Medical Hypotheses 118 (2018) 26–28

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

Should all women with postpartum depression be screened for bipolar disorder?

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ARTICLE INFO

Keywords:
Bipolar
Depression
Postpartum
Hypomania
Treatment

ABSTRACT

The term postpartum depression is used generically to denote occurrence of a depressive episode after childbirth. Emerging research suggests that bipolar disorder is common among women with postpartum depression. Due to the lack of awareness of its existence, bipolar postpartum depression is often misdiagnosed as major depressive disorder, causing long delays for women to receive appropriate treatment. We hypothesize that screening all women with postpartum depression for bipolar disorder would help correctly identify subgroups of women based on the underlying psychiatric diagnosis. This suggested approach could improve the outcome of postpartum depression and facilitate timely disorder-specific treatment interventions.

Introduction

Approximately 6.5%–12.9% of women have a major or minor depressive episode in the first 12 months postpartum [1]. Depression may begin for the first time after childbirth; however, for the vast majority of women it is a recurrence of either major depressive disorder or bipolar disorder. Depression is the most common type of recurrence in women with bipolar disorder [2]. In one study, nearly 19% of women with bipolar I disorder, and 29% of women with bipolar II disorder had episodes of major depression after childbirth in spite of prophylactic drug treatment [3].

Postpartum depression (PPD) has historically been considered a manifestation of major depressive disorder; however, recent research developments have prompted a reappraisal of the diagnostic status of PPD. By allowing the use of the peripartum-onset specifier (occurrence of a depressive episode during pregnancy or first four weeks postpartum) to denote cases of bipolar II disorder in addition to major depressive disorder and bipolar I disorder, the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition [4] has expanded the repertoire of PPD and highlighted the need to differentiate between unipolar depression and subtypes of bipolar depression.

Childbirth and ubiquity of hypomania

Hypomanic symptoms occur in 9.6%–20.4% of women after childbirth [5]. The unique role of childbirth in the induction of hypomanic symptoms was highlighted in a longitudinal study from the United Kingdom that found an eight-fold increase in the prevalence of hypomanic symptoms in the first week postpartum compared to during pregnancy; however, there was no significant increase in cases of depression from pregnancy to the postpartum period [6].

The majority of studies on postpartum hypomania have used the Highs scale, a self-rating scale based on the Schedule for Affective Disorders and Schizophrenia-Lifetime Version [5]. Currently, there are no studies on the prevalence of postpartum hypomania using the DSM-5 diagnostic criteria. Similarly lacking are studies on the DSM-5 diagnostic profile of women with hypomanic symptoms in the postpartum period. Also, we do not know whether hypomanic symptoms can occur alone, or are invariably accompanied by depressive episodes.

Notwithstanding the lack of studies addressing these issues, it is clear that the hypomanic symptoms are followed by depressive episodes in some women [7]. Glover and colleagues [7] reported that 50% of women with hypomanic symptoms, compared with 18% of women without these symptoms in the first postpartum week, scored 10 or higher on the Edinburgh Postnatal Depression Scale (EPDS) at six weeks postpartum. Using an EPDS cut off of 13, another study found that 25% of women with hypomanic symptoms after childbirth compared with 5.2% of women without these symptoms had depressive symptoms at eight weeks postpartum [8].

PPD and bipolar disorder

There is accumulating evidence that a large number of women with PPD have hypomanic or manic symptoms. Hannah et al. [9] used a

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https://doi.org/10.1016/j.mehy.2018.06.016
Received 23 March 2018; Accepted 19 June 2018
0306-9877/

semi-structured interview to retrospectively assess prevalence of hypomania in women with new-onset PPD and found that 20.5% of them had hypomanic symptoms in the early postpartum period compared with only 8.7% in the control group. Heron and Oyebode [8] estimated that approximately 20% to 25% of women with PPD have antecedent hypomania. More recent studies have reported a higher prevalence of hypomania among women with PPD. Wisner and colleagues [10] found that 22.6% of women who screened positive on the EPDS (a score of 10 or more) in the postpartum period, had bipolar disorder. Among women with an EPDS cut off of 13, a higher proportion (26.7%) had bipolar disorder. This was likely an underestimation because the study participants were only screened for depression and not for bipolar disorder. A Polish study found that 23.7% of women had a positive Mood Disorder Questionnaire (MDQ) screen using the alternate scoring (a score of ≥ 7), and 4.6% of women scored positive using the traditional scoring (a score of > 7, co-occurrence of symptoms, and accompanying moderate or serious functional impairment) [11]. A register-based study from Denmark found that postpartum women with first-onset mood disorder who were treated with antidepressants were at increased risk of developing bipolar disorder compared to women who had a first-onset episode outside of the postpartum period [12].

