper treatment can lead to treatment refractoriness [85], and delays in initiating mood stabilizers can lead to a deterioration in social functioning, greater risk of hospitalization, and increase the risk of attempted suicide [86]. Due to the emerging evidence that there is an elevated risk for experiencing episodes of bipolar spectrum disorder during the postpartum period, women with postpartum depression should be routinely screened for mania and hypomania.

Those at risk require close monitoring by a clinician qualified in the management of bipolar spectrum disorder beginning before or during pregnancy and continuing throughout the postpartum period. This is especially critical due to the potential for serious consequences for some women if bipolar spectrum disorder is left untreated, such as abuse or neglect [59,60], which may impact child development. As well, bipolar spectrum disorder left untreated increases the risk of developing severe manic and psychotic episodes [45,47,54] as well as the risk of symptoms related to severe depression such as thoughts of self-harm and suicidal ideation, attempts, and completion [6,58].

Identification of both (hypo)manic and depressive mood episodes can be particularly challenging in the postpartum period, as mood symptoms are common following childbirth. For this reason all women should be screened and closely monitored for both (hypo) manic and depressive symptoms during the postpartum period, especially if they are at risk (e.g., personal history or positive family history of a mood disorder). In the absence of a validated clinical diagnostic tool for detecting bipolar spectrum disorder specifically related to the postpartum period, screening instruments such as the Mood Disorder Questionnaire [37] may be used [87,88] in conjunction with a comprehensive clinical interview. Symptoms such as racing thoughts, hypersomnia, psychotic symptoms and atypical depressive features may be indicative of an underlying bipolar diathesis, and a diagnosis of bipolar spectrum disorder should be carefully considered when these features are present [24,89].

Diagnostic confirmation is the first step in proper management and the diagnosis should be made based on information drawn from multiple sources including clinical interviews and screening instruments, as well as family history and family reports. Once a diagnosis of bipolar spectrum disorder is established, treatment and management of the disorder can still be challenging [1]. Furthermore, as bipolar I or II disorder has a high rate of comorbidity with other mental health disorders (e.g., anxiety), careful assessment to establish other comorbid disorders is necessary and will assist in improving the treatment plan. Treatment plans can be further complicated for women during the postpartum period due to issues such as breastfeeding. Moreover, due to a lack of research and evidence-based guidelines specifically related to postpartum bipolar spectrum disorder management, definitive recommendations have not and cannot be made. For the time being, management should follow the same guidelines as for nonpuerperal bipolar spectrum disorder and tailored to breastfeeding women.

General options for the acute management of bipolar depression include quetiapine, lamotrigine, lithium, valproate, quetiapine plus lamotrigine, and lithium plus lamotrigine. Options for prophylactic treatment include lithium, lamotrigine, or atypical antipsychotics such as quetiapine and olanzapine [76,90]. Whenever possible psychopharmacolologic agents found to be effective in managing the symptoms of bipolar I or II disorder prior to pregnancy should be considered for treatment in the postpartum period even if interrupted during pregnancy. Antidepressant monotherapy should be avoided in favor of mood stabilizers and neuroleptics [91]. Furthermore, antidepressants can induce mood instability making polypharmacy necessary; for these reasons caution must be exercised when prescribing antidepressants [90]. In addition, while all psychopharmacologic agents pass in varying quantities from mother to infant through breast milk, some are recommended as less innocuous than others with breastfeeding. Specifically, valproate, carbamazepine, and olanzapine have been classified as 'safer' medications by American College of Obstetricians and Gynecologists [65]. Efforts to reduce the number of medications prescribed while breastfeeding should be made. However, this may be challenging as there is some evidence that the postpartum period is a time when treatment resistance may predominate [91], although early identification of symptoms and prompt treatment may increase treatment success [90].

Empirically supported psychotherapies may be beneficial alone or, more often, as adjunct to pharmaceutical treatment. While there are no studies examining psychotherapeutic treatment for postpartum bipolar spectrum disorder specifically, recent research shows that certain forms of psychotherapy have an important role to play in the management of bipolar spectrum disorder. Regardless of whether women are receiving psychotherapy alone or on combination with pharmacotherapy, close monitoring is essential for early recognition of emerging symptoms.

Conclusion

Bipolar spectrum disorders are challenging disorders to manage and can be even more challenging to diagnose. This is especially true during the postpartum period when women commonly experience mood symptoms

resulting from natural physiological and environmental changes. Swift and accurate diagnosis can lead to improved management of the disorder while delays in identifying the disorder can have adverse consequences on treatment prognosis. Diagnosing or ruling out postpartum bipolar spectrum disorder should be based on a combination of validated screening assessments, as well as evidence taken from clinical interviews with the patient and, when possible, an informant. The interview should not only cover acute symptoms but should also consist of a comprehensive assessment of historical mood symptoms and family history. Treatment decisions should be based on a careful risk–benefit assessment considering the advantages for managing mood symptoms against the disadvantages associated with infant exposure to psychotropic drugs. In addition, psychoeducation or other forms of empirically supported psychotherapy should be offered to improve medication adherence and manage psychosocial complications. Bipolar I and II disorders are chronic and serious disorders and more research is needed to better identify and treat these disorders. Comprehensive assessment of at-risk women, in addition to early intervention and careful monitoring, can improve the prognosis and enhance the quality of life of women experiencing bipolar depression in the postpartum period.

