Breastfeeding and Medication

Breastfeeding and Post operative analgesia

Provision of effective analgesia is important, with an awareness of potential side effects of any drugs that may pass into breastmilk, particularly when using opioid based drugs. Regional anaesthesia provides an effective and safe option and should be considered wherever applicable. Simple analgesics such as paracetamol, NSAIDS and COX-II inhibitors are safe with breastfeeding. When used in combination, regional anaesthesia and use of regular simple analgesia may reduce the requirement for opioids, however a mother may require stronger pain relief depending on the nature of surgery, and these should not be withheld on the grounds that she is breastfeeding. A discussion of the potential side effects to watch for in her baby should be undertaken in order for her to ensure her baby's safety when taking opioid base analgesia. Short acting opioids can be utilised intraoperatively and it is safe to continue breastfeeding as soon as a mother is alert after surgery, conversely these agents do not provide postoperative analgesia. Strong opioids may be used, however it is important to take into account the age and maturity of the baby. In many cases, the amount of drug passing to the baby will be negligible, and well below any therapeutic dosing level. When using strong opioids in conjunction with breastfeeding, frequent clinical assessment of the baby is important, and the mother should be warned of the risk of sedation and drowsiness and breathing difficulties and advised to withhold breastfeeding if symptoms develop and seek medical advice. When opioids are used, it is important to use the lowest effective dose for the shortest period of time. Mothers may be offered PCA devices set to deliver low dose morphine.

Analgesic agents

Individual patient needs for analgesia should be taken into account due to individual response. Use of opiates should be offered at low doses initially to opiate naïve patients.

- Paracetamol: Although there seems to be wide variation in the milk concentrations in studies, the amount of acetaminophen an infant could ingest via breastmilk is most likely significantly less than the paediatric therapeutic dose.

NSAIDS/COX-II Inhibitors:

- Ibuprofen: Ibuprofen has been used extensively for postpartum pain and during lactation, and is recommended for use during breastfeeding.

- Diclofenac: Small amounts are detected in breastmilk but it has been used extensively during lactation and is recommended for use during breastfeeding.

- Celecoxib: The relative dose that infants are exposed to via milk is very low and breastfeeding is safe to continue.

- Ketorolac, Parecoxib Levels detectable in breastmilk without demonstrable adverse effects in the neonate. Safe for use with breastfeeding.

Opioids

Remifentanil

There is no published data on maternally administered remifentanil use and its effect on the breast-fed infant. Due to its short context sensitive half-life of <10min it may be considered safe in lactating women, however is not useful for acute postoperative pain.

Fentanyl/Alfentanil

After a single dose of fentanyl intravenously, minimal amounts were detected in breastmilk. Breastfeeding is considered acceptable following single doses of fentanyl to the mother. This is also extrapolated to alfentanil.

Morphine: Morphine is transferred to human milk in small amounts. It also has an active metabolite morphine-6-glucoruonide which is more potent. Administration of a single dose of morphine to the mother is not expected to cause detrimental effects to infants however with repeated doses, the infant should be monitored for signs of sedation and respiratory depression. The use of morphine delivered by patient-controlled-analgesia is not recommended with lactation (Dalal 2013). Morphine has been recommended as the opioid of choice if potent analgesia is required in breastfeeding mothers (Ito 2000).

Oxycodone: breastfed infants may receive >10% of a therapeutic dose. May pose a greater risk of causing infant sedation and that this risk is dose-related. Poor CYP2D6 metabolisers may have decreased clearance of oxycodone and ultrarapid metabolisers higher concentrations of the more potent metabolite oxymorphone, leading to sedation. Multiple case reports and studies have reported sedation, respiratory depression and difficulty feeding in infants exposed to oxycodone via breast milk; especially at doses higher than 30 mg/day (LactMed). As with any opioids, caution should be used when giving oyxcodone as a single dose intra-opepratively, and the infant monitored for sedation after breastfeeding. The conclusion drawn is that oxycodone does not appear to be safer than codeine, particularly for continued use for acute postoperative pain. Repeated dosing of oxycodone should be avoided when breastfeeding.

