

Guidelines

Guidelines for anaesthesia and sedation for patients who are breastfeeding

Guidelines from the Association of Anaesthetists

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Summary

Introduction Breastfeeding is acknowledged widely as one of the most effective ways to ensure the health and well-being of both child and birth parent. Historically, advice given to patients who required an anaesthetic while breastfeeding was variable and inconsistent, sometimes resulting in the interruption of feeding for ≥ 24 h, or expressing and discarding breastmilk because of concerns regarding the possible adverse effects secondary to medicines passing into the breastmilk. This can be a contributory factor in the early cessation of breastfeeding. Peri-operative decisions can normally be made on the basis of pharmacokinetic data rather than on the precautionary principle.

Methods This multidisciplinary consensus guideline included anaesthetists, pharmacists, midwives, infant feeding advisers and people with lived experience relevant to these guidelines. Following the targeted literature review, a three-round modified Delphi process was conducted to produce and ratify recommendations.

Results Any patient with a child aged < 2 y should routinely be asked if they are breastfeeding or expressing breastmilk during their pre-operative assessment for a procedure involving anaesthesia or sedation. Anaesthetic, sedative and analgesic medicines are transferred to breastmilk in only very small amounts. For almost all medicines used peri-operatively, there is no evidence of adverse effects on the breastfed child. Patients should be advised that discarding of breastmilk after anaesthesia ('pumping and dumping') is not necessary and that 'sleep and keep' is now recommended.

Discussion This pragmatic, multidisciplinary guideline aims to facilitate the peri-operative management of patients who are breastfeeding. It is hoped that these will be of value to both clinicians and patients in determining the optimal anaesthetic management strategy to support breastfeeding in the peri-operative period while ensuring minimal risk to the breastfed child.

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Plain Language Summary is available on the journal website.

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Key recommendations

- 1 Any patient with a child aged < 2 y should routinely be asked if they are breastfeeding or expressing breastmilk during their pre-operative assessment for a procedure involving anaesthesia or sedation. However, it is important to consider that patients may continue to breastfeed a child beyond the age of 2 y.
- 2 Patients should be supported to breastfeed immediately before surgery, preferably directly, or by expressing if that is their preference. Patients should be supported to resume breastfeeding after the procedure once they are alert, orientated and able to feed their child or express independently.
- 3 Anaesthetic, sedative and analgesic medicines are transferred to breastmilk in only very small amounts. For almost all medicines used peri-operatively, there is no evidence of adverse effects on the breastfed child.
- 4 Patients should be advised that discarding of breastmilk after anaesthesia ('pumping and dumping') is not necessary and that 'sleep and keep' is now recommended.
- 5 For patients who are breastfeeding and who are admitted for urgent or emergency surgery or inpatient care, it is important that the patient and child remain together wherever possible with appropriate support for care of the child.
- 6 Anaesthetic departments should have a breastfeeding champion to support colleagues with patient discussions and advocacy in the peri-operative period, and to provide departmental and patient education.
- 7 Hospitals are encouraged to engage with the United Nations Children's Fund Baby Friendly Initiative, an evidence-based programme to support the starting and continuation breastfeeding.
- 8 Hospitals should provide a suitable environment for breastfeeding such as a single room, where another adult can be present to care for the child as required.
- 9 For all patients, including those who are breastfeeding or expressing milk, postoperative analgesia should be multimodal and opioid sparing when possible.
- 10 If opioid pain relief is required, codeine is not recommended due to concerns related to differences in metabolism which may result in excessive sedation in some children.
- 11 Patients who are breastfeeding should have appropriate opioid analgesia if needed, and the lowest effective dose should be used for the shortest period of time. Dihydrocodeine or morphine are the preferred medicines.

- 12 Where possible, day surgery is preferable to avoid disrupting normal routines. Consider moving breastfeeding patients to first on the list for their procedure to minimise time away from their child.
- 13 Breastfeeding while on chemotherapy is not recommended due to the passage of the medication into milk with associated adverse effects.
- 14 Patient information leaflets and additional resources should be available containing information on the compatibility of anaesthetic medicines, sedatives and analgesics during breastfeeding, and guidance on breastfeeding support in the peri-operative period.

Why were these guidelines developed?

Accessing information on the risks of medicines during breastfeeding can be challenging, as many of the resources used most commonly, such as the British National Formulary, err on the side of caution in line with the manufacturers' recommendations and licences. Specialist information sources on breastfeeding are available but not accessed routinely. The Association of Anaesthetists produced guidelines on anaesthesia and sedation in patients who are breastfeeding in 2020 [1]. Since then, several new medicines have entered routine clinical practice. This guideline has been updated to provide information for all health professional groups involved in the peri-operative care of patients who are breastfeeding.

