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Antidepressant Use in Pregnancy

Depression affects approximately 10% of pregnant people and is associated with adverse parental and foetal outcomes, including compromised parenting, which can impact on child development.[1] Some data suggest that antidepressants may increase the risk of spontaneous abortion, preterm delivery and low birth weight; however, these risks can also be attributed to untreated depression. Selective serotonin reuptake inhibitors (SSRIs) have the most pregnancy safety data.

Risks associated with antidepressant use in pregnancy

	First trimester exposure	Possible adverse foetal and parental outcomes
SSRIs citalopram escitalopram fluoxetine paroxetine sertraline	Small increased risk of cardiac malformations OR* 1.25 (95% CI 1.15–1.37; NNH 388).	SSRIs have been associated with spontaneous abortion, decreased gestational age (usually a few days) and decreased birth weight (mean 175 g).[2] Late pregnancy exposure: • Neonatal adaptation syndrome (NAS) develops in up to 30% of newborn infants.[3] • Small increased risk of persistent pulmonary hypertension (PPHN) in the newborn. The absolute increase in risk is small (about 0.6 per 1000 live births).[4] • Small increased risk of postpartum haemorrhage. The absolute increase in risk is small (about 1 per 80-100 exposed women).[5,6] • Small increased risk of gestational hypertension or pre-eclampsia from mid pregnancy (RR 1.14, 95% CI 1.00-1.30 and RR 1.32, 95% CI 0.99-1.78; respectively).[7]
venlafaxine	Small increased risk of cardiac malformations OR* 1.3 (95% CI 0.99–1.71).	As for SSRIs.
mirtazapine	Fewer data than SSRIs.	Fewer data than SSRIs. Effects similar to SSRIs cannot be excluded.
bupropion *(unapproved use)*	Small increased risk of cardiac malformations OR* 1.23 (95% CI 1.01–1.49).	Fewer data than SSRIs. Effects similar to SSRIs cannot be excluded.
moclobemide	Fewer data than SSRIs.	Data too limited to fully assess safety.
TCAs	Wide use over several decades. No increased risk of cardiac malformations OR* 1.02 (95% CI 0.82–1.25).	Wide use over several decades suggests any risk is very small. Effects similar to SSRIs.

- CI = confidence interval. NNH = number needed to harm. RR = relative risk.
- OR* = odds ratio (95% confidence interval) of first trimester antidepressant use (SSRIs, venlafaxine, bupropion or TCAs) and the presence of cardiac defects, from a meta-analysis of 20 studies involving approximately 5 million pregnancies. The OR for individual drugs within each antidepressant class may vary. Cardiac defects include atrial septal defects, right ventricular outflow tract obstructions, bulbus cordis anomalies and anomalies of cardiac septal closure.[8]
- NAS: symptoms include; poor feeding, vomiting, diarrhoea, tremors, irritability, lethargy, hyper/hypotonia, body temperature instability, nasal congestion, tachypnoea, hypoglycaemia. The symptoms may relate to adverse effects of the antidepressant (e.g. serotonin toxicity) or withdrawal symptoms. In most infants symptoms are mild and self-limiting, usually within 72 hours. Continuing to breastfeed may help reduce the severity of symptoms.
- PPHN: a rare condition that occurs in about 2 per 1000 live births.
- TCAs = tricyclic antidepressants (e.g. amitriptyline, clomipramine, dosulepin, imipramine and nortriptyline).

Long term neurodevelopmental outcomes

Some data suggest that antidepressants may increase the risk of learning and behavioural disorders in children. However, these can also be attributed to major depression. A cohort study (including 145,702 antidepressant-exposed and approximately 3 million unexposed pregnancies) found no significant increase in risk when confounding factors were controlled for. For example, analysis of antidepressant-exposed siblings (SSRIs, serotonin noradrenaline re-uptake inhibitors, TCAs and bupropion) with unexposed siblings found no increase in risk for any neurodevelopmental disorder (hazard ratio 0.97; 95% CI 0.88-1.06).[9]

Pharmacokinetics in Pregnancy

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

General Recommendations

Choice of antidepressant is best guided by what is most effective for the individual. Consider remaining with the current antidepressant if it is effective rather than switching, to minimise the risk of relapse. Use the lowest effective dose and avoid polypharmacy. Tapering or stopping antidepressants before birth is not recommended as it may leave the mother without antidepressant cover at a vulnerable time.

Key points

1. The risks of untreated maternal depression outweigh the risks associated with antidepressants.
2. Switching antidepressants is not recommended in pregnant people already established on an effective agent.
3. Also see our bulletin on antidepressants and breastfeeding.

References

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