Breastfeeding and Medication

Breastfeeding and Opiate pain relief

If greater pain relief is required than is offered by regular, full dose paracetamol and ibuprofen, tramadol, Oramorph or dihydrocodeine are all breastfeeding compatible options. Codeine should not be prescribed to opiate naïve mothers or those who it makes feel sick or dizzy as they are more likely to be rapid metabolisers (see below).

- Dihydrocodeine or co dydramol is widely used post c section and is now the opiate analgesic of choice due to the fact that it has a cleaner metabolism.

- Morphine is subject to extensive first pass metabolism so actually reaches low levels in milk. Oramorph is widely used

- Tramadol reaches low levels in babies but can make mum very sleepy. Watch the baby for signs of drowsiness too.

The following data is extracted from my book Breastfeeding and Medication 2018

Dihydrocodeine or Co-dydramol – paracetamol 500 mg and dihydrocodeine 10 mg

Preferred compound analgesic due to cleaner metabolism than codeine. Use for as short a time as possible. Observe baby for drowsiness. If baby becomes drowsy stop drug immediately and seek medical advice.

Tramadol

Tramadol is an opiate analgesic used for moderate to severe pain. Its use would appear to have increased as a result of concern over codeine preparations. It is subject to first-pass metabolism. It has an elimination half-life of six hours. Tramadol inhibits the reuptake of noradrenaline and serotonin and may potentiate the action of other drugs with similar action, e.g. SSRI anti-depressants.

Ilett et al. (2008) studied 75 breastfeeding mothers who were given 100 mg tramadol post-caesarean section on days two–four. They collected milk and plasma samples of four or more doses to reflect steady state. Additionally, he observed the infants together with matched controls not

exposed to tramadol. He determined a relative infant dose quoted as 2.24% for tramadol and 0.64% for its metabolite. No difference was noted in the behaviours of the infants exposed compared with the controls and the authors therefore concluded that short-term maternal use of tramadol is compatible with breastfeeding.

In 2015 the FDA recommended that tramadol is not used in breastfeeding mothers. When tramadol is taken, it is changed in the liver to O-desmethyltramadol (known as M1). Both tramadol and M1 relieve pain and are responsible for side effects that some people may experience, but M1 has stronger opioid effects than the tramadol. Tramadol is metabolised in the liver by enzyme cytochrome P450 isoenzyme 2D6 (CYP2D6). Some people have a variation of this enzyme that changes codeine to morphine and tramadol to M1 faster and to a greater extent than in other people. These individuals are called CYP2D6 ultra-rapid metabolisers. Just as in codeine, this can produce an accumulation of the drug in breastmilk. This genotype is present in up to 10% of the white population in Europe and North America, but only 4% of black African Americans (FDA 2015).

As with other opiates, exposure of premature infants should be undertaken with caution because of the risk of apnoea and sedation. Amount probably too small to be harmful, but manufacturer advises avoidance (BNF).

Avoid if possible although the amount in breastmilk is probably too small to be harmful. Use for as short a time as possible. Observe baby for drowsiness. If baby becomes drowsy stop drug immediately and seek medical advice.

- FDA, Use of Codeine and Tramadol Products in Breastfeeding Women, FDA, 2015.
- Ilett KF, Paech MJ, Page-Sharp M, Sy SK, Kristensen JH, Goy R, Chua S, Christmas T, Scott KL, Use of a sparse sampling study design to assess transfer of tramadol and its o-desmethyl metabolite into transitional breastmilk, Br J Clin Pharmacol, 2008;65(5):661–6.

Morphine

Therapeutic doses of morphine in the breastfeeding mother are unlikely to be harmful to baby in the short term, e.g. post-operatively. Infants under 4 weeks of age have a prolonged elimination half-life and clearance does not approach adult levels until 2 months of age. Respiratory difficulties may be important to be aware of with premature babies or others at risk of apnoea. The oral absorption of morphine is very poor and first-pass metabolism is high. It is therefore frequently used post-caesarean section as Oramorph solution.

Robieux et al. (1990) reported a single case of an infant who was breastfed while his mother was receiving low doses of morphine. Morphine concentration in his serum was in the analgesic range (4 ng per millilitre), while concentrations in the milk varied substantially from 10–100 ng per millilitre. The authors calculated that the baby had received 0.8–12% of the maternal dose. Oberlander et al. (2000) studied one baby born to a mother who received morphine intrathecally during and after pregnancy. Minimal levels were determined in breastmilk over seven weeks and the infant's development and feeding up to seven months were normal. Baka et al. (2002) also studied women receiving patient-controlled analgesia post-caesarean section and noted that the concentrations of morphine in breastmilk were very small (<1 to 274 ng per millilitre) with a m/p ratio <1. Relative

infant dose is quoted as 9.1% (Hale 2017 online access). Therapeutic doses unlikely to affect infant (BNF).