What other guideline statements are available on this topic?

Online and print resources include lactation specific database such as the UK Drugs in Lactation Advisory Service (UKDILAS) [2], the Drugs and Lactation Database (LactMed) [3], e-lactancia [4] and the Manual of Lactational Pharmacology by Hale and Krutsch [5]. There are other publications that give guidance on the compatibility of breastfeeding following anaesthesia, but which have not been updated for several years [1, 6–10]. The Breastfeeding Network 'Drugs in Breastmilk' service [11] provides information suitable for patients on the use of anaesthesia while breastfeeding and is a support service for both patients and healthcare professionals to ensure evidenced-based and consistent information.

How and why does this statement differ from existing guidelines?

This guideline contains pharmacokinetic data on medications used during anaesthesia to ensure anaesthetists have the required knowledge to minimise

interruptions to breastfeeding in the peri-operative period. This is in accordance with recommendations from the National Institute for Health and Care Excellence (NICE) [12] which also provides advice on peri-operative care for patients who are breastfeeding. This document uses recommended inclusive language in the form of 'people' and 'patients' rather than terms such 'woman' and 'mother' [13]. 'Breastfeeding' is used to describe all people who are lactating and providing nutritional support for children, either by directly breastfeeding or feeding using expressed breastmilk. The term 'neonate' is used to describe children aged ≤ 28 days and 'infant' for children aged > 28 days but < 1 y.

Introduction

Breastfeeding is acknowledged widely as one of the most effective ways to ensure the health and well-being of both the child and the birth parent. Its advantages span across nutritional, immunological, emotional and economic fields. Breastmilk is a living fluid that is continually changing according to the needs of the child. It provides antibodies and protection for the child from infections. Breastfeeding has been shown to decrease the risk of a baby developing a range of illnesses and chronic health conditions including: respiratory infections; diarrhoea; necrotising enterocolitis; otitis media; diabetes; asthma; heart disease; obesity; and sudden child death syndrome [14]. Breastfeeding also protects the lactating parent from breast and ovarian cancers, type 2 diabetes and supports the building of relationships between parent and baby, benefiting parental and child mental wellbeing [14]. Increasing breastfeeding rates around the world to near universal levels could prevent 823,000 annual deaths in children aged < 5 y and 20,000 annual deaths from breast cancer [14]. In the UK, increases in breastfeeding rates could lead to substantial economic benefits for the NHS, with estimated savings exceeding £40 million (US\$54 million, €46 million) per annum [15].

For some parent and child dyads there can be additional value placed on breastfeeding: for example, if a child is unwell or has a long-term condition or for cultural reasons, such as the importance placed on breastfeeding in Islam where breastfeeding is encouraged until 2 years of age [16]. It is also important to support a parent to achieve their breastfeeding goals and not force them to stop before they are ready, especially when based on misinformation, as this can lead to feelings of guilt, anxiety or anger [17].

Historically, advice given to patients who required an anaesthetic while breastfeeding was variable and

inconsistent, sometimes resulting in the unnecessary interruption of feeding for ≥ 24 h, or expressing and discarding breastmilk ('pumping and dumping') because of concerns regarding the possible adverse effects secondary to medicines passing into the breastmilk [18]. This can be a contributory factor in the early cessation of breastfeeding [19]. It should be noted that, while there may be an absence of research studies on a medicine, this does not imply risk. Decisions can normally be made on the basis of pharmacokinetic data rather than on the precautionary principle.

Improved knowledge and updated practice relating to anaesthesia-related breastfeeding counselling might positively impact patient health outcomes and satisfaction in patients who are breastfeeding, but would require improved training of all professionals who encounter a lactating patient during the peri-operative period [20, 21].

The World Health Organization (WHO) recommends exclusive breastfeeding up to 6 months of age and continued breastfeeding along with complementary foods up to 2 years or beyond [22]. Hospitals across the UK are encouraged to engage with the United Nations Children's Fund (UNICEF) Baby Friendly Initiative, an evidence-based programme to support the starting and continuation of breastfeeding [23]. This includes initiating breastfeeding after anaesthetic interventions, including general anaesthesia in an obstetric setting. However, formal support for patients receiving anaesthesia beyond the immediate post-partum period is not as well established. Anecdotally, incorrect advice often remains problematic in the peri-operative period.

While the prevalence of breastfeeding beyond six months is still relatively low in Western European countries compared with other high-income countries (28.5% vs. 42.9%) [24], active measures are in place to encourage and support ongoing breastfeeding. Therefore, it is important that appropriate consideration is given to patients who require surgical or medical procedures and who have children up to 2 years of age (or even beyond), as they may still be breastfeeding [25].

