Breastfeeding and Medication

The dilemma of medication and breastfeeding: pharmacokinetics introduction for midwives

The number of mothers advised that they cannot take medication whilst breastfeeding is sadly large, if the number of contacts to the BfN Drugs in Breastmilk Service and my own website Breastfeeding and Medication is representative. We know that purely deciding to breastfeed discourages some mothers from taking anything purely to preserve the purity of breastmilk.

Schirm showed that 65.9% of women have taken a drug whilst breastfeeding a baby in the first 6 months after birth whilst 79.6% of formula feeding mothers have taken a drug during the same time period. However, in my PhD research I found that 56.5% of breastfeeding received some meds in the first 5 days after delivery mostly analgesics and antibiotics as we might expect. In my experience mothers will "put up" with pain or other symptoms rather than interrupt breastfeeding. An unknown number of women never seek help for mental health problems fearing either that they will be told that they must stop breastfeeding or that they will be seen as such poor mothers that "they" will take their babies away.

So how can the midwife help?

Many women reach the point of delivery without knowing whether they can breastfeed on drugs they have continued to take during pregnancy or which

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they need to restart. So, my first request of you would be that you find time during booking appointments to check if the mother you are talking to is in this position. Can you imagine how tough it is to have delivered but suddenly you are told you can't put the baby to the breast because no one knows if your medication is safe? What if this is midnight and there is no one on call to ask? Those first precious hours of skin to skin and early feeds are lost. Might the mum be discharged before she knows and miss your expertise on positioning and attachment? Do you need to challenge a doctor who has said that a mother cant breastfeed? Maybe you know where to look for sources of information other than the BNF. We all know midwives support junior doctors through their placements and just maybe this is another part of their education.

This is my first take-home message:

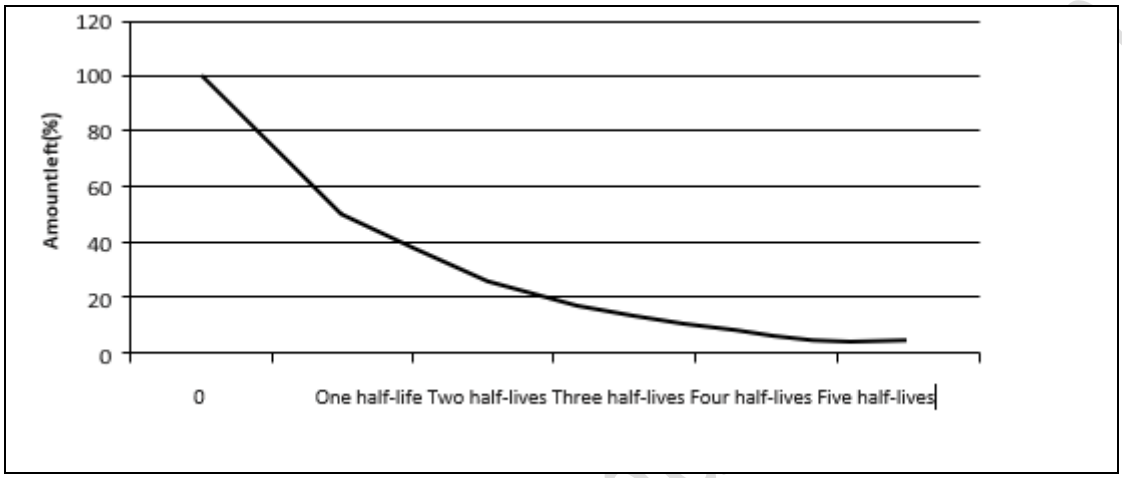
If a mother needs medication long term check the evidence on use in breastfeeding during pregnancy. Do not rely on the BNF check with specialist sources (NICE PH11)

Pharmacokinetics

I remember having a panic when I first was asked to talk about the pharmacokinetics of drugs in breastmilk but I'm going to try to make it as easy as possible for you with lots of diagrams and one-word descriptions. Hopefully you will be able to answer the questions of doctors after you qualify because I know they largely don't understand it! First, what does pharmacokinetics mean? It is the branch of pharmacology concerned with the movement of drugs within the body. So how the body absorbs drugs, moves them into the blood and then into milk. Do not forget that once the baby has consumed the milk, he/she also has to absorb it, metabolise it and transport it before it is going to have an effect so there are a lot of barriers between the mother being given a medication and the baby responding to it.

Half-life

The half-life of a drug is the time it takes to be metabolised to half the original level. So, if at minute 1 there was 100mcg and the half-life is two minutes – after two minutes there is 50mcg left, after four minutes 25mcg and so on. After five half-lives the amount left is regarded as so small that it can effectively be said to have left the body.

