Canterbury District Health Board
Te Poari Hauora ō Waitaha

Clinical Pharmacology Bulletin

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Antidepressant Use in Pregnancy – Part 1

Depression affects approximately 10% of pregnant women and can be associated with adverse maternal and foetal outcomes. The decision to use or continue antidepressants in pregnancy centres around the risks to the mother and baby of untreated maternal depression, the effectiveness of non-pharmacological therapies and the risks associated with antidepressants in pregnancy. Individualised treatment is key. This is the first of two bulletins which aim to discuss the potential pregnancy risks associated with the most commonly prescribed antidepressants in New Zealand: the selective serotonin reuptake inhibitors (SSRIs), venlafaxine and mirtazapine.

Effects of Depression on Pregnancy and the Foetus

Depressed pregnant patients are more likely to experience hyperemesis, hypertension (and pre-eclampsia) and gestational diabetes, and are at increased risk of alcohol and substance abuse, smoking and suicide. Maternal depression is also associated with pre-term birth, low birth weight, lack of obstetric care and a six-fold increase in the risk of post-natal depression. Post-natal depression is particularly associated with poor maternal-infant attachment, inadequate nutrition, and poorer long-term developmental outcomes for the child. Children born to mothers with perinatal depression are found to have higher cortisol concentrations than those born to mothers without depression. These higher cortisol concentrations continue into adolescence and may underlie child temperament and behavioural problems. Adequate treatment of perinatal depression has been shown to normalise infant cortisol concentrations.

Evidence Limitations

Most antidepressant studies assessing pregnancy outcomes have been observational and have included patients with potentially significant confounding factors, such as underlying maternal condition, substance use and increased body mass index. Studies comparing depressed women who used antidepressants during pregnancy with those who did not may be confounded by severity of depression. Antidepressant use may also be a marker for a group of women with different risk factors in pregnancy to the general population.

The SSRIs, particularly fluoxetine and paroxetine, are the most studied of the antidepressants, with respect to safety in pregnancy. Sertraline appears to cause the least placental exposure, although the significance of this is uncertain. The use of venlafaxine in pregnancy is not as well studied as SSRIs and there are only limited safety data for mirtazapine.

General Recommendations

Choice of antidepressant and/or non-pharmacological therapy is best guided by what is most effective for the individual woman. Exposure to an ineffective drug or switching antidepressants may risk more harm than a small chance of an adverse effect from a beneficial antidepressant. It is recommended to use the lowest effective dose and avoid polypharmacy. Tapering or stopping antidepressants before birth does not affect pregnancy outcomes and may leave the mother with no antidepressant cover at a vulnerable time.

Pharmacokinetics in Pregnancy

The physiologic changes occurring during pregnancy begin early and fluctuate during the third trimester. These can affect drug absorption (e.g. hyperemesis), increase drug volume of distribution and drug clearance (liver enzyme induction and increased glomerular filtration rate). These changes result in lower drug concentrations in the blood. In some women, antidepressant doses may need to be increased during pregnancy to maintain efficacy.

Risks associated with specific antidepressant drugs (most studied first)

Risk / Drug	Congenital Malformations 1st trimester use	Cardiovascular Malformations 1st trimester use	Spontaneous Abortion	Reduced Birth Weight	Pre-term birth	Other
SSRIs: fluoxetine paroxetine sertraline citalopram escitalopram	anencephaly craniosynitosis omphalocele gastroschisis reported - very rare birth defects - no consistent pattern - data conflicting -?causality	Very small (<1% of exposed infants) ↑ risk of: - atrial septal defects, - ventricular outflow tract obstruction. paroxetine (?most studied) -probably a class effect ?detection bias	?Small ↑ risk Data conflicting Confounded by - gestational age - underlying maternal mental illness	Associated with a↓ birth weight by 75 g (31-117 g). ?clinical significance. Data inconsistent Confounded by - underlying illness - substance use	Probable small ↑ relative risk (OR: 1.3) Usually by a few days ?clinical significance	No association with stillbirth
venlafaxine	No association so far – an effect similar to SSRIs cannot be excluded.	No association so far – an effect similar to SSRIs cannot be excluded.	Small ↑ risk Similar confounders to SSRIs	Small ↑ risk of "small for gestational age" from 2nd trimester use.	Small ↑ risk Fewer data than SSRIs	No association with stillbirth
mirtazapine	Tracheomalacia Vesicoureteral reflux reported but ?causality	No association so far – an effect similar to SSRIs cannot be excluded.	Small ↑ risk Similar confounders to SSRIs	Small ↑ risk Fewer data than SSRIs	Small ↑ risk Fewer data than SSRIs	No association with stillbirth