



WeMeReC Bulletin

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Prescribing in breastfeeding

Breastfeeding clearly has substantial benefits for the infant. However, many mothers need to take medicines during the time they are breastfeeding and there is great concern that this may adversely affect the infant. The benefits and risks of drug therapy as well as the benefits of breastfeeding must all be considered. This applies whether initiating or continuing drug therapy.

As with the use of medicines in pregnancy, few studies have been done on the effects of drugs taken by a mother on her breastfed infant. Evidence for safety or harm is primarily based on case reports, clinical experience and anecdotal reports. For most drugs, very little information is available to allow a comparison of the risks of exposure to the drug with the disadvantages of discontinuing breastfeeding. However, estimates of drug concentrations reached in an infant's

Summary

- The decision to initiate or continue a medicine during breastfeeding involves considering the benefits of breastfeeding and the risks and benefits of drug therapy.
- The potential for causing harm when using a medicine during breastfeeding depends on many factors related to the drug, the infant and the mother.
- Most drugs are excreted in breast milk but are present in low concentrations; few drugs are contra-indicated during breastfeeding.

plasma allow reasoned judgement of potential harm in many cases.¹ Although most drugs are excreted in breast milk, for many drugs the plasma concentrations reached in an infant are insufficient to cause concern.^{1,2}

General principles

- Only prescribe drugs for breastfeeding mothers when necessary. Monotherapy is preferable to multiple-drug regimens.
- Assess the risk/benefit ratio for both the mother and infant.
- Avoid drugs known to be associated with serious toxicity in adults or children.
- Drugs licensed or accepted for use in infants are generally considered safe for use while breastfeeding.
- Prescribe older, more established drugs in preference to newer drugs. Information on the passage of new drugs into breast milk and their effect on infants is usually scarce.
- Counsel breastfeeding mothers to seek advice when considering over-the-counter products.
- Avoid drugs with long half-lives and sustained-release preparations if possible.
- If the drug has an appropriately short half-life the risk of drug effects in the infant may be minimised by dosing after breastfeeding.²
- Drug clearance is lower in premature infants, putting them at greater risk of drug effects.^{1,3} Similarly, neonates (up to one month old) are at greater risk than older infants.^{1,3} However, the young and premature benefit most from breast milk.
- If significant exposure of an infant to a drug is expected, monitor the infant for signs of adverse effects.
- It may be possible to resume breastfeeding after a short course of therapy with a contra-indicated drug if milk is expressed and discarded during therapy and for four to five half-lives after the last dose.

Manufacturers' data sheets and summaries of product characteristics should be consulted for full prescribing information. For some drugs mentioned in this bulletin, use during breastfeeding is not licensed although it may be established medical practice. It is important for doctors to recognise the responsibility that prescribing these drugs entails.

Benefits of breastfeeding

Apart from the obvious benefits of providing optimum nourishment, breastfeeding is associated with decreased infant mortality and morbidity. This includes decreased risk of gastro-intestinal, urinary tract and respiratory infections and decreased risk of developing atopic disease and insulin-dependent diabetes mellitus.³⁻⁶ Health benefits for the mother, including reduced risk of ovarian and pre-menopausal breast cancer, have been documented.^{3,6} Breastfeeding is recommended during the first six months of life or longer.⁷

Drug content of breast milk and infant exposure

Exposure of an infant to maternal drugs in breast milk is different from exposure to drugs *in utero*. Drugs that should be avoided during pregnancy may be safe for use during breastfeeding. In the immediate postpartum period, the potential effect of drugs used during labour may need to be considered.⁸

The extent to which a drug will be excreted in breast milk is affected by its physicochemical properties (e.g. pKa, protein-binding capacity, lipid solubility and molecular weight) and the dose, administration route and pharmacokinetics of the drug in the mother.^{2,5,9} During the first few weeks after delivery, drug disposition in the mother varies as physiological processes return to the non-pregnant state.⁹ Milk composition, which varies during a feed as well as over the longer term, is also a complicating factor.^{3,9}

Ratios of the concentration of a drug in secreted milk to those in maternal plasma are commonly quoted. For most drugs this ratio is less than one, but about 25% of drugs have a ratio greater than one indicating that they are concentrated in milk.⁵ This may not be clinically relevant if the absolute amount of the drug is low, because the infant's exposure will be low. It is more appropriate to estimate the daily dose of drug ingested by the infant, which can then be related to doses used therapeutically in infants or to adult doses adjusted for weight.^{1,5}

Apart from the amount of a drug ingested by an infant, its bioavailability and clearance in the infant are the most important factors that determine exposure to the drug. Some drugs such as insulin and heparin are destroyed in the gut and do not enter the systemic circulation of the infant.

Risk/benefit assessment

The age and health status of the infant must be considered. For example, prematurity, low birth weight or illness put an infant at higher risk of drug effects.^{4,8} If possible, exposure to drugs in breast milk should be avoided in such infants. Additional risk factors for the infant include renal or liver impairment, glucose-6-phosphate dehydrogenase deficiency,⁴ and dehydration.

The health of the mother is also important. For example, chronic antipsychotic or antidepressant medication may be essential to enable a mother to care for her infant, even if their use precludes breastfeeding.

