

Clinical pharmacology

Principles of using medication in breastfeeding mothers

Health care professionals are often required to make decisions regarding the use of medications during breastfeeding. Unfortunately, good-quality information on drugs in lactation is not readily available. Maternal medication is often unnecessarily viewed as a reason to discontinue breastfeeding. It is important to systematically evaluate the mother's need, infant factors and the data on specific drugs to avoid depriving infants of the benefits of breastfeeding.

This article sets out to provide practical guidance to assist the health care professional in deciding whether mothers of breast-fed infants may continue breastfeeding or whether the safest option would be for the baby to be bottle fed.

Factors to consider when choosing a drug for a lactating mother

Assessing the safety of breastfeeding during maternal drug therapy requires an individualised risk:benefit analysis. The following factors should be considered:

Dosage and duration of therapy

Drugs that are potentially harmful to the infant may not necessarily contraindicate nursing. They may require only a short abstinence period. On the other hand, drugs usually considered safe during breastfeeding may be potentially problematic when given in a high dose or for a long period of time.

Age of the infant

Newborn, especially premature infants may be more susceptible to the pharmacological effects of drugs than older infants. Newborns are also more likely to be exclusively breastfed.

Experience with drugs in infants

Years of experience with a drug in infants allows a more confident prediction of the risks. There is usually very limited safety, pharmacokinetic and dosage data available on newly marketed drugs.

Quantity of milk consumed

As infants become older, breast milk may become less important in the diet. Therefore, the dose to the infant is reduced.

Oral absorption by the infant

Drugs that are poorly absorbed orally (e.g. insulin, aminoglycoside antibiotics and sucralfate) are generally safe as minimal absorption is likely in the infant.

Potential long-term effects

Few studies have evaluated the effects of long-term maternal therapy on the nursing infant. It would be prudent to minimise exposure of the infant to drugs which may potentially affect their development in the absence of safety data.

Possible interference with lactation

Certain drugs, including furosemide and chlorthalidone, may decrease the supply of breast milk. This may go unrecognised and result in under-nourishment or suboptimal growth.

Non-dose-related toxicities

These include sensitisation, antimicrobials affecting gastrointestinal flora, haemolytic anaemia in infants with glucose-6-phosphate dehydrogenase deficiency, aplastic anaemia due to chloramphenicol and agranulocytosis due to phenothiazines. Although these rare adverse reactions do not necessarily contraindicate the use of these drugs in breastfeeding mothers, extra monitoring of the infant may be required.

Stepwise approach to minimising exposure

The aim is to minimise infant exposure to drugs in breast milk with minimal disruption of breastfeeding. The information below should be read in conjunction with the available information on the drugs being considered and the factors mentioned above.

Withhold drug from the mother

Drugs that are not essential, e.g. multi-ingredient cold and flu preparations for symptomatic relief, should be withheld with the mother's co-operation.

Choose drugs that pass poorly into breast milk

Some classes of drugs (e.g. beta-adrenergic blocking agents) exhibit large differences in the amount excreted into breast milk. Choosing a drug that is poorly excreted into breast milk and that does not have active or potentially active metabolites helps to minimise the exposure.

Choose an alternative route of administration

Decreasing the maternal plasma drug concentration will decrease concentration in the milk and consequently the infant's dose. Inhaled or topically applied corticosteroids and inhaled bronchodilators and nasal decongestants should be substituted for oral preparations.

Avoid nursing at times of peak drug concentrations in milk

Generally peak concentrations occur in milk 1 - 3 hours after an oral dose. In older infants, nursing just before a dose is taken may help to avoid the peak concentration effect. This strategy may not be successful in newborn infants in whom nursing is frequent and irregular and when long-acting drugs and extended-release products are used.

Administer the drug before the infant's longest sleep period

If the drugs can be given once daily, administration to the mother just before the infant's longest sleeping period should minimise drug exposure. A middle-of-the-night bottle feed can be substituted if needed.

Temporarily withhold breastfeeding

When drug therapy is short-term, e.g. sedatives or anaesthetics for dental or surgical procedures, breastfeeding can be withheld for a certain period of time depending on the toxicity of the drug. If possible the mother could use a breast pump to obtain extra milk before the procedure, refrigerating it for use during the period of abstinence from nursing. Alternatively, formula could be substituted or a 'wet nurse' used.

Discontinue nursing

Sometimes drugs that are necessary for the mother's health are too toxic, e.g. cytotoxics, to allow nursing. In these cases it is best to discontinue breastfeeding altogether.

Methods of Estimating Infant Drug Exposure

Milk/plasma ratio (M/P ratio)

This ratio has often been used as an indication of the extent of drug passage into breast milk. However, it has severe limitations. Firstly, there is no standard definition for the milk/plasma ratio, and various authors have applied the term differently. Secondly, calculation of the M/P ratio at non-steady-state concentrations 'gives no absolutely reliable expression of the relationship between the concentration of drugs in milk and plasma'.

It must be emphasised that the M/P ratio itself, regardless of the method of calculation used, has no inherent clinical meaning. It can however be used in the absence of a measured drug concentration in milk to calculate average or worst-case milk concentrations using the following equation:

drug concentration in milk = maternal plasma concentration x M/P ratio

Percentage of maternal dose

This value is calculated by dividing the estimated amount of drug excreted into milk during a stated time period (which varies by author) by the maternal dose and multiplying by 100 to derive a percentage. In general, the dose in milk is calculated either from concentrations measured in a clinical trial or by use of some form of the M/P ratio together with an estimate of milk intake.

Table I. Drugs considered compatible with breastfeeding

Antibiotics: amoxicillin, penicillin G & V, cephalosporins, erythromycin

Antidepressants: amitriptyline, sertraline

Antihypertensives: captopril, enalapril, verapamil, propranolol, labetalol

Analgesics: paracetamol

NSAIDs: diclofenac, ibuprofen

Antihistamines: brompheniramine, loratadine

Antidiarrhoeals: kaolin-pectin

Laxatives: psyllium

Gastrokinetic agents: domperidone, metoclopramide

Contraceptives: depot-medroxyprogesterone, progestogen-only oral contraceptive

Hormones: insulin

Infant dosages

This is calculated by multiplying the drug concentration in milk by the volume of milk ingested:

infant dosage = drug concentration in milk x volume of milk ingested

The dosage of drug received by an infant in breast milk is more relevant than both of the above ratios. Because instantaneous milk drug concentrations and milk volumes are clinically impossible to determine, estimates of drug concentration and milk volume must be made. When the average estimate of ingested milk volume (150 ml/kg/day) and the average dose-adjusted milk concentration for a drug (approximately the concentration at the midpoint of the dosing interval) are used, an average drug dosage received by the infant can be calculated. Once the infant's dose is estimated, this dose can be compared with the infant dose or adult dose (if the infant dose is unknown) in mg/kg to determine whether the infant is likely to receive a pharmacologically important amount of drug via breast milk.

In conclusion, it is often not possible to determine whether a specific drug is safe to use during breastfeeding, for the following reasons:

- many drugs have not yet been investigated
- conclusions are drawn from single or a few case reports or from theoretical risks
- data are incomplete in the literature.

In such cases a risk-benefit assessment needs to be performed and the decision should be based on the following:

- whether this drug is needed or not
- whether there is a safer alternative
- the socio-economic circumstances of the mother, i.e. whether she will be able to afford formula milk or not.

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