Antidepressants in pregnancy and breastfeeding

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Summary

Maternal depression and anxiety during pregnancy and the early years of an infant's life cause substantial problems to the mother, her infant and her family. Suicide is an ever-present risk with depression along with adverse effects on infant growth and birth weight. Balancing these risks against accumulating evidence of the effects of selective serotonin reuptake inhibitors on the fetus and infant presents a challenge to the treating doctor. Careful explanation to the woman and her partner of the risks of both the condition and the treatment, using a biological, psychological and social treatment approach, is likely to provide the most benefit.

Key words: depression, infants, lactation, selective serotonin reuptake inhibitors.

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Introduction

Depression in pregnant and lactating women is a common problem. In attempting to find the best treatment options for these women, doctors work with less knowledge and more risks than with other patients. Drug trials always exclude pregnant and lactating women and therefore practice is guided by data accumulated from clinical experience. Clinicians must consider the risk of damage from the medications and the effects of the illness itself on both the mother and the baby.

Harmful effects of maternal depression

There is increasing evidence that antenatal and postnatal anxiety and depression potentially have enduring effects on offspring.

Pregnancy

Although some studies differ, most document maternal antenatal depression as causing slightly shorter gestational length and lower birth weight in newborns.[1] Antenatal anxiety has shown a strong association with raised cortisol levels in 10-year-old offspring, with the potential for increased vulnerability to psychopathology in these children.[2] Boys whose depressed mothers show ambivalence to them in early months have increased rates of behavioural problems and learning difficulties by the age of five years.[3]

Lactation

The relationship between postnatal depression and breastfeeding is emerging as complex. Women who develop postnatal depression are more likely to stop breastfeeding than women who are not depressed. Likewise, women who establish and maintain breastfeeding are less likely to develop depression than women who have difficulties with breastfeeding.

Harmful effects of antidepressants

Antidepressant use in Australia has changed in the last two decades. Tricyclic antidepressants have fallen from favour and many have been withdrawn. Their adverse effects and risk of fatality from overdose make them hazardous. However, some doctors continue to prescribe them after considering the risks and the benefits. There have been few documented problems arising from their use, but this is perhaps due to lack of extensive research. A small study on the use of dothiepin in lactation suggested better outcomes for children of depressed mothers taking the drug compared to those whose mothers chose no medication.[4] Case reports suggest that doxepin may be harmful to infants and should be avoided in breastfeeding.[5]

Data on mirtazapine are sparse and therefore this drug should not be used as a first-line treatment in pregnancy. Recent work cautiously suggests that levels of mirtazapine are low in breastfed infants.

Venlafaxine use in early pregnancy has been associated with increased rates of spontaneous abortion but not fetal abnormality. There are also now many case reports of neonatal effects so it should be used with great caution in pregnancy. Venlafaxine has the potential to accumulate in the breastfed baby with prolonged treatment.[6]

Drugs used to treat bipolar depression include sodium valproate which is highly teratogenic and is best avoided in the first trimester. However, it is probably safe to use during lactation. Lithium may also cause fetal abnormalities and is generally advised against in early pregnancy and during lactation. However, a recent review of its use in the first trimester has shown lower rates of cardiac abnormalities than previously documented. Its use in lactation has suggested it is relatively safe in compliant mothers with healthy babies.[7] Infants must be monitored for lithium concentrations in serum as well as renal

and thyroid function. Specialist advice is highly recommended with lithium. This is also the case for lamotrigine.

SSRIs during pregnancy

First trimester: Early prospective trials on SSRIs suggested they were safe with no teratogenic effects. However, recent data have challenged this and suggest a small increase in birth defects. These results were not statistically significant and should be interpreted with caution.[8,9] Paroxetine has been associated with cardiovascular abnormalities[10], although recent analysis suggests this risk is only at doses greater than 25 mg per day.[11]

Second and third trimesters: Recent studies show a small but significant risk of shorter gestational length and lower birth weight in infants of mothers who used SSRIs in later pregnancy even compared to babies of untreated mothers with depression.[1]

Third trimester: Increases in mild respiratory distress, irritability and feeding problems have been observed in infants of mothers taking SSRIs in late pregnancy. Some but not all research suggests that paroxetine may cause more neonatal difficulties.[12] These effects are self-limiting and have generally settled by 14 days. It is unclear whether these neonatal effects are withdrawal or toxic effects.[13]There have also been reports of persistent pulmonary hypertension of the newborn[14] and possibly intraventricular haemorrhage.[12]

SSRIs during lactation

Many SSRIs are highly protein bound and little drug is transferred from the mother to the infant during lactation. We can therefore be more confident in prescribing SSRIs in lactation.[5] However, there is individual variability in infant levels of SSRIs and there are occasional case reports describing adverse effects.[15] Less data are available on the use of other antidepressant drugs during lactation.