Obstetric surgery immediately preceding delivery is undertaken frequently, with little concern about the passage of anaesthetic medicines across the placenta and potential effects on the neonate [26]. Immediately after delivery, the intercellular gaps in the milk glands are wide open to facilitate the passage of immunoglobulins to line the gut of the baby, and during this period medicines are also freely able to pass into breastmilk. However, patients having a caesarean section are encouraged to breastfeed as soon as they are alert and able to hold the baby in the

post-anaesthesia care unit (PACU). There is considerable overlap between the medicines used in anaesthesia after the peripartum period and those used during caesarean section, yet the intercellular gaps close soon after birth so passage of medicines into breastmilk is much lower.

The risk:benefit balance of stopping breastfeeding peri-operatively should take into consideration possible consequences that include: breast engorgement/blocked ducts or mastitis, which potentially requires antibiotic treatment; refusal of the child to feed from a bottle; and reactions to cows' milk protein and increased risk of cows' milk protein allergy by exposure through artificial formula.

In addition to the health benefits of breastfeeding, the carbon footprint of formula milk cannot be ignored. The cost of production, transportation and heating of child formula milk has significant environmental costs. The water footprint of powered cows' formula milk is approximately 4700 l.kg⁻¹ [27] and in the UK the energy costs of heating formula milk over the first year of life produce over 1.5 million kg of carbon dioxide [28]. Compared with formula feeding, exclusively breastfeeding for six months saves an estimated 95–153 kg carbon dioxide equivalent per child [29]. The production of unnecessary formula milk exacerbates environmental damage and should be a matter of increasing global concern.

We aimed to produce multidisciplinary guidelines on behalf of the Association of Anaesthetists for the peri-operative management of patients who are breastfeeding.

Methods

In line with recommended practice [30, 31], a multidisciplinary working party was convened that included a diverse authorship selected on the basis of clinical or academic expertise relating to breastfeeding and/or guideline production. A targeted literature review was performed with particular focus on articles published since the previous guidelines from the Association of Anaesthetists in 2020 [1].

We conducted the literature search using PubMed, using the following search terms: 'anaesthesia'; 'breastfeeding'; 'breastmilk'; and 'surgery'. We also consulted relevant sources of information identified by the Working Party including: lactation specific databases [3, 5, 11, 32–34]; the World Health Organization; current guidelines; breastfeeding expert journals; and relevant websites (e.g. <https://www.medicinescomplete.com/>). A list of medicines used peri-operatively was compiled, including reference to the Association of Anaesthetists National Essential Anaesthesia Drugs List (<https://anaesthetists.org/Home/Resources-publications/Guidelines/National-Essential-Anaesthesia-Drugs-List-NEADL>).

Following the literature review, a modified Delphi process was conducted to formulate and ratify recommendations. An initial long list of recommendations was produced relating to conduct of breastfeeding during the peri-operative period, including organisational and logistical principles. These were refined by a virtual round table discussion of the Working Party members. A modified Delphi process was then conducted to ratify recommendations [35].

Authors were asked to rate recommendations as 'include', 'exclude' or 'revise', and provide anonymised comments. Recommendations with $\geq 80\%$ inclusion agreement proceeded into subsequent rounds; those with 50–79% agreement were revised; and those with $< 50\%$ agreement were discarded. Final recommendations were then shared with relevant supporting organisations for approval.

Results

Patients who donate breastmilk (milk donors)

Milk donors should discuss with their own milk bank regarding temporary restrictions on donation due to hospital admission and medication use. A list of medications administered in hospital should be provided to the patient. It is likely that any milk expressed in hospital which would normally be for donation will have to be discarded. This is because donated milk is often used for very-low birth weight babies (< 1500 g) receiving care in the neonatal intensive care unit.

For milk donors having surgery who are donating while feeding their own child: treat as per patients who are currently breastfeeding. For milk donors having surgery who are exclusively donating: treat as per patients who are breastfeeding with regards to peri-operative care and encourage their normal expressing regimen.

Pre-operative factors: assessment, consent and peri-operative planning

Historically, breastfeeding was not considered pre-operatively and yet was a cause of considerable anxiety and concern in patients. A patient may not mention that they are breastfeeding at the time of pre-operative assessment as they may not have considered this to be significant information or may be concerned that they will be subjected to judgemental comments, especially if they are continuing to feed an older child. Patients may also be expressing breastmilk after the loss of a child.

As there is considerable variability in the timeframe between being listed for surgery and anaesthetic pre-operative assessment, it is vital that surgical,

Box 1 Pre-operative considerations for patients who require surgery and are breastfeeding.

