Prescribing psychotropic drugs for women who are pregnant

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Prescribing in pregnancy

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Background risks

- The spontaneous abortion rate in confirmed early pregnancy is 10–20% and the risk of spontaneous major malformation is 2–3% (approximately 1 in 40 pregnancies).
- Smoking, poor diet and drinking alcohol during pregnancy can have adverse consequences for the foetus.
- Moderate maternal caffeine consumption may be associated with low birth weight.
- Pre-pregnancy obesity increases the risk of neural tube defects.
- Psychiatric illness during pregnancy is an independent risk factor for congenital malformations and peri-natal mortality.
- Affective illness increases the risk of pre-term delivery.
Effect of medicines

• Drugs account for a very small proportion of abnormalities (approximately 5% of the total). Potential risks of drugs include
  – major malformation (first-trimester exposure)
  – neonatal toxicity (third-trimester exposure)
  – longer-term neurobehavioural effects and increased risk of physical health problems in adult life.

• The safety of psychotropics in pregnancy cannot be clearly established because robust, prospective trials are obviously unethical
  – We rely on database studies, prospective data from teratology information centres and published case reports. At worst there may be no human data at all, only animal data from early preclinical studies.

• The patient’s view of risks and benefits will have paramount importance.
General principles of prescribing in pregnancy

In all women of child bearing potential
- Try to avoid drugs that are contra-indicated during pregnancy (especially valproate and carbamazepine). If prescribed, women should be made fully aware of teratogenic potential. Consider prescribing folic acid.

If mental illness is newly diagnosed in a pregnant woman
- Try to avoid all drugs in the first trimester (when major organs are being formed).
- If non-drug treatments are not effective/appropriate, use an established drug at the lowest effective dose.

If a woman taking psychotropic drugs is planning a pregnancy
- Consider discontinuing treatment if the woman is well and at low risk of relapse.
- Discontinuation of treatment for women with SMI and at a high risk of relapse is unwise, but switching to a low risk drug may be appropriate.

If a woman taking psychotropic medication discovers that she is pregnant
- Abrupt discontinuation of treatment in women with SMI and at a high risk of relapse is unwise.
- Consider remaining with current (effective) medication rather than switching, to minimise the number of drugs to which the foetus is exposed.

In all pregnant women
- Ensure that the parents are as involved as possible in all decisions.
- Use the lowest effective dose of the drug with the lowest known risk to mother and foetus.
- Prescribe as few drugs as possible both simultaneously and in sequence.
- Consider referral to specialist peri-natal services.
- Ensure adequate foetal screening.
- Be aware of potential problems with individual drugs around the time of delivery.
- Inform the obstetric team of psychotropic use and possible complications.

improving lives
Psychosis

• Pregnancy does not protect against relapse

• During the month after childbirth there is a 20-fold increase (to 30-50%) in the relative risk of psychosis

• The risk of perinatal psychosis is 0.1–0.25% in the general population, but is about 50% in women with a history of bipolar disorder

• The risk of recurrent post-partum psychosis is 50–90%

• The mental health of the mother in the perinatal period influences foetal well-being, obstetric outcome and child development

• The risks of not treating psychosis include harm to the foetus or neonate (ranging from neglect to infanticide)
Antipsychotic treatment

- People with schizophrenia are more likely to have minor physical anomalies than the general population - complicates assessment of the effects of antipsychotic drugs.

- Older, first generation antipsychotics are generally considered to have minimal risk of teratogenicity.
  - There may be an association between haloperidol and limb defects, but if real, the risk is likely to be extremely low
  - Neonatal dyskinesia has been reported with FGAs
  - Neonatal jaundice has been reported with phenothiazines

- Data relating to second generation antipsychotics are growing.
  - Most data for olanzapine
    - associated with both lower birth weight and increased risk of intensive care admission, and with macrosomia and gestational diabetes.
    - no clustering of congenital malformations
  - Limited data for risperidone and quetiapine
  - Clozapine associated with gestational diabetes and neonatal seizures. Theoretical concerns re agranulocytosis in the foetus/neonate.
Recommendations – psychosis in pregnancy

• Patients should be advised to discuss a planned pregnancy as early as possible
• Drug-induced hyperprolactinaemia may prevent pregnancy.
• Antipsychotics usually required during and after pregnancy.
• There is most experience with chlorpromazine (constipation and sedation can be a problem), trifluoperazine, haloperidol, olanzapine and clozapine (gestational diabetes may be a problem with both SGAs).
• NICE recommends avoiding depot preparations and anticholinergic drugs in pregnancy
Depression

• 10% of pregnant women develop a depressive illness and a further 16% a self-limiting depressive reaction.

• There is a significant increase in new psychiatric episodes in the first 3 months after delivery. At least 80% are mood disorders, primarily depression.

• Women who have had a previous episode of depressive illness (postpartum or not) are at higher risk of further episodes during pregnancy and post-partum. The risk is highest in women with bipolar illness.

• Unclear if depression increases the risk of spontaneous abortion, having a low birth weight or small for gestational age baby, or of pre-term delivery.
Antidepressant treatment

- **The relapse rates are high** in those with a history of depression who discontinue medication.

- Antidepressants may increase the risk of spontaneous abortion, pre-term delivery, respiratory distress in the neonate, a low APGAR score at birth and admission to a special care baby unit.