Future perspective

Research on bipolar spectrum disorder in the postpartum period is still preliminary and much more work needs to be done. Through the course of this review a number of areas in need of further investigation were identified. A better understanding of the influential factors for developing postpartum mood episodes would be clinically helpful to assist in identifying individuals at risk. Additionally, there are a number of physiological changes that occur during the peripartum period; a better understanding of how these changes (e.g., changes in gonadal hormone levels or changes in immune system functioning) affect the course of bipolar spectrum disorder may have implications for both prevention and treatment. With regard to diagnosis, more information to help differentiate unipolar depression from bipolar depression specifically during the postpartum period would be highly useful clinically. In addition, large controlled studies are needed of both clinical and nonclinical populations to determine the prevalence of postpartum hypomania and to better differentiate it from normal elation and mood fluctuation following childbirth.

Further information is also needed regarding the use of psychopharmacotherapy for the treatment of bipolar I or II disorder during the postpartum period specifically related to transfer through breast milk and infant safety. Such research would allow for specific guidelines to be set outlining the management of bipolar I and II disorder during the postpartum period. Moreover, treatment recommendations regarding the pharmacological management of bipolar I and II disorder during pregnancy can have implications for illness course and management during the postpartum period. As treatment recommendations and information regarding pharmacotherapy during pregnancy are also lacking, research should also focus on better understanding the safety of psychopharmacotherapy for bipolar I and II disorder during pregnancy.

At present, a limited number of studies have reported that for women with a history of bipolar I or II disorder discontinuation of mood stabilizers during pregnancy is associated with high risk for recurrence and overall maternal morbidity. On the contrary, continuation of mood stabilizers, such as lithium [10,74] and lamotrigine [10,68] are associated with a marked reduction in such risks. Furthermore, Viguera and colleagues report that women with bipolar I disorder were more likely than those with bipolar II disorder to continue mood stabilizer treatment during pregnancy, to be maintained with lithium as the primary mood stabilizer, and to be treated with adjunctive psychotics [10].

Currently, there are no studies specifically on psychotherapy for the management of bipolar spectrum disorder during the postpartum period. CBT, IPSRT and psychoeducation for bipolar spectrum disorder in general have shown evidence of efficacy and may have similar or additional benefits for women who are trying to manage the disorder in the postpartum period. Future research focused on attaining empirically supported treatments for the management of bipolar spectrum disorder, particularly during the postpartum period, is encouraged.

While not previously discussed in this review, transcranial magnetic stimulation may be a beneficial noninvasive treatment for severe cases of postpartum depression [92] and electroconvulsive therapy is a promising option during pregnancy for manic, mixed and depressive episodes [93,94]. It is possible that either of these treatment options may be desirable for the treatment of postpartum bipolar I or II disorder in place of psychopharmacology in women who are breastfeeding. However, considerable further research is required to establish the efficacy and safety of treating postpartum bipolar I and II disorder with either of these interventions.

A number of lifestyle factors, as they relate to postpartum bipolar spectrum disorder, would also benefit from further exploration. The role of sleep disruption in eliciting or exacerbating postpartum hypomanic, manic or mixed episodes, and its possible role in

postpartum depression, requires further study. Furthermore, the role of perceived and objective social support on the illness course of bipolar spectrum disorder requires further study. While some information exists regarding the relationship between depressive episodes and perceived social support, information regarding the relationship of manic episodes and social support is lacking [49].

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Executive summary

Background

- Bipolar I or II disorders are chronic and severe psychiatric disorders that, if improperly managed, can lead to potentially devastating consequences.
- Women with bipolar I or II disorder are at risk of experiencing the disorder during their child-bearing years making bipolar I or II disorder in women of child-bearing potential an essential public health concern.
- Women are more prone to experiencing both mixed features as well as rapid cycling, and spend more days in the depressive phase of the illness compared with their male counterparts.

Prevalence & illness course

- Episodes of bipolar spectrum disorder can arise in the postpartum period for the first time or may be a recurrent episode of an existing disorder.
- Recognition of hypomanic episodes during the postpartum period can be challenging frequently resulting in misdiagnosis.

Risk

- Women with a diagnosed mood disorder are at increased risk of experiencing a mood episode during the postpartum period, with women with bipolar I disorder being at the highest risk.
- Close monitoring of women with depressive symptoms is necessary as there may be an underlying bipolar diathesis.
- A number of factors have been identified as potential risk factors for postpartum bipolar episodes and clinicians should enquire about these risk factors when trying to determine if a diagnosis of a bipolar spectrum disorder is appropriate.

Comorbidity

- Individuals with bipolar I or II disorder have a high risk for comorbid disorders, particularly anxiety disorder, behavioral disorders and substance use disorders.

Parity

- Parity appears to play a role in the illness course of bipolar I or II disorder.

Consequences

- Bipolar I or II disorder has significant repercussions for the mother, her infant and her family, especially if the disorder is not well managed.

Psychopharmacology

- The mainstay treatment for bipolar I or II disorder is psychopharmacological treatment; however, treatment with pharmaceutical agents presents with unique problems with regard to breastfeeding.
- Currently no specific guidelines exist regarding the pharmaceutical management of bipolar I or II disorder during pregnancy or the postpartum period.

Psychotherapy

- Psychoeducation, cognitive behavioral therapy, and interpersonal and social rhythm therapy have shown to be efficacious in managing bipolar I or II disorder when combined with pharmacological treatment.

Lifestyle considerations

- Enlisting the help of others to help care for the infant may be helpful in reducing maternal stress and maintaining mood stability.

Expert commentary

- Distinguishing between unipolar disorder and bipolar spectrum disorder is necessary as optimal management of these conditions differs and improper treatment can have devastating consequences.
- Diagnostic confirmation should be made based on information drawn from multiple sources including clinical interviews, screening instruments, as well as family history and family reports.

Future perspective

- A better understanding of factors that can assist in the early identification of women at risk of postpartum mood disorders is urgently needed.
- Further information is also needed regarding the use of pharmacotherapy and psychotherapy for the management of bipolar I or II disorder during the postpartum period.

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