- Does the patient wish to continue to breastfeed? In general, this should be assumed and supported regardless of the age of the child. The clinician's role is not to discuss the patient's choice of child feeding, beyond encouraging the continuation of breast feeding should the patient so wish.
- What is the impact on ongoing lactation if interrupted by expressing and discarding breastmilk including the risk to the patient of blocked ducts/mastitis or the risks of exposure to artificial formula in an allergic child? These factors should be set against any hesitations that the patients may have about potential adverse effects from medicine transfer into breastmilk.
- Is the child able to feed from another container (such as a bottle or cup) or eating solid foods alongside breastfeeding? This may facilitate care of the child at home. Not all children who are exclusively breastfed will take expressed milk from a bottle; this may lead to dehydration if breastfeeding is interrupted.
- In pre-term children, the risk of necrotising enterocolitis needs to be considered if breastmilk is replaced, even temporarily, by formula milk.
- Discuss with the patient:
 - Their wishes to continue to breastfeed.
 - The most suitable type of anaesthesia that is the least disruptive to breastfeeding. Early return of consciousness after general anaesthesia is desirable. Assure the patient that effective analgesic and anti-emetic strategies will be used.
 - The transfer of medicines to breastmilk, both intra-operative and postoperative, and any potential risks of this vs. the benefits of continuing breastfeeding.
- Document a plan to recommence breastfeeding as soon as possible after surgery, in line with locally developed guidelines.
- Discuss expressing and storing of breastmilk if the child is unable to stay with the patient on the ward, or if surgery is prolonged. This should be carried out with input from an expert in child feeding, or other specially trained member of staff.

pre-operative and anaesthetic teams are aware of the evidence-based information available to support patients who wish to continue to breastfeed during the peri-operative period. This will ensure that the correct guidance is given starting from the decision to proceed with surgery and should improve patient experience [36]. Factors that should be considered are shown in Box 1.

Electronic pre-operative questionnaires should include questions about whether the patient is breastfeeding and whether they wish to continue in the peri-operative period. This should be highlighted to the anaesthetic and surgical teams to allow appropriate planning. Day surgery is preferable for patients who are breastfeeding. Local guidelines should provide information for staff regarding additional support services including contact information for local child feeding advisors. This information should be accessible to pre-operative assessment staff to assist in planning including additional considerations and support, such as expressing and storage of milk, especially if the patient requires an overnight stay.

Departments will benefit from identifying a breastfeeding champion with an interest in this area of practice. As well as supporting colleagues with patient discussions and advocacy in the peri-operative period, champions may also provide departmental education; develop in-hospital networks to support child feeding; and create local guidelines and patient information literature. This includes ensuring appropriate information is incorporated in relevant policies and processes to care for patients who are breastfeeding in the peri-operative period. An example of a peri-operative breastfeeding patient pathway is available in online Supporting Information Appendix S1.

Peri-operative management

The WHO/UNICEF Baby Friendly Initiative encourages support for patients who wish to continue breastfeeding [23]. Patients who are having an operation will have normal peri-operative anxieties and concerns, as well as disruption of their normal breastfeeding routines. It is important, therefore, that the hospital provides a suitable environment

for breastfeeding; this is likely to include a single room where family members can accompany the patient; attention to minimising the time in the theatre suite; and timing the surgery so that the patient can feed the child just before leaving the ward for surgery. A specific hospital guideline will make it easier to accommodate all these factors.

When scheduling theatre lists, the patient who is breastfeeding should be first on the list if possible. Fasting times should be minimised to avoid dehydration in accordance with national guidance. The Centre for Perioperative Care recommends a 'Sip Til Send' protocol unless there are specific contraindications (<https://www.cproc.org.uk/guidelines-and-resources/guidelines-resources/resources/sip-til-send>).

Anaesthetic options should aim to ensure the delivery of anaesthesia and postoperative analgesia that minimise any impact on breastfeeding in the postoperative period. It is important to consider factors that are important to the patient as part of shared decision-making. Patients should be advised that expressing and discarding of breastmilk after anaesthesia ('pumping and dumping') is not necessary, and the 'sleep and keep' is now recommended. However, some patients may wish to ensure that their child is not exposed to any medication at all. Prior expression and storage of milk may be possible. If a patient chooses to express and discard after medication exposure, evidence-based material should be provided on the elimination time of the medicines so that normal breastfeeding can be resumed as soon as the patient wishes (see later sections).

Patients should be supported to feed immediately before surgery, preferably directly, or by expressing (if that is their preference). Patients should be encouraged to resume breastfeeding after the procedure once they are alert, orientated and able to feed their child or pump independently. Parents and carers should be informed that, to facilitate access to the child to continue breastfeeding, another adult should be assigned to care for the child. This could be the other parent, other member of the family or friend but cannot be assumed to be the responsibility of ward staff.

