Breastfeeding and Medication

Breastfeeding and anaesthesia

Every hospital should have a policy in place to support patients to continue to breastfeed during hospital admission. These should include:

- access to trained breastfeeding support,
- availability of a breast pump if required and suitable private space to express as well as storage availability of expressed milk
- understanding by **all staff** of the long-term benefits of breastfeeding (to the age of 2 years and beyond
- an appreciation that informing a mother that she needs to interrupt breastfeeding has implications (risk of engorgement and mastitis, child refusal to feed from a bottle or cup, risk of allergy to cow's milk protein in artificial formula)

Anaesthetic drugs

Transfer of medications into breast milk depends on pharmacological properties of the drug including oral bioavailability, first pass metabolism, protein binding, lipid solubility, molecular weight, drug half-life, and maternal plasma level of the drug. The impact on the infant depends on the age and maturity of the infant, particularly relating to hepatic and renal function, volume of milk consumed and frequency of feeding, potential duration of action of drug in the infant, and therapeutic range. (Hale 2017, Jones 2018).

The ideal drug would be one with high maternal protein binding, high degree of ionization, short half, poor bioavailability and low lipid solubility, with a milk-plasma ration of <1. It is also good to avoid agents with active metabolites. Further explanation of these pharmacokinetic factors is given in Jones 2018

Detailed pharmacokinetic data on the most common agents used during anaesthesia is given in the tables below. The data enables practitioners to undertake a risk:benefit assessment for each drug to facilitate ongoing breastfeeding as soon as the mother is awake and alert following surgery.

References

- Hale TW Medications and Mothers Milk Springer 18th Ed 2019
- Jones W Breastfeeding and Medication 2nd Ed Routledge 2018
- LactMed actmed.nlm.nih.gov

Pharmacokinetic data of agents used in anaesthesia and their safety in breastfeeding

Intravenous Anaesthetic Agents

Drug	plasma protein binding	milk:plasma ratio (aim <1)	half life	relative infant dose (aim <10%)	Medications & Mother's Milk. Hale TW	LactMed
Propofol	99%		1-3 days	4.4	From these data it is apparent that only minimal amounts of propofol are transferred to human milk.	Amounts of propofol in milk are very small and are not expected to be absorbed by the infant. Although one expert panel recommends withholding nursing for an unspecified time after propofol administration,[1] most recommend that breastfeeding can be resumed as soon as the mother has recovered sufficiently from general anesthesia to nurse and that discarding milk is unnecessary.
Thiopentone	60-96%	0.3-0.4	3-8 hours	1.77-5.94	This medication appears to be suitable for use in lactation, the mother should resume breastfeeding after her procedure only once she is alert, orientated and able to feed her infant or pump on her own.	Amounts of thiopental in milk are very small. Existing data indicate that no waiting period is required before resuming breastfeeding after thiopental anesthesia. Breastfeeding can be resumed as soon as the mother has recovered sufficiently from general anesthesia to nurse
Etomidate	76		75 mins		Etomidate appears to be suitable for use in lactation. The mother should resume breastfeeding after her procedure once she is alert, orientated and able to feed her infant or pump on her own.	Amounts of etomidate in milk are very small and decrease rapidly. Existing data indicate that no waiting period is required before resuming breastfeeding after etomidate anesthesia. Breastfeeding can be resumed as soon as the mother has recovered sufficiently from general anesthesia to nurse.

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Sedative Agents

Drug	plasma protein binding	milk:plasma ratio (aim <1)	Half life	relative infant dose (aim <10%)	Medications & Mother's Milk. Hale TW	LactMed
Ketamine	47%		2.5 hours		It has a short half-life of 2.5 hours but its redistribution half-life out of the plasma (to muscle and tissues) is brief (10-15 min), thus milk levels are likely to be low	Breastmilk levels of ketamine have not been measured after administration to humans. Minimal data indicated that ketamine use in nursing mothers may not affect the breastfed infant or lactation. Until more data are available, ketamine should only be used with careful monitoring during breastfeeding.
Midazolam	97%	0.15	3 hours	0.63	Midazolam is a short acting benzodiazepine primarily used as an induction or preanesthetic medication. Midazolam has a quick onset of action, rapid elimination and is more potent than diazepam. With a half-life of only 3 hours, it is preferred for rapid induction and maintenance of anesthesia. The amount of midazolam transferred to an infant via early milk is minimal, particularly if the baby is breastfed more than 4 hours after administration.	The small amounts of midazolam excreted into breastmilk would not be expected to cause adverse effects in most breastfed infants. Two expert panels advocates waiting for at least 4 hours after a single intravenous dose of midazolam (e.g., for endoscopy) before resuming nursing. However, no waiting period or discarding of milk might be necessary before resuming breastfeeding after a single dose of midazolam in the mothers of infants over 2 months of age. After general anesthesia, breastfeeding can be resumed as soon as the mother has recovered sufficiently from general anesthesia to nurse

Diazepam	99%	0.2-2.7	43 hours	0.88% - 7.14%	The acute use such as in surgical procedures is not likely to lead to significant accumulation. Some reports of lethargy, sedation, and poor suckling have been found.	After a single dose of diazepam, as for sedation before a procedure, there is usually no need to wait to resume breastfeeding, although with a newborn or preterm infant, a cautious approach would be to wait a period of 6 to 8 hours before resuming nursing.

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	

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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.
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			

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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

Anti emetics

Drug	plasma protein binding	milk:plasma ratio (aim <1)	Half life	relative infant dose (aim <10%)	Medications & Mother's Milk. Hale TW	LactMed
Ondansetron	70-75%		3-4 hours		At this time there are no data regarding the transfer of ondansetron into human milk; however, based on this medications shorter half-life, larger volume of distribution and moderate oral bioavailability we predict a relatively small exposure to the infant via breast milk	Little published information is available on the clinical use of ondansetron during breastfeeding, although it is apparently frequently used for nausea after cesarean section, usually in doses of 4 to 8 mg intravenously Use after cesarean section appears to not affect the onset of breastfeeding.No adverse infant effects have been reported and the drug has been used in infants. If ondansetron is required by the mother, it is not a reason to discontinue breastfeeding;
Metoclopramide	30%	0.5-4.06	5-6 hours	4.7% - 14.3%	In breastfeeding, it is sometimes used in lactating women to stimulate prolactin release from the pituitary and enhance breastmilk production.	Metoclopramide is excreted in variable amounts in breastmilk. Most infants would receive less than 10% of the maternal weight-adjusted dosage, but some receive doses that achieve pharmacologically active serum levels, elevated serum prolactin and possible gastrointestinal side effects. Although most studies have found no adverse effects in breastfed infants during maternal metoclopramide use, many did not adequately observe for side effects

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Domperidone	93%	0.25	7-14 hours	0.01% - 0.35%	The medication is not recommended in patients with a preexisting arrhythmia, history of cardiac disease or those taking other medications which can also prolong the QTc interval.	Data available from 4 small studies on the excretion of domperidone into breastmilk are somewhat inconsistent, but infants would probably receive less than 0.1% of the maternal weight-adjusted dosage. No adverse effects have been found in a limited number of published cases of breastfed infants whose mothers were taking domperidone.