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Title:
Peripartum antidepressant use is associated with an increased risk of postpartum hemorrhage

Authors: Jane B Ford, Jonathan M Morris

Commentary on: Palmsten K, Hernández-Díaz S, Huybrechts KF, Williams PL, Michels KB, Achtyes ED, Mogun H, Setoguchi S. Use of antidepressants near delivery and risk of postpartum hemorrhage: cohort study of low income women in the United States. BMJ. 2013 Aug 21;347:f4877

Context
Increased incidence of postpartum hemorrhage is reported in a number of high resource settings since the 1990s.[1] The increase appears unrelated to factors such as rising rates of caesarean section or increasing maternal age.[1] Recent studies have investigated the association between antidepressant use at different stages of pregnancy and postpartum hemorrhage, with two studies demonstrating a 1.20[2], and 1.45-fold[3] increased risk of bleeding at delivery and another study[4] reporting no association. Selective serotonin uptake inhibitors (SSRIs) are increasingly prescribed and may impair platelet function by blocking serotonin uptake into platelets and impairing their homeostatic ability. The authors in the current study aimed to assess the association between exposure to antidepressants, particularly SSRIs, at the time of delivery and postpartum hemorrhage.

Methods
This US study used nationwide Medicaid data comprising a 2000-2007 cohort of pregnancies among low income women. The authors restricted their population to inpatients/outpatients with ICD9 diagnoses of mood and anxiety disorders. Exposure to antidepressants categorized as serotonin reuptake inhibitors or non-serotonin reuptake inhibitors was based on prescription dispensing date and supply relative to delivery date. Women exposed to more than one drug type were excluded from analysis. Four mutually exclusive exposure groups were assessed relative to delivery: current exposure (women with a supply date overlapping the delivery date), recent exposure (at least one day in the month prior), past exposure (supply ending 1-5 months pre-delivery) and unexposed (no supply of antidepressants in the last five months). Postpartum hemorrhage was identified using ICD9 coding during the admission for delivery (inpatients), or within three days of the delivery date (outpatient deliveries). Confounders assessed included: year, age, race, multiple pregnancy, coagulopathies, diabetes, proxies of mood disorder severity and comorbidity, indications for antidepressants, use of psychotropic drugs, and other drugs associated with bleeding risk. Generalized estimating equations were used to identify relative risks (and risk differences) for postpartum hemorrhage among women exposed and unexposed to antidepressants.

Findings

Of the 106,000 pregnant women with diagnoses for mood or anxiety disorders, 15.1% had a supply of antidepressants overlapping their delivery date including 12,710 (12%) with exposure only to serotonin reuptake inhibitors (SRI) and 1,495 (1.4%) with exposure only to non-serotonin reuptake inhibitors (non-SRI). The risk of postpartum hemorrhage was 2.8% among women with mood/ anxiety disorders but no exposure to antidepressants and ranged from 2.5-4.0% in the groups exposed to SRIs and non-SRIs. Compared with no exposure, women with current exposure to SRI had a 1.47-fold increased risk of postpartum hemorrhage (95% CI 1.33-1.62) and women with current non-SRI exposure had a 1.39-fold increased risk (1.07-1.81). Recent SRI exposure and past non-SRI exposure showed borderline associations with postpartum hemorrhage with adjusted relative risks of 1.19 (1.03-1.38) and 1.26 (1.00-1.59) respectively.

Commentary

In the context of differing published findings, the authors of this study sought to harness the strengths of nationwide data to investigate differing windows of exposure to antidepressants in pregnancy and subsequent postpartum hemorrhage.

While strengths of using population-based data include high generalisability of findings, the restriction to low-income women on single therapy potentially negates this advantage. Further, the study is limited by likely under-ascertainment of women with mood or anxiety disorders in pregnancy, measurement of antidepressant exposure based on prescription date and supply (versus use) and lack of data on severity of postpartum hemorrhage.

The authors appropriately conclude that potential confounding by unmeasured factors cannot be ruled out. There are some important confounders that this study could not assess including obesity, parity and previous postpartum hemorrhage. Notably the Salkeld study[4] accounted for previous hemorrhage and reported no statistically significant association of SSRI use in the past 30 days with postpartum hemorrhage.

The study indicates that there may be one excess case of postpartum hemorrhage for every 80 to 100 women using antidepressants near the time of delivery. This provides further reason to counsel women of reproductive age who commence SSRIs about their possible effects in pregnancy. In addition to postpartum hemorrhage, SSRIs have been described to increase the risk of miscarriage, fetal anomalies and autism. Discontinuation at any stage of pregnancy needs to be based on balancing the risks of discontinuing or substituting antidepressants against other risks, which at birth include postpartum hemorrhage. In this context, further studies that can determine the association with severe hemorrhage are warranted.

Taken with findings from other studies, it would be reasonable to take into account recent history of antidepressant use as a potential risk factor for postpartum hemorrhage when counseling women about where to deliver. The consistent increase in incidence of postpartum hemorrhage across multiple international locations is unlikely to be attributable entirely to antidepressant use, but this may be one of a myriad of factors that contribute to the increase.

References

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