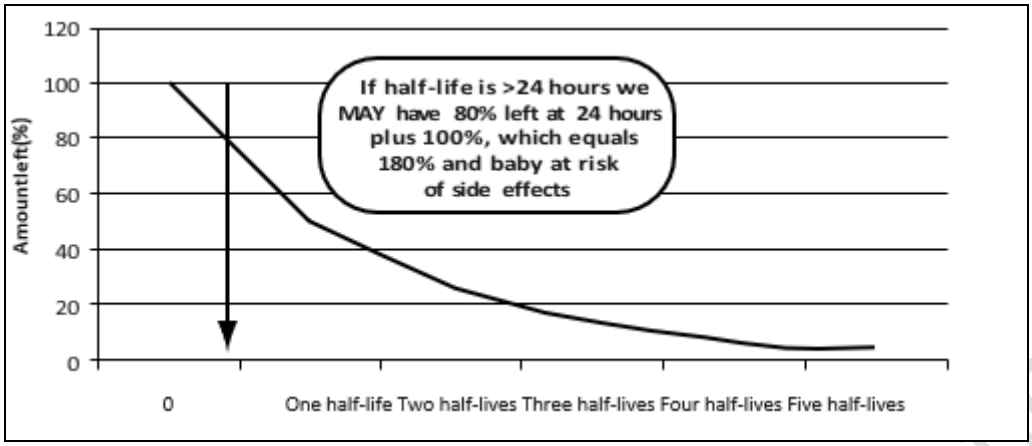


The problem comes when a drug is taken every day, but the half-life is more than 24 hours, particularly if the baby is under 6 weeks and has immature kidney and liver function. Worse still there are at least two commonly used drugs fluconazole and pethidine, where the half-life in a neonate is considerably longer than that in an adult.

Fluconazole: half-life in an adult is 30 hours. But in the baby, it is 88.6 hours at birth, 55.2 hours at 2 weeks of age (Pacifici 2016)

Pethidine: half-life in an adult 2.4 hours (normeperidine active metabolite 15-30 hours). But in the baby, it is 13 hours (normeperidine active metabolite 63 hours) (Hale 2019)

These drugs therefore begin to accumulate because so much drug is left every day when the mother takes more. This can lead to toxicity. Babies exposed to pethidine in the neonatal period may become sleepy and feed poorly. In my experience babies under 6 weeks exposed to fluconazole via breastmilk often display symptoms of tummy pain, vomiting and often weight loss.



Oral bio-availability

The oral bio-availability of a drug is the percentage of the drug absorbed into the system having passed through the gut, liver, vagina, rectum or lungs. Most drugs given by injection only (i.e. there is no oral formulation available) have poor bio-availability e.g. insulin, heparin. If a drug cannot be absorbed from the gut, it doesn't matter how much gets into milk, the baby can't absorb it e.g. gentamycin, infliximab.

The extent of plasma protein binding of the drug

When drugs enter the maternal bloodstream after absorption, they either become bound to plasma proteins or remain free. Only the free part of the drug can penetrate the biological membranes. The more drug that is bound, the less is free to diffuse. Highly protein-bound drugs are unable to penetrate breastmilk e.g. most penicillins. Drugs with high protein binding are the drugs of choice for administration to lactating mothers. Some drugs compete for binding sites normally occupied by bilirubin in the first week after birth. Drug displacement of unconjugated bilirubin may result in kernicterus and brain damage in the infant and a theoretical risk exists with some drugs e.g. co-trimoxazole.

An analogy that I often use is that the drug is attached to a Lego® brick so it becomes too big to pass through the cell membranes.

Milk–plasma ratio

This measurement refers to the concentration of the protein-free fractions in milk and plasma. Any ratio over 1 implies that the drug may be unsuitable to