Drugs that may affect milk supply

Bromocriptine, ergotamine and oestrogens may suppress milk production whereas dopamine receptor antagonists, such as metoclopramide and domperidone, stimulate milk production.^{3,5} Because of the effect of oestrogens, progestogen-only oral contraceptives are preferred to combined oral contraceptives. Large doses of some thiazides have been reported to decrease milk production but thiazides are generally considered to be safe for the infant.^{4,10}

Risk categories of drugs

Drugs may be grouped into three main categories with regard to breastfeeding.³

Class 1: Drugs considered to be unsuitable (see examples in Table A). These drugs have high intrinsic toxicity (e.g. antineoplastic agents) or documented serious effects in infants (e.g. lithium).

Class 2: Drugs that should be used with caution and adequate monitoring. These include drugs for which minor or reversible adverse effects have been reported or may be anticipated in breastfeeding infants, or those that have low toxicity in adults but for which no information is available in breastfed infants. Examples include sedating antihistamines and theophylline. A decision to use these drugs must be made on an individual basis. Mothers requiring combinations of some drugs, such as antipsychotics or anti-epileptics, should breastfeed only upon the advice of a specialist. Methadone use (up to 80 mg per day) to treat addiction in breastfeeding mothers is considered to be justified, in conjunction with monitoring and support of the infant.⁵

Table A: Some drugs that should be avoided during breastfeeding^{1-5,10}

Drug	Possible effect on infant
Amiodarone	theoretical risk of neonatal hypothyroidism
Antineoplastic agents	immunosuppression, neutropenia
Aspirin	theoretical risk of Reye's syndrome, case of metabolic acidosis
Cocaine	cocaine toxicity
Gold salts	accumulation – effect unknown
Iodides	thyroid dysfunction
Lithium	lithium toxicity
Pethidine (multiple doses)	potential accumulation, neurobehavioral depression
Radioactive isotopes	radiation toxicity
Vitamin D (high-dose)	case of hypercalcaemia

Class 3: Drugs that are considered safe and any risk associated with their use is clearly outweighed by the benefits of breastfeeding (see examples in Table B). These drugs are either not excreted in milk in significant quantities (e.g. enalapril,

warfarin), are not absorbed from the infant's gut (e.g. heparin), or have sufficiently low intrinsic toxicity (e.g. penicillin, paracetamol). In addition, for many of these drugs there is clinical experience of safe use.

Table B: Some drugs considered to be safe during breastfeeding for the normal, healthy, full-term infant (in routine general practice)^{1-5,8-10}

This list is not exhaustive; for further information see the sources of information on page 4.

Analgesics (short-term): paracetamol, ibuprofen, diclofenac, codeine, morphine (low-dose)
Anticoagulants: warfarin, heparin (unfractionated and low-molecular-weight)
Anti-asthmatic drugs: salbutamol, terbutaline, inhaled corticosteroids
Antidepressants: tricyclic antidepressants (except doxepin)
Anti-epileptics (not high-dose or combination therapy): carbamazepine, phenytoin, sodium valproate
Antihistamines: cetirizine, loratadine
Antimalarials (prophylactic use): chloroquine, proguanil
Antimicrobials: penicillins, cephalosporins, macrolides, aciclovir, rifampicin
Cardiovascular drugs: captopril, enalapril, diltiazem, nifedipine, verapamil, labetalol, propranolol, methyl dopa, furosemide (frusemide), thiazide diuretics, digoxin
Endocrine drugs: insulin, levothyroxine
Gastrointestinal drugs: antacids, ranitidine, famotidine, cyclizine, bulk laxatives
Glucocorticoids (low-dose): prednisolone
Homeopathic (not herbal) remedies: from reputable sources, if highly diluted
Oral contraceptives: progestogen-only pill
Vaccines

Sources of information

- ♦ BNF, Appendix 5: Breast-feeding.
- ♦ Local medicines information centres.
- ♦ Pharmaceutical company medical information departments.
(For medico-legal reasons these often cannot recommend the use of a drug in breastfeeding but may have information from case reports.)
- ♦ UK Lactation Information and Advisory Service at www.ukmicentral.nhs.uk
West Midlands Medicines Information Service, Good Hope Hospital, Sutton Coldfield.
(Tel: 0121 311 1974)
Trent Regional Medicines Information Service, Leicester Royal Infirmary, Leicester.
(Tel: 0116 255 5779)
These provide enquiry-answering services to all health professionals.
- ♦ Specialist textbooks:
Briggs GC, Freeman RK, Yaffe SJ. Drugs in pregnancy and lactation. 6th Edition, Williams & Wilkins, Baltimore, 2001 (cost: £83).
Lee A, Inch S, Finnigan D. Therapeutics in pregnancy and lactation. Radcliffe Medical Press, Abingdon, 2000 (cost: £19.95).

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5. Ito S. Drug therapy for breast-feeding women. *N Engl J Med* 2000; 343: 118-126.
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7. WHO. Child and adolescent health and development. Nutrition and infant feeding. www.who.int/child-adolescent-health/nutrition/infant.htm, 2001.
8. Auerbach KG. Breastfeeding and maternal medication use. *J Obstet Gynecol Neonatal Nurs* 1999; 28: 554-563.
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10. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. Policy statement. *Pediatrics* 2001; 108: 776-789.

A bulletin on prescribing in pregnancy (WeMeReC Bulletin Vol. 7, No. 3) was published in November 2000. A Case Study Pack containing the bulletin and distance-learning module on prescribing in pregnancy was sent to all GP practices in spring 2001. Further copies are available from WeMeReC.