- Some antidepressants have been associated with specific congenital malformations, many of which are rare.

- TCAs have been widely used throughout pregnancy without apparent detriment to the foetus.

- SSRIs appear not to be major teratogens;
  - most data supporting the safety of fluoxetine
  - possible association of SSRIs with PPH of the newborn, and cardiac septal defects.
  - No apparent increase in risk of postpartum haemorrhage

- Moclobemide, reboxetine and venlafaxine seem to be relatively safe.
- Few data for mitrazepine.
- Bupropion associated with an increased risk of ADHD
Recommendations – depression in pregnancy

• Patients who are already receiving antidepressants and are at high risk of relapse are best maintained on antidepressants during and after pregnancy.

• Those who develop a moderate or severe depressive illness during pregnancy should be offered treatment with antidepressant drugs.

• There is most experience with amitriptyline, imipramine and fluoxetine. Paroxetine may be less safe than other SSRIs.

• When taken in late pregnancy, SSRIs may increase the risk of persistent pulmonary hypertension of the new-born.
Mood stabilisers in pregnancy

• **Lithium** should be avoided if possible.
  – Increases the risk of Ebstein’s anomaly (relative risk is 10–20 times more than control, but the absolute risk is low at 1:1000). The period of maximum risk to the foetus is 2–6 weeks after conception
  – The risk of atrial and ventricular septal defects may also be increased
  – High-resolution ultrasound and echocardiography should be performed at 6 and 18 weeks of gestation
  – Monitor plasma levels every month during pregnancy and immediately after birth.
  – Neonatal goitre, hypotonia, lethargy and cardiac arrhythmia can occur

• **Valproate**
  – Known increased risk of neural tube defects, atrial septal defects and cleft palate
  – Risk is dose related
  – Folate supplementation should be used.

• **Carbamazepine**
  – Similar range of risks to valproate but less frequent
  – 3rd trimester use may necessitate maternal vitamin K administration

• **Lamotrigine**
  – Risks much lower than with valproate/cbz
  – Associated with cleft palate.
  – NICE recommends lamotrigine should not be routinely prescribed in pregnancy
<table>
<thead>
<tr>
<th>Psychotropic group</th>
<th>Recommendations</th>
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<tbody>
<tr>
<td>Antidepressants</td>
<td>Nortriptyline</td>
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<tr>
<td></td>
<td>Amitriptyline</td>
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<td></td>
<td>Imipramine</td>
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<td></td>
<td>Fluoxetine</td>
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<tr>
<td>Antipsychotics</td>
<td>Conventional drugs have been widely used, although safety is not fully established. Most experience with chlorpromazine, haloperidol, and trifluoperazine. No clear evidence that any antipsychotic is a major teratogen, although data for SGAs other than olanzapine and clozapine are scarce</td>
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<tr>
<td>Mood-stabilisers</td>
<td>Consider using an antipsychotic as a mood-stabiliser rather than an anticonvulsant drug</td>
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<td></td>
<td>Avoid anticonvulsants unless risks and consequences of relapse outweigh the known risk of teratogenesis. Women of childbearing potential taking carbamazepine or valproate should receive prophylactic folic acid. Avoid valproate and combinations where possible</td>
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<tr>
<td>Sedatives</td>
<td>Non-drug measures are preferred</td>
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<td></td>
<td>Benzodiazepines are probably not teratogenic but are best avoided in late pregnancy. Promethazine is widely used but supporting safety data are scarce</td>
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General principles of prescribing psychotropics in breast-feeding

- In each case, the benefits of breast-feeding to the mother and infant must be weighed against the risk of drug exposure in the infant.
- Premature infants and infants with renal, hepatic, cardiac, or neurological impairment are at a greater risk from exposure to drugs.
- The infants should be monitored for any specific adverse effects of the drugs as well as for feeding patterns and growth and development.
- It is usually inappropriate to withhold treatment to allow breast-feeding where there is a high risk of relapse. Treatment of maternal illness is the highest priority.
- Where a mother has taken a particular psychotropic drug during pregnancy and until delivery, continuation with the drug while breast-feeding may be appropriate as this may minimise withdrawal symptoms in the infant.
- Women receiving sedating medication should be strongly advised not to sleep with the baby in bed with them.

Wherever possible:

- use the lowest effective dose
- avoid polypharmacy
- time the feeds to avoid peak drug levels in the milk or express milk to give later (this may be impractical in small infants feeding every 1–3 hours).
<table>
<thead>
<tr>
<th>Drug group</th>
<th>Recommended drugs</th>
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<tbody>
<tr>
<td>Antidepressants</td>
<td>Paroxetine or sertraline (others may be used – see table)</td>
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<tr>
<td>Antipsychotics</td>
<td>Sulpiride; olanzapine (others may be used – see table)</td>
</tr>
<tr>
<td>Mood-stabilisers</td>
<td>Often best to switch to <strong>mood-stabilising antipsychotic</strong> (see table). Valproate can be used but only where there is adequate protection against pregnancy (breast-feeding itself is not adequate protection). Beware risk of hepatotoxicity in breast-fed infants</td>
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<tr>
<td>Sedatives</td>
<td>Lorazepam for anxiety; <strong>zolpidem</strong> for sleep (others may be used – see table)</td>
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