Tramadol: Tramadol and active metabolite O-desmethyltramadol are excreted into breastmilk. There have been case reports of respiratory depression and death associated with the use of this medication. FDA issued a statement in April 2017 contra-indicating tramadol whilst breastfeeding. The UKDILAS has reviewed this statement, and recommended that 'despite the FDA warning,

tramadol can continue to be used (with caution) during breastfeeding', however the infant should be observed for increased sleepiness signs of respiratory depression, sedation and decreased alertness.

Dihydrocodeine:Dihydrocodeine is metabolised in the liver by CYP2D6, to dihydromorphine, which has potent analgesic activity. The analgesic effect of dihydrocodeine still appears to be mainly due to the parent compound. In addition, the CYP2D6 pathway only represents a minor route of metabolism for dihydrocodeine, with other metabolic pathways being involved. However, there is no data to confirm whether polymorphism of CYP2D6 has implications on potential side effects following dihydrocodeine use. Advice is to use dihydrocodeine at lowest effective dose for shortest time possible and to observe for drowsiness or sedation in the baby.

Codeine: Codeine is secreted in breastmilk due to high lipophilicity and weak protein binding. Maternal use of codeine during breastfeeding can cause infant drowsiness, central nervous system depression with case reports ending in death of the infant. It is metabolized to morphine by cytochrome P450 hepatic enzyme system isoenzyme CYP2D6, which has considerable genetic polymorphism. Patients who are ultrarapid metabolisers produce much higher concentrations of morphine in breastmilk, which in extreme cases may lead to severe neonatal depression and death in the infant. Conversely, patients who are poor-metabolisers will have little analgesic effect from codeine themselves. There are large ethnic differences in the frequencies of variant alleles, with the proportion of ultrarapid metabolisers up to 29% in Middle Eastern and Northern African populations, 3-5% of Caucasian population, and lower (0.5%) in Asians; the proportion of poor metabolisers is 8-10% of Caucasian population but lower in Asians and African Americans.

Numerous professional organizations and regulatory agencies recommend that other agents are preferred over codeine during breastfeeding. In the vast majority of mothers, codeine taken in moderation and for a short duration was suitable for their breastfed infant. However, due to the inability to predict which infants will be sensitive to codeine in lactation, this product is not recommended for use in breastfeeding women.

August 2018 *The information on this sheet is based upon my professional experience as a pharmacist with a specialised interest in the safety of drugs in breastmilk, supported by evidence from expert sources. However, I cannot take responsibility for the prescription of medication which remains with the healthcare professionals involved. I am happy to discuss the evidence by email wendy@breastfeeding-and-medication.co.uk*

Analgesics

Drug	plasma protein binding	milk:plasma ratio (aim <1)	Half life	relative infant dose (aim <10%)	Medications & Mother's Milk. Hale TW	LactMed
Paracetamol	10-25%	0.91-1.42	2 hours	6.41% - 24.23%	Although there seems to be wide variation in the milk concentrations in these studies, the amount of acetaminophen an infant could ingest via breastmilk is most likely significantly less than the pediatric therapeutic dose.	Acetaminophen is a good choice for analgesia, and fever reduction in nursing mothers. Amounts in milk are much less than doses usually given to infants. Adverse effects in breastfed infants appear to be rare.
Ibuprofen	>99%	0.84-1,59	1.85-2 hours	0.1-0.7	Based on years of clinical experience with ibuprofen for postpartum pain and its use in lactation it is one of the analgesics of choice in breastfeeding women.	Because of its extremely low levels in breastmilk, short half-life and safe use in infants in doses much higher than those excreted in breastmilk, ibuprofen is a preferred choice as an analgesic or antiinflammatory agent in nursing mothers
Diclofenac	99.70%		1.1 hours		Pediatric Concerns: None reported via milk. Milk levels are extremely low.	Data on excretion of diclofenac into milk are poor, but the drug has a short half-life and little glucuronide metabolite formation. Most reviewers consider diclofenac to be acceptable during breastfeeding