Patients who are breastfeeding may have increased fluid requirements due to milk production. An effective anti-emetic strategy should be used, which should include prophylactic treatment. Where general anaesthesia is required, the use of propofol-based total intravenous anaesthesia (TIVA), with processed EEG monitoring where appropriate, may reduce the risk of postoperative nausea and vomiting (PONV) [37, 38].

Performing surgery under regional anaesthesia (including spinal anaesthesia) has the advantage of the least interference with the patient's ability to care for their child. However, regional anaesthesia for upper limb surgery may impact upon the ability of the patient to hold the child postoperatively.

It is important to consider opioid-sparing analgesia as part of a general anaesthetic. In line with existing guidelines, local anaesthetic supplementation (including regional anaesthesia) should be encouraged to reduce the need for systemic analgesics [39]. Multimodal analgesia with non-opioid medicines including paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) and cyclo-oxygenase-2 inhibitors is compatible with breastfeeding. When used in combination, paracetamol and NSAIDs are synergistic and highly effective [40].

Patients who are breastfeeding should have appropriate opioid analgesia if needed, and the lowest effective dose should be used for the shortest period of time [24, 25]. If opioids are used, effects may vary from person to person because of greater or lesser metabolism (pharmacokinetic differences) or from a different sensitivity to the same blood level (pharmacodynamic differences). Dihydrocodeine or morphine are the preferred medicines (see later sections). If using strong opioids during breastfeeding, parents should observe their child for a change in behaviour; if sedation and drowsiness develop in the child, breastfeeding should be withheld and medical advice sought. It may be necessary to identify a responsible adult other than the patient to help observe the child postoperatively if opioids are required [41]. Pre-term babies are more sensitive to opioids because of immature hepatic and renal function; extra caution should be taken in neonates and infants < 6 weeks of age (corrected for gestation). It is also advisable to seek signs of excessive sedative effects in the patient as an indicator of potential child effects.

Care should be taken when positioning patients for surgery, avoiding additional pressure on breast tissue during patient positioning; prone positioning may predispose to mastitis. Where prolonged surgery or postoperative recovery is expected, consideration must be given to the potential for milk expression to maintain milk supply and avoid the risk of engorgement or mastitis. This may require the support of the child feeding team and should be part of the peri-operative plan [42].

Patients should be given advice on who to contact with queries after discharge. Although current day surgery guidelines now advise that some patients can be

discharged without a home escort as part of the 'No-One at Home' (NOAH) protocol [43], this policy is not recommended for patients who are breastfeeding. Patients who are breastfeeding should be cautious if bed-sharing or sleeping while feeding the child in a chair in the postoperative period, as they may not be as responsive as normal. Patients should be advised on a strategy for stepping down analgesic medication that includes stopping opioid medication first, then NSAIDs and finally paracetamol. Online supporting information contains links to further information for professionals and patients (online Supporting Information Appendix S2), and a sample patient information leaflet (online Supporting Information Appendix S3).

Special circumstances: emergency care

The same principles apply to provide support for patients who are breastfeeding who are admitted for urgent or emergency surgery or inpatient care. It is important that the patient and child remain together wherever possible with appropriate support for care of the child as highlighted previously. Local information should be available for staff including information on access to a breast pump if required and safe storage of breastmilk. Specialist child feeding support should be accessed as required. It is important to ensure that breastfeeding can continue safely with any additional medicines that may be required (e.g. antibiotics). This could be from the local pharmacy department or internet-based resources such as those detailed in online Supporting Information Appendix S2. If the patient is unable to breastfeed or no longer wishes to breastfeed, effective management and gradual cessation is important to prevent complications. Sudden cessation of breastfeeding can impact acutely on the health of the patient, including the development of complications such as mastitis and associated morbidities that can prolong hospital stay.

Sedation on the ICU

The Intensive Care Society recommends that routine aspects of neonatal care, including breastfeeding, should be supported within the ICU [44]. Advice should be accessed from child feeding co-ordinators to support the patient and staff to provide appropriate care. However, there are limited data relating to breastfeeding in patients who are critically ill and receiving care on the ICU. One retrospective study from the USA involved 102 patients who were admitted to the ICU immediately postpartum [45]. Of the patients who received mechanical ventilation of their lungs, lactation (including breastfeeding, breast pumping

or hand expression of breastmilk) was initiated in 47/58 patients and continued until discharge in 38/58.

Sedation in the presence of critical illness present several challenges in relation to breastfeeding. Many clinical trials exclude patients who are breastfeeding, thereby limiting the evidence base. As such, the pharmacological recommendations for critical care are generally extrapolated from those used in the elective peri-operative setting, especially in relation to sedative and analgesia medicines.

