Canterbury District Health Board
Te Poari Hauora ō Waitaha

Clinical Pharmacology Bulletin

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Antidepressant Use in Pregnancy

Depression affects approximately 10% of pregnant women and is associated with adverse maternal and foetal outcomes. Non-pharmacological measures such as psychotherapy, relaxation techniques, exercise and positive activities are the ideal as drugs have potential adverse effects on a developing foetus. However, this approach is often not possible. This bulletin aims to discuss the potential risks associated with the use of the following antidepressants in pregnancy: selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs) and serotonin noradrenaline reuptake inhibitor (SNRIs).

Effects of Depression on Pregnancy and the Foetus

Depressed patients are more likely to experience complications of pregnancy (e.g. nausea, vomiting, hyperemesis and pre-eclampsia), and are at increased risk of alcohol and substance abuse, smoking and suicide. Untreated maternal depression is also associated with a six-fold increase in the risk of post-natal depression. Data regarding maternal depression and low birth weight or size are conflicting. Infants born to mothers with untreated depression have an increased risk of irritability, reduced activity and attentiveness, fewer facial expressions, poor maternal-infant attachment, inadequate nutrition, and poorer long-term developmental outcomes for the child. The long-term effects of maternal depression on infant development are unclear.

Effects of Antidepressants on Pregnancy and the Foetus

It is important to note that most antidepressant studies assessing pregnancy outcomes have been observational and have included patients with potentially significant confounding factors, such as underlying maternal condition and the use of drugs, smoking and alcohol. Compared with SSRIs, there are less safety data available for TCAs and SNRIs (even less for).

Antidepressants in general are likely to be associated with preterm birth (up to 1 week) and neonatal withdrawal effects. There are limited data on the long-term effects of antidepressants on cognition and behaviour. However, most studies have not reported negative effects. See table below for other risks associated with individual antidepressant classes.

Stopping / Dose-Reducing Antidepressants in Pregnancy

The risks of treating depression in pregnancy should be weighed against the risks of not treating (i.e. maternal relapse), ideally prior to conception. There is no evidence that tapering antidepressants prior to birth has positive neonatal outcomes. Further, it leaves the mother with no antidepressant cover at a vulnerable time. If withdrawn, antidepressants (except fluoxetine) should be tapered over at least 4 weeks. Fluoxetine has a long half-life and, theoretically, can be stopped without down-titration. However, adverse effects may still occur.

Antidepressants in Breastfeeding

Antidepressants that are considered reasonable to use while breastfeeding (where clinically indicated) include amitriptyline, nortriptyline, citalopram, escitalopram, paroxetine, sertraline and venlafaxine. Fluoxetine significantly transfers into breastmilk and has a long half-life, and for this reason, should only be used in certain patients. Infants should be observed for signs of drug exposure such as altered bowel and sleep habits, poor suckling, irritability and jitteriness. Ideally the antidepressant should be taken just after a feed (when the period between feeds is greatest). A bulletin covering this in more detail will follow later.

Conclusions

Treatment of depression in pregnancy is a risk/benefit decision (where benefits often outweigh risks). If considered necessary, the lowest effective dose of antidepressant should be used. There is no preferred choice of drug with regards to safety in pregnancy, and treatment should be individualised.

Risks associated with specific antidepressant drugs

Risk / Drug	Congenital Malformations	Respiratory Distress (use >20wks gestation)	Spontaneous Abortion/Foetal Loss	Neonatal Withdrawal Effects	Other
SSRIs - citalopram - fluoxetine - paroxetine - sertraline - escitalopram	No increase in overall malformations. ? Small ↑ in absolute risk of CV malformations (data conflicting; most consistent with paroxetine & fluoxetine, but class effect likely).	Neonatal respiratory distress. Probable ↑ in risk of persistent pulmonary hypertension of the newborn (PPHN) of likely <0.5% (background rate is 1-2 /1000 live births). PPHN is associated with considerable morbidity & mortality.	Unclear – data limited, conflicting, and often confounded.	Mild, transient symptoms in 15-30% of newborns which resolve within 2 wks. Symptoms involve GI, CNS, respiratory & motor systems (e.g. tachypnoea, weak / absent cry, tremor, temperature instability, irritability, hypoglycaemia, seizures).	Maternal / neonatal bleeding - SSRIs reduce platelet aggregation & cause bleeding in up to 1% of patients. Data regarding this are sparse. However, there are concerns over their effects in the neonatal and post-partum period.
TCAs - amitriptyline - nortriptyline -clomipramine	Data not concerning.	No known association.	No known association.	Jitteriness, irritability and convulsions (rarely) reported.	Maternal cardiotoxicity in overdose.
SNRIs - venlafaxine	No association so far – an effect similar to SSRIs cannot be excluded.	Respiratory distress similar to SSRIs reported.	No known association.	Low Apgar score, hypoglycaemia & convulsions reported.	Bleeding risk may be increased, as with SSRIs.

Key: CV= cardiovascular. GI=gastrointestinal. CNS=central nervous system.