Naproxen	99.70%	0.01	12-15 hours	3.30%	Although the amount of naproxen transferred via milk is minimal, one should use this with caution in nursing mothers because of its long half-life. Short term use postpartum or infrequent or occasional use would be compatible with breastfeeding	Limited information indicates that levels of naproxen in breastmilk are low and adverse effects in breastfed infants are apparently uncommon. However, because of naproxen's long half-life and reported serious adverse reaction in a breastfed neonate, other agents may be preferred while nursing a newborn or preterm infant.
Celecoxib	97%	0.84-1.59	11 hours	0.3-0.7	The relative dose that infants are exposed to via milk is very low and breastfeeding would probably not be a threat to the infant	Because of the low levels of celecoxib in breastmilk, amounts ingested by the infant are small and would not be expected to cause any adverse effects in breastfed infants. No special precautions are required.
Fentanyl	80-85%		2-4 hours	1.9-5	When used parenterally, its half-life is exceedingly short.The transfer of fentanyl into human milk has been documented but is low.	No waiting period or discarding of milk is required before resuming breastfeeding after fentanyl is used for short procedures (e.g., for endoscopy). After general anesthesia, breastfeeding can be resumed as soon as the mother has recovered sufficiently from anesthesia to nurse
Alfentanil	92%		1-2 hours	0.26% - 0.4%	Following a dose of 50 µg/kg IV (plus several additional 10 µg/kg doses during the procedure), the mean level of alfentanil in colostrum at 4 hours was 0.88 µg/L, a level probably too small to produce overt toxicity in a breastfeeding infant	
Morphine	35%	0.84-1.59	1.5-2 hours	9.09% - 35%	The oral absorption of morphine is very poor and its fist pass metabolism is high. It is estimated that the amount of drug that would actually reach the infants systemic circulation would be 2-3 µg/100 mL and 10- 20 µg/100 mL via maternal epidural and IV/IM routes, respectively.	Morphine is metabolized to inactive morphine-3-glucuronide (60%) and to active morphine-6-glucuronide (10%). Morphine has an oral bioavailability of about 30% in adults. Morphine-6-glucuronide has an oral bioavailability of about 4%, but is probably converted back to morphine in the infant's gut and absorbed as morphine. The plasma clearance of morphine is prolonged in very young infants compared to older infants and children. Usual therapeutic intravenous doses of morphine in infants are 10 mcg/kg/hour or 50 to 100 mcg/kg as a single dose. Usual single oral doses of morphine in infants are 100 to 500 mcg/kg.

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Oxycodone	45%	0.84-1.59	2-4 hours	1.01% - 8%	Oxycodone may pose a greater risk of causing infant sedation and that this risk is dose-related. The use of doses greater than 40 mg/day are discouraged in opiate naive breastfeeding mothers. Higher doses maybe acceptable in breastfeeding mothers whom received opiates regularly during their pregnancy.	A maximum oxycodone dosage of 30 mg daily is suggested, although some sources recommend avoiding oxycodone during breastfeeding. Oxycodone elimination is decreased in young infants with much inter-individual variability. Monitor the infant closely for drowsiness, adequate weight gain, and developmental milestones, especially in younger, exclusively breastfed infants.
Tramadol	20%	2.4	7 hours	2.86	Caution is recommended as this medication also has an active metabolite via CYP 2D6 metabolism. No significant neurobehavioral adverse effects were noted between controls and exposed infants (post c section).	The excretion of tramadol into milk is low and even lower amounts of the active metabolite, O-desmethyltramadol, are excreted. With usual maternal dosage, the amount excreted into breastmilk is much less than the dose that has been given to newborn infants for analgesia. A study of breastfeeding in breastfed newborn infants found no adverse effects attributable to tramadol
Dihydrocodeine			3.5-5 hours			
Codeine	7%	1.35-2.5	2.9 hours	0.6% - 8.1%	Ultimately, each infant's response to codeine exposure in milk should be independently determined. In the vast majority of mothers, codeine taken in moderation and for a short duration was suitable for their breastfed infant. However, due to the inability to predict which infants will and will not tolerate codeine in lactation this product is not recommended for use in breastfeeding women.	Maternal use of codeine during breastfeeding can cause infant drowsiness, central nervous system depression and even death, with pharmacogenetics possibly playing a role. Excessive sedation in the mother often correlates with excess sedation in the breastfed infant

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