Bipolar disorder is particularly common among women referred to tertiary care centres with a suspected diagnosis of PPD. A study at our clinic found that 54% of these women met the DSM-IV criteria for bipolar disorder [13]. In a study from Korea of women hospitalized after committing or attempting filicide, postpartum-onset of depression predicted a change in diagnosis from major depressive disorder to bipolar disorder. Of the patients with major depressive disorder at admission, 64.7% were subsequently classified as having bipolar disorder based on prospective occurrence of hypomanic or manic episodes [14].

To sum, several studies have reported a high prevalence of hypomanic or manic symptoms in women with PPD. These symptoms are more prevalent in women with more severe PPD or women attending specialized psychiatric clinics.

Subthreshold bipolar disorder and the peripartum onset specifier

With a lifetime prevalence of 2.4%, subthreshold bipolar disorder was the most common type of bipolar disorder in the National Comorbidity Survey replication, accounting for nearly 50% of all cases [15]. Rates of receipt of treatment were much lower in individuals with subthreshold bipolar disorder compared to bipolar I or bipolar II disorder. In the Bipolar Disorders: Improving Diagnosis, Guidance and Education (BRIDGE) study, approximately half of the patients presenting with a major depressive episode in the context of bipolar disorder were misdiagnosed as having major depressive disorder using a definition just slightly broader than the DSM-IV criteria. The clinical and safety profile of patients with subthreshold bipolar disorder was more similar to threshold bipolar disorders rather than major depressive disorder, suggesting that these patients should be managed with treatments normally indicated for bipolar disorder [16].

Only a handful of studies have reported on the prevalence of subthreshold bipolar disorder in the postpartum period. Wisner et al. [10] found that approximately 19% of women with bipolar disorder met the DSM-IV criteria for bipolar disorder not otherwise specified (NOS). Another study reported that 29% of women seen at a specialty clinic for PPD met the diagnostic criteria for bipolar disorder NOS [13].

The DSM-5 has replaced the DSM-IV bipolar disorder NOS diagnosis with specified bipolar or related disorder. It now includes subthreshold presentations such as hypomanic episodes of two to three days duration, or fewer than four symptoms of hypomania in patients with a major depressive episode. The DSM-5 peripartum onset specifier allows its use to characterize hypomanic/manic or depressive episodes; however, the specifier cannot be used to denote subthreshold hypomanic symptoms [4]. As is the case outside of the postpartum period [15], specified bipolar or related disorder may be the most common presentation of bipolar disorder after childbirth.

Postpartum diagnostic conversion

The frequency with which hypomanic symptoms occur in the postpartum period among women with major depressive disorder has been the subject of two Canadian studies. One study found that women with an antecedent diagnosis of major depressive disorder were at risk of developing hypomania in the first six months postpartum. In fact, compared to the rates of switching in populations not undergoing parturition, the results showed that the rate of diagnostic switching to bipolar II disorder (6.52%) was at least 11- to 18- fold higher [17]. According to the results of another study, 34.6% of women with major depressive disorder experienced hypomania or mania defined by an Altman Self-Rating Mania scale score of ≥ 6 during the postpartum period [18].

An international study conducted in secondary care facilities found that the risk of converting to bipolar disorder among women with first-onset of depression in the postpartum period was three-fold higher compared to rate of switching in women with a non-postpartum onset of depression. Depending on the diagnostic criteria used, 15%–50% of women with first-onset of depression in the postpartum period were thought to have bipolar disorder [16]. A population-based study from Denmark found that approximately 14% of women with first-time psychiatric contacts during the first month postpartum converted to a bipolar diagnosis within the 15-year follow-up period compared with 4% of women with a first psychiatric contact unrelated to childbirth [19].

In summary, childbirth appears to be a potent trigger for de novo occurrence of hypomanic and manic symptoms in women with a history of PPD emphasizing the need to routinely screen for manic symptoms in women with ‘unipolar’ depression.

