

Systematic review and meta-analysis

Exposure to selective serotonin reuptake inhibitors in late pregnancy increases the risk of persistent pulmonary hypertension of the newborn, but the absolute risk is low

10.1136/eb-2014-101786

Nancy Byatt,¹ Marlene P Freeman²

¹Department of Psychiatry and Obstetrics and Gynecology, University of Massachusetts Medical School/UMass Memorial Medical Center, Worcester, Massachusetts, USA; ²Department of Psychiatry, Harvard Medical School/Massachusetts General Hospital, Boston, Massachusetts, USA

Correspondence to: Dr Nancy Byatt, Department of Psychiatry and Obstetrics and Gynecology, University of Massachusetts Medical School/UMass Memorial Medical Center, 55 Lake Avenue North, Worcester, MA 01655, USA; nancy.byatt@umassmemorial.org

Commentary on: Grigoriadis S, Vonderporten EH, Mamisashvili L, *et al.* Prenatal exposure to antidepressants and persistent pulmonary hypertension of the newborn: systematic review and meta-analysis. *BMJ* 2014;348:f6932.

Implications for practice and research

- Persistent pulmonary hypertension in newborns (PPHN) is rare and, despite a small increased risk when selective serotonin reuptake inhibitors (SSRIs) are used in late pregnancy, the absolute risk of PPHN remains low.
- Considering the risk of relapse into depression, the available evidence does not support discontinuation of SSRIs during pregnancy due to concerns about PPHN.
- Future research needs to consistently either examine or control for factors that may be associated with PPHN, including treatments for underlying maternal psychiatric illness.

Context

Depression in pregnancy is common and has adverse effects on birth outcomes, mother–infant attachment, and the behaviour and development of infants and children.^{1–4} While effective evidence-based treatments are available,⁵ treatment with antidepressants is complicated by the need to carefully consider and discuss the risks, benefits and alternatives of in utero medication exposure. Exposure to antidepressants during pregnancy has been inconsistently associated with the risk of PPHN. With a baseline prevalence of 1.9/1000 live-births, PPHN is a rare but serious condition, which can result in mild-to-severe respiratory distress soon after birth. Grigoriadis and colleagues' systematic review and meta-analysis aimed to determine the extent to which antidepressant exposure in pregnancy is associated with PPHN.

Methods

Multiple data sources were searched using keyword combinations for studies examining newborn PPHN and antidepressant exposure during pregnancy. Two abstractors independently screened the titles and abstracts of all studies using the Strengthening and Reporting of Observational Studies (STROBE) criteria. Seven articles (five cohort studies and two case-control studies) that met the inclusion criteria and quality threshold were included in the analysis and review. When available, adjusted risk estimates were extracted; if risk estimates were not available, crude ORs and sample variances were computed based on the available data. Quality of the studies was assessed using the Systematic Assessment of Quality in Observational Studies (SAQOR) assessment tool.

Findings

SSRIs were the only class of antidepressants that were analysed quantitatively because other classes of antidepressants did not have enough comparable data for analysis. Exposure to SSRIs limited to early pregnancy was not associated with PPHN, while late exposure was significantly associated with PPHN (pooled OR=2.5). The absolute risk for developing PPHN after exposure to an SSRI in late pregnancy was 2.9 to 3.5 in 1000 births. Thus, for one additional case of PPHN to occur, 286–351 women would need to be treated with an SSRI during late pregnancy. Owing to limitations in the included studies, several covariates that may increase the risk of PPHN were not assessed, including caesarean section, body mass index, preterm delivery and depression severity.

Commentary

Grigoriadis and colleagues' study demonstrates a small association between PPHN and SSRI use throughout and late in pregnancy. However, the absolute risk of PPHN is low. As a meta-analysis, the review is limited by the small number of studies included. Several covariates were not assessed, and cause and effect cannot be determined; it is unclear whether the antidepressant itself or other factors related to underlying disorders explain the association.

It is imperative to consider the clinical significance of these findings. It is well established that depression in pregnancy is common and has a negative impact on maternal and infant outcomes. In addition to the risks of medication exposures, maternal psychiatric disorders also constitute a risk for women and their babies. Evaluation of the risks of stopping an antidepressant on a patient-by-patient basis is crucial. Mood and anxiety disorders among women vary in severity and impact on functioning, morbidity and even mortality. Individualised treatment decisions are ideally made collaboratively with well-informed patients. Although important, non-pharmacological treatments are often inadequate for women with moderate-to-severe depression. The timing of the association between PPHN and antidepressant use in late pregnancy raises challenges because antenatal depression and anxiety are risk factors for postpartum depression. As delivery nears and women prepare to care for a newborn child, it is essential to provide effective mental healthcare for these women. The postpartum period is a demanding time that can leave women vulnerable; it is vital to optimise the mental health of pregnant women in order to promote maternal and child health.

Competing interests None.



References

1. Wisner KL, Sit DK, McShea MC, *et al.* Onset timing, thoughts of self-harm, and diagnoses in postpartum women with screen-positive depression findings. *JAMA Psychiatry* 2013;70:490–8.

2. Grote NK, Bridge JA, Gavin AR, *et al.* A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. *Arch Gen Psychiatry* 2010;**67**:1012–24.
3. Paulson JF, Keefe HA, Leiferman JA. Early parental depression and child language development. *J Child Psychol Psychiatry* 2009;**50**:254–62.
4. Deave T, Heron J, Evans J, *et al.* The impact of maternal depression in pregnancy on early child development. *BJOG* 2008;**115**:1043–51.
5. Weissman MM, Pilowsky DJ, Wickramaratne PJ, *et al.* Remissions in maternal depression and child psychopathology: a STAR*D-child report. *JAMA* 2006;**295**:1389–98.