So what is a doctor to do?

When a woman presents early in pregnancy with depression a very careful assessment should be made, preferably with her partner or other family member as additional historian. An assessment of risk of self-harm or suicide is vital. Other risks such as poor antenatal care are increased with depression. Once safety issues and general self-care have been addressed, a biological, psychological and social treatment plan should be explored relating to the patient's needs and wishes, and the severity of the depression. Sufficient information should be provided to the patient so they can make an informed decision about their treatment. Careful documentation of these discussions is important for medicolegal reasons.

Pre-conception counselling for women already taking antidepressants must explore the relative risks of the depression itself compared to the risks of using antidepressants in pregnancy. Anxiety about medication use in pregnancy may be high. For a woman whose depression has receded, a trial of slow cessation of medication before conception may be successful, but her mental state should be monitored in case of a relapse.

Unplanned conceptions for women on antidepressants can cause alarm and some women will abruptly cease their medication. Unfortunately, up to 75% of women who do so may develop a recurrence of their depression before delivery.[13] Careful reassessment of relative risks will reassure many women that continuation of their medication is appropriate.

If a pregnant woman decides to continue taking the drug, doctors should be aware that pharmacokinetics change during pregnancy. In the event of a relapse, a woman might need higher doses of many drugs including SSRIs to maintain clinical improvement.

Later in pregnancy, concerns over neonatal toxicity and withdrawals guide some doctors to lower SSRI doses until after delivery. Anecdotally, many women can manage this well, provided good psychosocial support is available. Some women will choose to continue on current doses with support, and appropriate management of the neonate.

Which antidepressant to use?

Experts differ in their assessments of the relative risks of the antidepressants, but in general, SSRIs are preferred to tricyclic antidepressants, combined serotonin and noradrenaline reuptake inhibitors and mirtazapine. Every antidepressant has been associated with some neonatal effects, and different studies show differing results. The data on paroxetine in higher doses cause concern.[11] While some perinatal psychiatrists prefer fluoxetine with its longer half-life and potential for slower neonatal withdrawal effects, many prefer the shorter-acting SSRIs, either citalopram, fluvoxamine or sertraline as the maternal response may be faster.

Useful sources of information

It is essential to frequently update information about best practice in this area as new information rapidly changes practice. Reliable websites such as the Organisation of Teratology Information Specialists (OTIS) (www.otispregnancy.org) and the Canadian www.motherisk.org are valuable to both doctors and patients. Most large Australian obstetric facilities also provide a pharmacy information service (see box), and if in doubt, a telephone call is appropriate. Telephone advice from a psychiatrist can be obtained privately or through GP PsychSupport on 1800 200 588. Pharmaceutical companies may have additional data about the effects of antidepressants on pregnancy and lactation.

Conclusion

The risks of the depression and its consequences must be weighed against the risks of the medications to both mother and

Pregnancy drug information centres

New South Wales

MotherSafe

Tel: (02) 9382 6539 / 1800 647 848 (toll free for NSW callers)

Queensland

Queensland Drug Information Centre (health professionals)

Tel: (07) 3636 7098

South Australia

Women's and Children's Hospital

Tel: (08) 8161 7222

Victoria

Royal Women's Hospital

Tel: (03) 9344 2277

Western Australia

Women's & Newborn Health Service

Tel: (08) 9340 2723

infant during the different phases of pregnancy and lactation. Careful history taking, close monitoring and good psychosocial care may be sufficient for many women with depression during pregnancy. When antidepressants are needed, the baby should be monitored postnatally for feeding, neurological and respiratory difficulties. Prescription of SSRIs postnatally appears less hazardous than in antenatal use, and potentially of benefit to mother and child.

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Further reading

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Self-test questions

The following statements are either true or false (answers on page 135)

3. It is safe to prescribe sodium valproate during early pregnancy.
4. Generally, SSRIs are safe to use during lactation.