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Codeine and Breastfeeding

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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.

During lactation analgesics such as paracetamol, ibuprofen or naproxen (unless contraindicated) should preferably be used and codeine or other opioid only considered as a third line analgesics.

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.

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).

To speak to a Breastfeeding Supporter call the National Breastfeeding Helpline 0300 100 0212

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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) .

Codeine combinations have in the past formed the mainstay of analgesic use, particularly in the early postpartum period. The genotype producing ultra rapid metabolism is rare but is impossible to identify without genetic testing.

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 recommendation from the MHRA to avoid codeine during lactation supersedes the information in 2007 that breastfed babies might "very rarely develop side effects due to the presence of morphine in breastmilk" (DSU 2007).

The UKMI Specialist Pharmacy Service issued information in October 2013 that dihydrocodeine and tramadol should be considered where breastfeeding mothers require opioids. If opioids are prescribed and adverse effects develop in breastfeeding infants, the possibility of opioid toxicity should be considered regardless of the maternal dose. In such cases, the opioid should preferably

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be replaced by an alternative non-opioid analgesic and breastfeeding interrupted until the cause of the symptoms is clear. (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).

Use of any opioid by breastfeeding mothers, if necessary (and only as third line choice of medication after the use of regular paracetamol and non steroidal anti-inflammatories - see Information sheet on Analgesics and breastfeeding on www.breastfeedingnetwork.org.uk), should be at the lowest effective dose, for the shortest possible duration, regardless of the baby's age and the mother made aware that she should cease the drug and seek medical advice, if she notices side effects in her baby such as:

- Breathing Problems
- Lethargy
- Poor Feeding
- Drowsiness
- Bradycardia – slow heart rate

If adverse effects develop in breastfeeding infants the possibility of opioid toxicity should be considered, regardless of maternal dose. The opioid should be replaced by a suitable non-opioid analgesic (LactMed Hale).

Breastfeeding should not be interrupted unless the symptoms are extreme e.g. necessitating admission, and then only for the shortest duration possible in line with NICE recommendations (NICE 2008).

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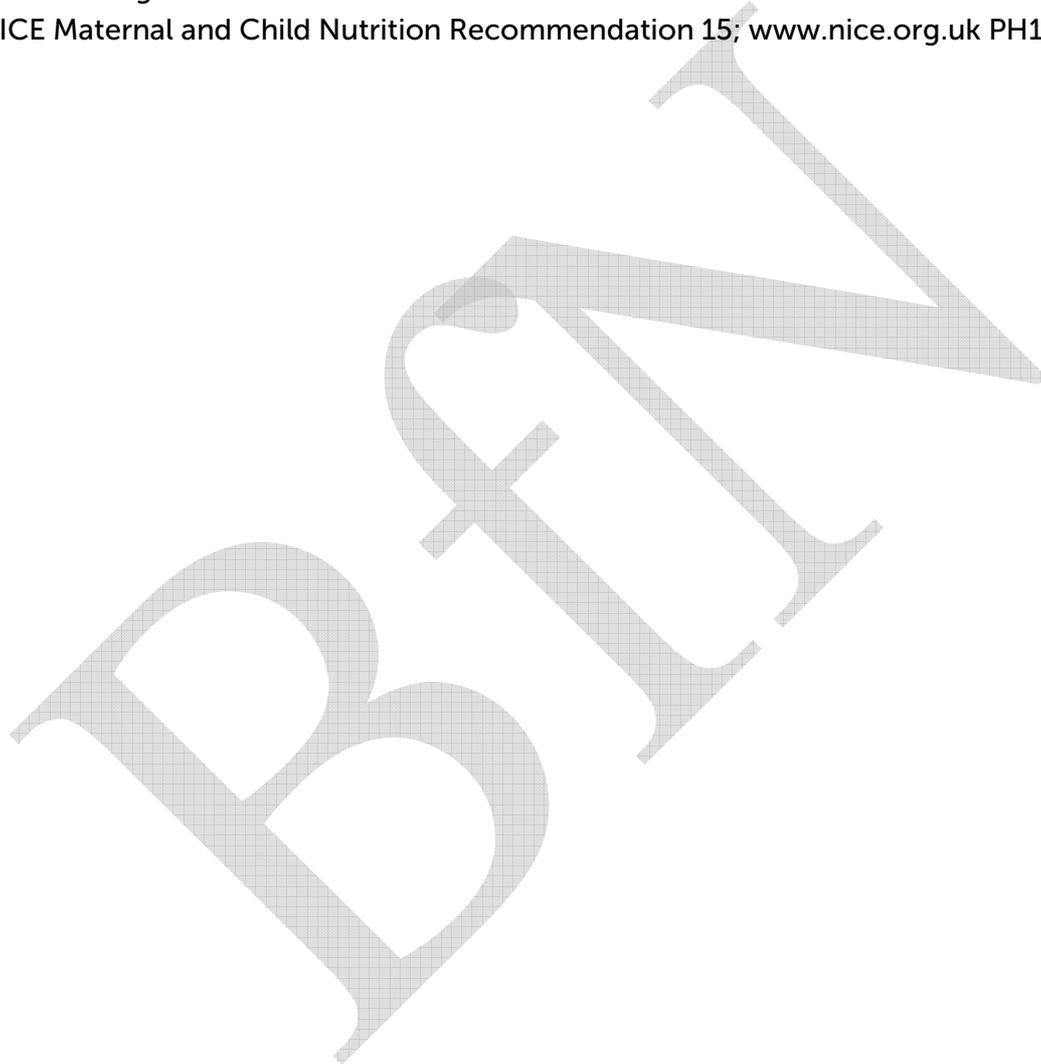
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- Specialist Pharmacy Service fact sheet updated March 2016 . Codeine and breastfeeding: Is it safe and what are the alternatives? www.sps.nhs.uk/articles/codeine-and-breastfeeding-is-it-safe-and-what-are-the-alternatives/
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- NICE Maternal and Child Nutrition Recommendation 15; www.nice.org.uk PH11 March 2008



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