Specific medicines that are used more commonly on critical care include vasopressors; glucocorticoids; anti-arrhythmic medicines; and proton pump inhibitors. Noradrenaline and adrenaline have a poor oral bioavailability and a short half-life meaning that administration is unlikely to affect the child. Both medicines may inhibit milk production. There are no data for vasopressin but as this is not orally absorbed this is unlikely to have any effect on the breastfeeding child. Hydrocortisone is a normal component of breastmilk and very low levels are excreted in breastmilk in response to exogenous administration, meaning that hydrocortisone is compatible with breastfeeding [3, 4]. Amiodarone has the greatest significance of anti-arrhythmic medicines as breastmilk levels can be variable and there is theoretical risk of neonatal hypothyroidism. A single intravenous dose of 450 mg corresponded to breastmilk levels that were < 1% of the paediatric dose [46]. This suggests that single doses for treatment of arrhythmias have a low risk of adverse events in the context of breastfeeding. Beta-blockers are excreted into breastmilk and are associated with a risk of hypoglycaemia and bradycardia; metoprolol and labetalol are associated with the lowest risk [47]. All currently used proton pump inhibitors are compatible with breastfeeding.

If a patient is sedated and unable to express milk independently, and where the patient wishes to continue breastfeeding are known, a relative or other appropriate person may need to express the milk both to avoid engorgement and to facilitate ongoing breastfeeding following recovery. If possible, appropriate consent should be sought from the patient or next of kin.

Surgery for cancer in a patient who is breastfeeding

Cancer rates in UK patients aged 18–49 y have increased by over 20% between 1995 and 2019 [48]; in patients who are biologically female, breast cancer is the commonest malignancy accounting for > 40% of diagnoses. Patients who are lactating may present for surgery before other therapies and have a desire to continue to breastfeed for as long as possible. The ability

to breastfeed may depend on surgery and, if the surgery is on the breasts, whether major ducts have been excised. It may be possible for the patient to continue to breastfeed if chemotherapy is not planned or until such time as treatment begins.

Breastfeeding while on chemotherapy is not recommended due to the passage of the medication into breastmilk with associated adverse effects. On the basis of a case report from 1985 [49], the Green Top Guidelines recommend “*There should be a time interval of 14 days or more from the last chemotherapy session to start of breastfeeding to allow drug clearance from breastmilk*” [50]. The guidelines also recommend that patients should not breastfeed while taking trastuzumab (Herceptin) or tamoxifen [50]. The half-life of chemotherapy medicines varies widely, and five half-lives should have elapsed before recommencing breastfeeding.

Following surgery, patients may experience nausea. If the patient has only stopped breastfeeding recently, the use of domperidone or metoclopramide (which increase prolactin levels) may lead to an increase supply of breastmilk or resumption of lactation, both of which may be traumatic for the patient and lead to a risk of mastitis. Ondansetron is the preferred anti-emetic following both surgery and chemotherapy.

Despite a diagnosis of cancer, a patient may express a desire to pump and discard their milk until treatment is complete or to re-lactate. This decision should be acknowledged and supported. However, the use of adjuvant therapy (e.g. tamoxifen) to prevent recurrence may make this incompatible with continued breastfeeding.

Transfer to breastmilk of medicines used peri-operatively

LactMed is a useful source for information on individual medicines [3]. Table 1 provides a summary of information on medicine transfer to breastmilk. Detailed pharmacokinetic data and pharmacokinetic principles involved in medicine transfer to breastmilk are available in online Supporting Information (Appendices S4 and S5, respectively). Individual medicines are discussed in detail below.

Intravenous anaesthetics

Most intravenous anaesthetic medicines have poor bioavailability and short half-lives [3, 5, 34] and so are compatible with use in patients who are breastfeeding. Small amounts remain in body fat stores for 24–48 h, but

Table 1 Transfer to breastmilk of medicines used peri-operatively.

Medicines used during anaesthesia and after surgery that pass in low levels into breastmilk and therefore patients can breastfeed as normal:

Intravenous anaesthetics	Propofol Thiopental Etomidate Ketamine
Inhalational anaesthetics	Sevoflurane Isoflurane Desflurane Halothane Nitrous oxide
Sedatives	Midazolam Diazepam (single-dose)
Analgesics	Paracetamol NSAIDs: - Ibuprofen - Diclofenac - Naproxen - Celecoxib - Ketorolac - Parecoxib Opioids: - Morphine - Dihydrocodeine - Remifentanyl - Fentanyl - Alfentanil
Local anaesthetics	All local anaesthetics in current practice
Neuromuscular blocking drugs	Suxamethonium Rocuronium Vecuronium Atracurium
Neuromuscular blocking drug antagonists	Neostigmine Sugammadex
Anti-emetics	Ondansetron Granisetron Cyclizine Prochlorperazine Dexamethasone Metoclopramide Domperidone

Use with caution while breastfeeding:

Analgesics	Tramadol: observe child for unusual drowsiness Oxycodone: increased risk of drowsiness in doses > 30 mg.day ⁻¹ Codeine: observe child for unusual drowsiness Pethidine: observe child for unusual drowsiness
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Contraindicated while breastfeeding:

Analgesic	Aspirin (analgesic doses)
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this does not preclude resumption of normal breastfeeding. A patient who is breastfeeding may need to take precautions if they normally bed-share with their child, as their natural responsiveness may be inhibited [51].