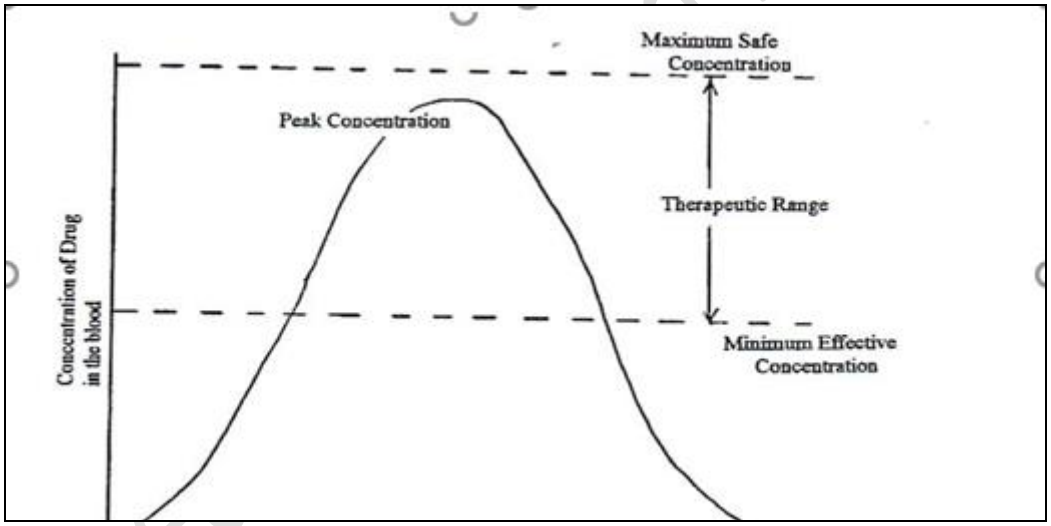
be prescribed for a lactating mother (because it concentrates in milk) and other factors need to be taken into consideration.

e.g. fluoxetine has a milk–plasma (m/p) ratio of 0.286, while the m/p ratio of dexamphetamine is quoted as 2.8–7.5, which means that the level in the milk is approximately 3 to 7.5 times that in the plasma. Milk plasma ratios of 26 have been reported in iodine which is why it should be avoided (this includes the use of seaweed and kelp in herbal remedies and application of Inadine® dressings)

The size of the drug molecule

The larger the molecule, the harder it is for it to pass into breastmilk. For example, low molecular weight heparins (molecular weight 6,000–20,000) and insulin (molecular weight >6,000) are restricted from passing into breast milk. These drugs are usually not orally bio available.

Therapeutic Range



Drugs which are licensed for use in children will almost invariably be safe for use during breastfeeding as they will reach levels below the minimum effective concentration. We aim to target the mother's dose into the therapeutic range. Sometimes mother and child will be taking the same drug simultaneously e.g., both on paracetamol or antibiotic. The amount passing through milk does not affect the dose that the baby is taking because these drugs have wide therapeutic indices. Both mother and baby can take their full normal doses.

So, the second take home message is:

- **Try to avoid drugs with long half-lives particularly in neonates**
- **Use drugs with high plasma protein binding > 90% if possible**
- **Choose drugs with milk plasma ratio less than 1**
- **Drugs with high molecular weights are limited in their passage into milk**
- **Drug licensed for use in children are ideal and will reach levels below effective concentration**

Timing medication and breastfeeds

Many mothers try to time breastfeeds to avoid the peak times that the drug is in milk. This only works for very acute exposure to drugs. When any drug is used for more than 3 days it reaches a steady state where the level is constant across the 24 hours. So, it isn't possible to reduce exposure with long term medication e.g. antidepressants

