

Metronidazole and Breastfeeding

Metronidazole is often indicated in infections affecting breastfeeding mothers, such as trichomoniasis, pelvic inflammatory disease and bacterial vaginosis. This bulletin reviews the safety of metronidazole in breastfeeding women.

Transfer into breast milk

- Nearly all drugs transfer into breast milk to some extent, with concentrations in milk usually following concentrations in maternal plasma.
- Metronidazole transfers into milk in relatively high amounts, with concentrations in milk only slightly lower than those in maternal plasma.
- To estimate infant exposure, the amount (dose) ingested via milk can be expressed as a percentage of the mother's dose (both adjusted for respective body weights); known as the relative infant dose or weight adjusted maternal dose (WAMD). For drugs that are not overtly toxic, a WAMD < 10% suggests safety in breastfeeding full-term, healthy infants.
- The reported WAMD for metronidazole varies and ranges from 12% to 24%. This is above the usually accepted safety cut-off of 10%. However, it is pertinent to remember that metronidazole is used in neonates, infants and children. Further, breastfed infants are likely to receive < 3 mg/kg/day from a maternal dose of 1500 mg/day (in divided doses), which is less than the therapeutic doses used in infants and children (7.5-30 mg/kg/day).
- One study found a stat 2 g oral metronidazole dose resulted in a 3 month-old exclusively breastfed infant ingesting 25 mg of metronidazole over 48 hours. This reflects significant exposure for young infants (close to the therapeutic dose used in this age-group). With a 12-hour discontinuation of breastfeeding post-dose, the 48-hour infant dose was reduced to 10 mg.

- Intravenous administration produces similar maternal plasma and milk concentrations to equivalent oral doses (metronidazole has almost 100% oral bioavailability).
- The rectal, vaginal and topical routes produce significantly lower plasma (and hence expected milk) concentrations than oral or intravenous administration, due to poorer bioavailability.

Unwanted effects in the infant

Numerous studies have shown virtually no untoward effects in breastfed infants. There are isolated and unsubstantiated reports of diarrhoea and candidiasis. Historically there has been some suggestion that metronidazole may impart a bitter taste to milk (perhaps related to the relatively common adverse effect of a 'metallic taste' found with therapeutic use); however, this is not supported by published evidence.

Mutagenic and carcinogenic risks

Historically, the safety of metronidazole in breastfeeding has been controversial due to data from animal studies showing that metronidazole is potentially carcinogenic and mutagenic. However, there is no substantive evidence of these effects in humans. Additionally, clinical experience, and the consensus of specialist opinion, is that there is no known established carcinogenic or mutagenic risk to breastfeeding infants whose mothers are receiving short-course treatment with metronidazole by any route.

Key recommendations

- A short course of metronidazole (i.e. 400-600 mg orally BD or 500 mg IV BD for 7-10 days) is considered reasonable to use in breastfeeding women with healthy, full-term infants.
- These doses are in line with recently updated CDHB dosing recommendations (see the Pink Book online and the Antimicrobial Stewardship Bulletin "Metronidazole" October 2015).
- Ideally, metronidazole exposure should be avoided in premature, breastfed infants, and those with renal or hepatic impairment.
- Avoid stat 2 g doses where possible. For those patients in whom this dose is necessary, consider discontinuation of breastfeeding for 12-24 hours post-dose. The breastfeeding mother should then be encouraged to:
 - store some expressed milk before the dose for the infant to use during the 12-24 hours post-dose.
 - express and discard milk during the 12-24 hours post-dose to maintain lactation.
- The rectal, vaginal and topical routes are considered safe in breastfeeding.
- As with all drugs in breastfeeding, infant exposure may be limited by:
 - breastfeeding just prior to the dose.
 - avoiding feeds at the time of maximum plasma (and hence milk) concentrations if possible (1-4 hours post-dose for metronidazole).
 - using the lowest effective dose for the shortest duration possible.
- The infant should be monitored for any change in bowel habit and poor feeding.
- Metronidazole should be used in preference to ornidazole (the alternative nitroimidazole antimicrobial available in New Zealand). Ornidazole has not been studied in breastfeeding.