Changing the paradigm

Misdiagnosis of bipolar disorder is common and can have serious consequences. This is particularly true in the postpartum period because the injudicious use of antidepressants may increase the risk of psychiatric hospitalization and compromise the safety of the mother and her infant. A diagnostic reconceptualization of PPD that emphasizes the hierarchical placement of bipolar depression over unipolar depression is needed. This means that clinicians will have to rule out a diagnosis of bipolar disorder before diagnosing a woman with PDD as having major depressive disorder. It is hypothesized that screening all women with PPD for bipolar disorder might improve the outcome of postpartum depression due to enhanced diagnostic accuracy, and the use of disorder-specific treatment interventions.

Screening

Diagnosing hypomania can be challenging, especially in the postpartum period. It may be difficult for women to differentiate between hypomania and the normal joy that accompanies childbirth. Women may deny or minimize the extent of hypomanic symptoms because a diagnosis of bipolar disorder is viewed less positively than depression [20]. The prevalent state of depression may make it difficult for women to recall and report symptoms of hypomania. Also, a lack of awareness of postpartum hypomania among physicians and consequent lack of routine screening for bipolar disorder may result in some women receiving a diagnosis of major depressive disorder.

The recently published Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) guidelines have recommended that all women with depression should be screened for bipolar disorder during and after pregnancy [21]. The MDQ, a 15- item self-report inventory that assesses the lifetime prevalence of hypomanic or manic symptoms is the most studied

questionnaire during or after pregnancy [17,22]. The MDQ is a screening tool that has been validated in the peripartum population [23]; however, additional evaluation is required for diagnostic confirmation of bipolar disorder due to its poor positive predictive value [24–26].

Diagnostic evaluation

Correct diagnosis is the most important prerequisite for optimal treatment of postpartum mood disorders. Women with unipolar PPD who are at risk of developing bipolar disorder, including those with concomitant mixed features, family history of bipolar disorder, first-onset of depression in the postpartum period, occurrence of depression in the early postpartum period, and psychotic features, should be identified and monitored for emerging symptoms of mania or hypomania.[17,24]. Women with a positive MDQ should be referred for psychiatric evaluation. A diagnosis of bipolar disorder can be expedited by asking women about symptoms of mania or hypomania who are presenting with symptoms of PPD and identifying the distinguishing features of bipolar depression [27]. Collateral information from a family member is often needed to help clarify the diagnosis of bipolar disorder.

Treatment

Treatment of depression in the postpartum period is challenging. Unfortunately, there are no controlled trials of mood stabilizers in women with bipolar PPD. Similarly there is a lack of data on the optimal treatment of women with PPD who are considered at risk of developing bipolar disorder. Classifying PPD into major depressive disorder and bipolar disorder would encourage consideration of diagnosis-specific treatment interventions including the use of treatments recommended for bipolar depression.

Conclusion

Bipolar depression is common after childbirth. There is preliminary evidence that bipolar depression may be as common as unipolar depression among women referred for PPD to tertiary care centres. Due to the lack of routine screening, women with bipolar disorder are often misdiagnosed as having major depressive disorder. The misdiagnosis and mismanagement of bipolar disorder as unipolar depression can have deleterious, and at times deadly, consequences [14]. According bipolar depression a higher diagnostic status than unipolar postpartum would likely facilitate timely identification and accurate diagnosis of bipolar disorder. A hierarchical approach to diagnosis might also improve the treatment of PPD by helping to identify subgroups of women based on the underlying psychiatric diagnosis. It is also hoped that the increased awareness of bipolar PPD among clinicians and the public would accelerate research on this topic, including its prevalence in both clinical and non-clinical settings, as well as its psychotherapeutic and pharmacological treatment.

Conflict of interest statement

Dr. Sharma has received grant support from, participated on scientific advisory boards for, or served on speakers' bureaus of Assurex, Genome Canada, Neurocrine Biosciences, Sage Therapeutics, Stanley Medical Research Institute, and Sunovion Pharmaceuticals.

Dr. Al-Farayedhi reports no financial relationships with commercial interests.

Ms. Doobay reports no financial relationships with commercial interests.

Ms. Baczynski reports no financial relationship with commercial interests.

Acknowledgement

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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