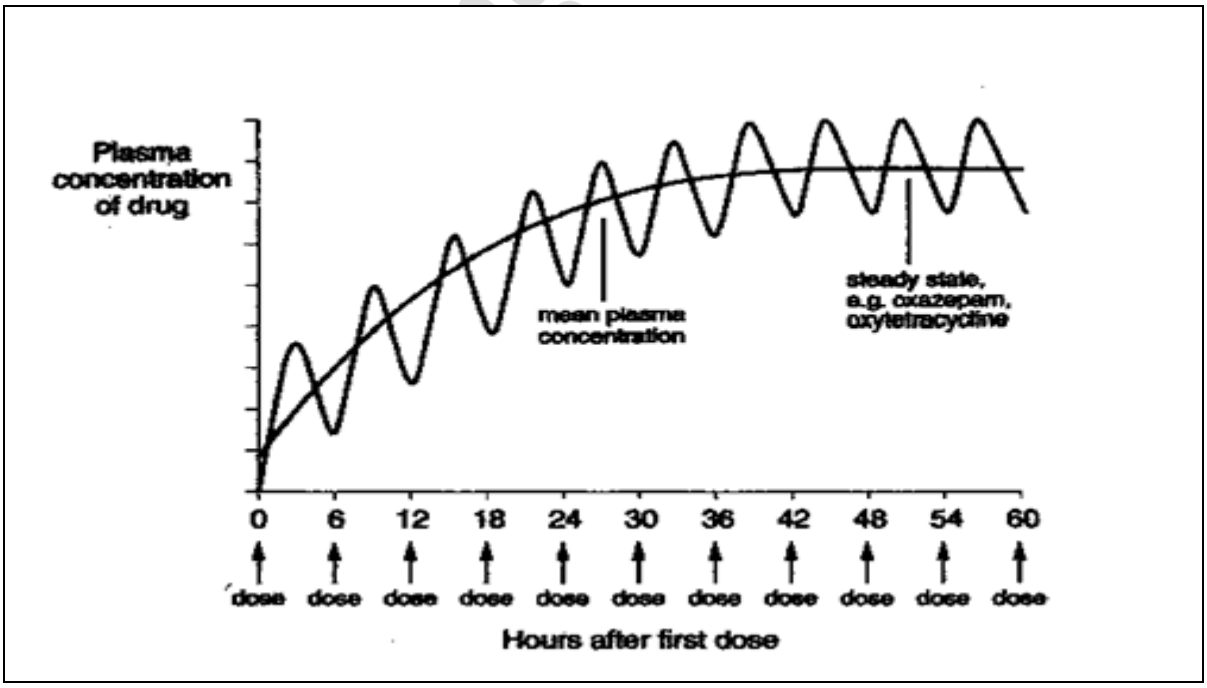


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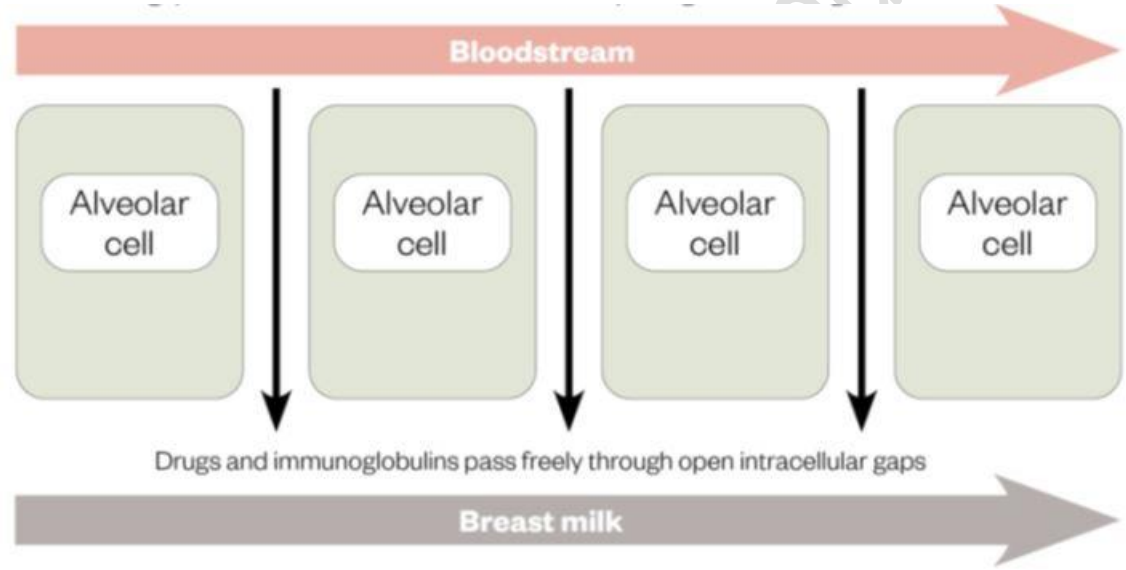
Diagram from McGavock 2005 How Drugs Work: Basic Pharmacology for Healthcare Professionals Radcliffe.

Passage of drugs into breastmilk immediately after delivery

The only time when a drug is free to pass into breastmilk is in the first few days after birth when the inter-cellular gaps are wide open to allow the passage of immunoglobulins to the baby for protection. This is, however, the time when we are most likely to prescribe drugs for the mother e.g., antibiotics, analgesics. However, obstetricians and paediatricians are more familiar with prescribing during breastfeeding and in general are confident than their fellow medical colleagues who may see mothers later in their lactation.



The intercellular gaps close around day 3 after birth and drugs then must pass through the cell membrane which is much more difficult.

Conclusion

I hope that this article has made something, which I believe makes many health professionals panic, clearer. The vast majority of drugs can be taken by breastfeeding mothers or there is an alternative.

- No breastfeeding mother needs to be left in pain because codeine is not recommended any more – she can have dihydrocodeine as well as paracetamol or another NSAID.
- No mother needs to stop breastfeeding to have an antibiotic or an anaesthetic.
- No mother should be asked to choose between having medication for mental health issues and breastfeeding.

I am always happy to help provide information if you are struggling – email me on wendy@breastfeeding-and-medication.co.uk or via the Facebook Page Breastfeeding and Medication. There are many factsheets on the Breastfeeding Network website or the Breastfeeding and Medication website – please share them with colleagues and good luck in your careers.

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