

## Drugs and breastfeeding

Most women take at least one drug during lactation, which may pose risk to the suckling infant. In addition, parental perception of the magnitude of risk may lead to non-compliance with drug therapy or unnecessary cessation of breastfeeding. Given the health, sociologic and economic benefits of breastfeeding, it is essential to have good data to guide decisions about drug use during breastfeeding.

### Drug transfer

All drugs transfer into breast milk to some extent (exceptions are very large molecules eg. insulin that are too big to cross biological membranes to get into milk). Most drugs transfer by passive diffusion with the extent of transfer depending on properties of the drug (eg. lipophilicity), and the different composition of blood and milk (eg. fat content is 2.5% and 19%, respectively). Drugs more readily distribute into milk if they are basic, lipophilic and have low protein binding.

### Milk to plasma ratio (M/P ratio)

$$\text{M/P ratio} = \frac{\text{drug concentration in breast Milk}}{\text{drug concentration in maternal Plasma}}$$

The M/P ratio is the most frequently reported index of drug transfer into breast milk. However, it is often used *erroneously* as an indicator of risk to the breastfed infant. It is *not* correct to assume that a drug with a high M/P ratio (eg. 5.0) is unsafe in breast-feeding, or that a drug with a low M/P ratio (eg. 0.1) is safe. This is because the M/P ratio does not necessarily tell us the 'dose' the baby receives in breast milk (see next section).

**The risk to the suckling infant** depends on:

**'Dose' ingested in milk.** This is dependent on the concentration of the drug in milk and the volume of milk ingested ie. dose = concentration x volume. The infant's dose in milk can be put into perspective by comparing it with the therapeutic dose for an infant of comparable age and weight. For example, babies receive up to 5mg/kg/day of paracetamol in milk during therapeutic maternal dosing, which is about 6-8% of the therapeutic infant dose (60-90mg/kg/day). In most cases therapeutic dosing data will not be available for infants (eg. consider the antidepressants). Therefore, it is more common practice to compare the infant's dose with the maternal dose:

$$\text{relative infant dose} = \frac{\text{infant dose in milk (mg/kg)}}{\text{maternal dose (mg/kg)}} \times 100 (\%)$$

If the relative infant dose is < 10% of the maternal dose (weight-adjusted), the drug is likely to be safe in breast-feeding unless the drug is toxic or the baby is very young. Many drugs eg. penicillins, macrolides and NSAIDs have a relative dose of around 1% and are regarded as 'safe' (see p152 of the Preferred Medicines List or "pink book").

The above can be illustrated by comparing sumatriptan which has a high M/P (4.9) and low relative dose (4%), and lithium which has a low M/P (< 1.0) and a high dose ( $\leq 80\%$ ). Sumatriptan is 'safe' whereas lithium is unsafe.

**Infant pharmacokinetics.** Oral availability and clearance are the two main parameters affecting drug concentrations in the infant's blood after exposure in milk. Drugs with low oral availability in adults (eg. gentamicin) are likely to be safe because the infant would also be expected to have low oral availability. Clearance is by far the most important factor since infants have reduced ability to eliminate drugs until they are about six months old because of immature renal and hepatic systems. Therefore, special care should be taken in neonates, especially if premature - a baby born early at 30 weeks' gestation will have one-fifth of the clearance of a term baby and will have five times higher plasma concentrations for a given 'dose' of a drug in milk.

**Drug toxicity.** In general, drugs with inherent toxicity (eg. cytotoxics, amiodarone) should be avoided because the risk to the infant is unacceptably high.

### What data are available to help you with decisions?

Many commonly available resources contain unhelpful information such as "...the drug was found to cross into human milk" or "caution is recommended". The information is often manufacturer driven and is inadequate to assist with clinical decision making. Contact Drug Information (ext. 80900) or your clinical pharmacist for specific questions about drug use during breastfeeding.

### Key points:

- Avoid all drugs if possible (the baby does not benefit from drugs exposure in milk)
- Select drugs with the best safety record
- Drugs should rarely preclude breastfeeding
- Monitor infant for adverse effects eg. poor suckling (but recognise that these are hard to detect)