Propofol: minimal amounts (0.025%) of propofol are transferred to breastmilk. This is not a concern even when propofol is used by infusion for maintenance of anaesthesia. Breastfeeding may be resumed as soon as the patient has recovered sufficiently from general anaesthesia to care for the baby [51].

Ciprrofol: half-life 2–4 h. There are no studies of use in patients who are breastfeeding. However, the duration of anaesthetic effect is short (5–10 min after a single bolus injection), largely due to rapid redistribution to peripheral tissues and swift hepatic metabolism [52].

Thiopental: amounts in breastmilk are very small; no waiting period is required before resuming breastfeeding [53].

Etomidate: rapidly redistributed from the central nervous system. Amounts of etomidate in milk are very small and decrease rapidly. No waiting period is required before resuming breastfeeding.

Ketamine: rapid redistribution from plasma makes adverse effects in the child unlikely. Ketamine and norketamine (active metabolite) concentrations in breastmilk are low with estimated child doses < 0.05 mg.kg⁻¹ and the relative child dose ≤ 0.95% [54, 55].

Inhalational medicines

Inhalational anaesthetic agents: these are eliminated predominately after anaesthesia by exhalation, with some metabolism. Because of their short half-life and rapid clearance [56], use will not preclude subsequent breastfeeding.

Methoxyflurane: there are no published studies on levels of methoxyflurane in breastmilk but due to its short duration of action it is compatible with continued breastfeeding soon after exposure with the same precautions of other inhalational anaesthetic agents. In utero exposure to methoxyflurane was not associated with an increased risk of adverse outcomes in the perinatal period [57].

Benzodiazepines

Midazolam: extensive first-pass metabolism results in low systemic bioavailability after oral doses, so blood levels in the child after breastfeeding can be expected to be low [33]. Breastfeeding can be resumed after a single dose of midazolam as soon as the patient has recovered from the procedure.

Diazepam: this has an active metabolite, desmethyldiazepam, which has a prolonged half-life. It is known to be transferred in breastmilk in significant levels. Use of diazepam may be considered as a one-off dose before a procedure [3].

Remimazolam: a newly emerging benzodiazepine that may be used for sedation or anaesthesia. It is rapidly metabolised by tissue esterase. No information is available on the use of remimazolam during breastfeeding. Current advice from the manufacturer recommends that breastfeeding patients pump and discard breastmilk after use, but this is at odds with the pharmacokinetics (elimination half-life of 0.7 h with no active metabolites [58]) and appears overly cautious. As with other intravenous anaesthetic medicines, breastfeeding can resume when the mother is alert and awake.

α-adrenoceptor antagonists

Dexmedetomidine: half-life 2–3 h [59] and relative child dose 0.034 [60]. It has a large volume of distribution, high percentage of protein binding (94%) [59] and has no active metabolites, meaning that there is negligible passage to breastmilk [60] even after continuous infusion [61]. No problems have been observed in the children of patients to whom dexmedetomidine has been administered, nor have problems with lactation or breastmilk production been reported [62]. Therefore, the patient can breastfeed as soon as they are awake and well enough.

Clonidine: may reduce prolactin secretion and therefore could conceivably reduce milk production in the early postpartum period. It is minimally secreted into breastmilk. There are no reports of neonatal toxicity during breastfeeding.

Non-opioid analgesic medicines

Peri-operative analgesia should be individualised. It is important that appropriate analgesia is given to patients after surgery including strong opioids if required; this includes after caesarean section, which has a 5% incidence of chronic postsurgical pain at 12 months [63]. It is essential that simple analgesics, including paracetamol and NSAIDs, are taken regularly as first line pain relief. If opioid analgesics are used, the lowest effective dose should be used for the shortest possible time in the postoperative period due to the risk of persistent postoperative opioid use (PPOU) and the risk of drowsiness in the baby [64]. Guidelines recommend that discharge analgesia after surgery should be of no greater than 7 days duration and should be reviewed appropriately if further analgesia is requested [39].

