Health and Drug Alerts

Persistent pulmonary hypertension of the newborn and maternal use of SSRIs

Reason for posting: Major depressive disorders affect one in 10 women of reproductive age, and selective serotonin reuptake inhibitors (SSRIs), with their generally favourable efficacy and safety profiles, are the most common medications used to treat these conditions. However, the results of a recent case–control study suggest that women taking the drugs in the latter half of their pregnancy may have an increased risk of their offspring developing persistent pulmonary hypertension of the newborn (PPHN).[1]

The drugs: PPHN is a rare but serious and sometimes fatal (about 10%–20% of the time) respiratory condition (Box 1, Box 2). In the current study, 377 women who delivered children with PPHN were enrolled. They were matched to 836 control women and their infants who did not have PPHN. Six months after delivery the women were asked to identify medications used in pregnancy, health history and demographic variables including age, ethnicity, number of years of education, presence of diabetes, cigarette use, pre-pregnancy body mass index (BMI) and their infant's sex. The results showed use of the antidepressants in general (and SSRIs specifically) before 20 weeks' gestation was not associated with PPHN. However, after adjusting for maternal ethnicity, BMI and diabetes, women using SSRIs after 20 weeks' gestation were more likely to have a child with PPHN than matched controls (adjusted odds ratio [OR] 6.1, 95% confidence interval [CI] 2.2–16.8). Adjustment for factors such as smoking, alcohol intake and use of NSAIDs did not change the results. Of note, only about one in 20 children with PPHN had mothers who used antidepressants during their pregnancy (a proportion similar to the control group). SSRIs used included citalopram, fluoxetine, paroxetine and sertraline.

The potential mechanism of this adverse effect is not certain, but SSRIs, which pool in the fetal lungs, may inhibit nitric oxide synthesis.[1] Alternatively, increased serotonin levels may vasoconstrict pulmonary vessels, or cause pulmonary smooth muscle cell proliferation and increased pulmonary vascular resistance.[1]

Box 1: Infants with persistent pulmonary hypertension of the newborn

- are born at or near term (> 34 weeks' gestation)
- are generally without other congenital anomalies
- have persistent elevation of pulmonary vascular resistance
- experience right-to-left shunting through a patent ductus arteriosus, foramen ovale or both
- have profound postnatal hypoxemia
- have severe respiratory failure requiring intubation and mechanical ventilation

Box 2: Possible associations with persistent pulmonary hypertension of the newborn

Fetal factors

- Male sex
- Meconium-stained amniotic fluid
- Neonatal sepsis
- Nonvertex presentation
- Pneumonia

Maternal factors

- Antenatal NSAID use
- Black or asian ethnicity
- Cesarean section
- Diabetes
- Fever
- Higher prepregnancy body mass index
- Lower educational level
- Maternal obesity
- Tobacco use
- Urinary tract infection

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What to do: These findings add to previously described problems of congenital malformations and neonatal adaptation syndrome seen in some pregnant women using SSRIs.[2,3] Although it is important to acknowledge the limitations of case–control studies (including their inability to establish causation and possible confounding by unmeasured variables) and a possible recall bias, the relative risk increase (6-fold) seen here is dramatic. Nevertheless, the absolute risks of having a child with PPHN still remain low. Women taking SSRIs in the second half of their pregnancy will see their baseline risk of having a child with PPHN increase from 0.1% to 0.6%, an absolute increase of 0.5%. Although there is a 99.5% chance that such a woman's child would be unaffected, the number needed to harm is only 200. Women should be made aware of this potential adverse effect and the benefits and risks of treatment considered on a patient-by-patient basis. Infants born to women using the drugs should be monitored closely postpartum. It's not clear whether lower SSRI doses were protective. Alternate antidepressants had a similar but slightly lower risk of PPHN relative to controls (adjusted OR 3.2, 95% CI 1.3–7.4).

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REFERENCES

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