Compatible with use short term during breastfeeding. Observe baby for sedation and poor feeding.

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Codeine or co-codamol 8/500. 15/500 or 30/500mg

In June 2013 the MHRA issued guidance that codeine should no longer be used by breastfeeding women EMA, MHRA 2013) . This is due to the concern that individuals vary in the way their bodies metabolise codeine and that breastfed babies might "very rarely develop side effects due to the presence of morphine in breastmilk" (DSU 2007) .

Codeine is converted to morphine in the liver by the CYP2D6 enzyme. There are many genetic variations of CYP2D6, which affect the extent of this conversion in individuals. This leads to differences in the plasma levels of morphine and different levels of pain relief. This then leads to a variable and unpredictable risk of side effects due to morphine's action on the brain and respiratory centre. For some this can result in no benefit from the drug, for others that they experience excessive drowsiness and constipation. For breastfeeding mothers in the latter group this may also lead their babies to experience respiratory depression.

Initial cautious recommendation of use during breastfeeding followed an adverse event report from Canada, where a breastfed baby died at 12 days of age. At post mortem he was found to have very high levels of morphine in his blood because his mother had multiple copies of the gene which metabolises codeine into morphine and was taking compound codeine analgesics for episiotomy pain. The mother had reported side effects of constipation and somnolence (sleepiness) in herself. She had sought medical help on several occasions prior to the baby's death as he was lethargic and had intermittent periods of difficulty in breastfeeding (Koren 2006) .

In another study (vanderVaart 2011) it was found that ultra rapid metabolisers chose to take less codeine than their counterparts complaining of dizziness and constipation. They chose instead, to take paracetamol and naproxen or naproxen alone which were options in the study protocol.

The MHRA have reported that to date, at least 44 cases of neonatal respiratory depression in breastfed infants of codeine-using mothers have been published (MHRA 2013) .

If a mother has never taken codeine preparations before she would be unaware of whether she might be an ultra rapid metaboliser putting herself and her baby at risk of adverse effects. Approximately 3% of Europeans have this genotype (vanderVaart 2011) . In most people only 10% of codeine is biotransformed into morphine but this can vary according to the genetic variation (and rapid metabolisers can biotransform 50% more codeine into morphine, whilst those with no active CYP2D6 genes convert almost no codeine into morphine and find it ineffective. Postpartum pain, due to either cesarean section (c-section) or episiotomy, is a major reason for the prescription of codeine, with an estimated 30% of North American women using the drug (vanderVaart 2011) .

Madadi et al (the group who have published most papers on codeine use during breastfeeding Motherisk.org) produced guidelines for safe use of medications that contain codeine during breastfeeding (2009) . They suggested that:

- In most cases, the occurrence of CNS depression is consistent between the mother and the baby. If the mother suffers from symptoms of CNS depression (e.g. somnolence, grogginess), a physician should examine the baby for signs of CNS depression as well.

- If the baby is not feeding well, does not wake up to be fed, does not gain weight, or shows limpness, he or she should be examined by a physician.

- Central nervous system depression in the baby appears to worsen after 4 days probably, owing to the accumulation of morphine with more breastfeeding. If possible, codeine should not be used for longer than 4 days. If pain still necessitates codeine, an attempt should be made to decrease the dose or to switch to non-codeine painkillers (e.g. NSAIDs).

The UKMI Specialist Pharmacy Service issued information in October 2013 that dihydrocodeine and tramadol should be considered where breastfeeding mothers require opioids (SPS 2016) .

The Sudden Infant Death Syndrome Institute reviewed all cases of infants referred for unexplained apnea, bradycardia and/or cyanosis in the first week of life (0.5-7 days) over a one year period (1984-85). The data demonstrated that opioids could have been a factor as 10 of the 12 infants were exposed to opioids and most of their mothers received more doses than the control group (Naumburg 1998).

Mothers should be fully informed of the risks before being sold or prescribed codeine or any opioid and to watch their nursling carefully for any signs of increased drowsiness – sleeping longer or more frequently. This can be evident whatever the age of the nursling and it should not be assumed that an older baby is not at risk.

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