Paracetamol: although studies show a wide variation in the concentration of paracetamol in breastmilk, the amount of paracetamol that a child would ingest via breastmilk is significantly less than the paediatric therapeutic dose and hence should be used as first line pain relief.

Nonsteroidal anti-inflammatory drugs: have limited transfer into breastmilk due to low lipid solubility and high protein binding resulting in very low relative child doses. One caveat is that NSAIDs should be avoided in patients who are breastfeeding and whose child has a ductal-dependent cardiac lesion [65], due to the risk of premature constriction of the ductus arteriosus [66]. Ibuprofen and diclofenac have been used extensively for postpartum pain and during lactation and are considered compatible with breastfeeding. Although naproxen has a longer half-life than diclofenac, it is used widely post-caesarean section, and breastfeeding may continue as normal. Similarly, the relative dose that a child is exposed to via breastmilk for celecoxib, parecoxib and ketorolac is very low, and breastfeeding may continue. Aspirin should not be used in analgesic doses due to the risk of Reye's syndrome in the child. If indicated, low-dose aspirin taken for its antiplatelet effects can be used in patients who are breastfeeding.

Magnesium: is a normal serum electrolyte that is often used as part of a multimodal analgesic strategy. In a study of 10 patients given intravenous magnesium for pre-eclampsia, although levels in breastmilk did increase, this was still within the normal range and had returned to the same levels as those seen in controls 24 h after administration [67].

Nefopam: is a non-opioid analgesic with a half-life of 3–8 h, plasma protein binding of 71–76% and relative child dose of 2.6% [68]. Breastfed babies should be observed for sedation and urinary output [3].

Opioid analgesics

Morphine: transferred to breastmilk in small amounts. It has an active metabolite (morphine-6-glucuronide) that is more potent than the parent drug. Morphine has been recommended as the opioid of choice if strong analgesia is required in patients who are breastfeeding [69]. Administration of a single dose of morphine to a patient who is breastfeeding would not be expected to cause detrimental effects to the child. There are limited studies of morphine patient-controlled analgesia following caesarean section. Transfer of morphine and morphine-6-glucuronide into breastmilk was low ($< 48 \text{ ng.ml}^{-1}$ and $< 1084 \text{ ng.ml}^{-1}$, respectively), and breastfed babies showed no

neurodevelopmental delays on day 3 following birth [70]. If repeated doses of morphine are used, the child should be monitored for signs of sedation and respiratory depression. This may be more likely if there are also signs of excessive adverse effects in the patient.

Codeine: half-life of 2.9 h, plasma protein binding 7% and a relative child dose 0.6%–8.1% [5]. Codeine is a prodrug, which is metabolised to the active drug morphine by the cytochrome P450 hepatic enzyme system isoenzyme CYP2D6. This enzyme has considerable genetic polymorphism. Patients who are poor metabolisers have little analgesic effect from codeine, whereas those who are ultrarapid metabolisers will have marked effects and adverse effects. There are large differences in the frequencies of variant alleles across ethnicities [71]. If a single dose of codeine is taken by a patient who is breastfeeding, there is no need to express and discard the milk. It may take 15 h for a normal metaboliser to have full clearance of a dose of codeine from the maternal plasma; however, ultrarapid metabolisers produce much higher concentrations of morphine in breastmilk, which in extreme cases may lead to severe neonatal depression and death in the child [72]. Families should be advised to observe the child for signs of excessive drowsiness and poor feeding.

It should be noted that the case report referenced above [72] has been questioned [73], with some publications based on this case retracted subsequently [74]. The original case report had been cited widely since its publication and its findings may have had a significant effect on the way that postpartum analgesic medication is prescribed, with one study from 2015 to 2016 showing that codeine was only prescribed to around 1% of patients in the postpartum period [75]. It has also influenced professional organisations and regulatory agencies; despite the concerns surrounding this case report, the US Food and Drug Administration (USFDA), European Medicines Agency and the UK Medicines and Healthcare Products Regulatory Agency (MHRA) still advise that patients who are breastfeeding should not take codeine [76–78].

Based on current international recommendations it is not possible to advocate use of codeine as a routine analgesic. There are alternatives which may be regarded as safer and more effective.

Dihydrocodeine: has oral bioavailability of 21% due to substantial first pass metabolism, with a half-life of 3.3–4.5 h [79]. It is metabolised in the liver by CYP2D6 to dihydromorphine, which has potent analgesic activity. However, the CYP2D6 pathway only represents a minor route of metabolism, with other metabolic pathways being involved. The metabolism of dihydrocodeine is not affected

by individual metabolic capacity as the analgesic effect is produced by the parent drug the analgesic effect appears to be mainly due to the parent compound [80]. Dihydrocodeine may be the preferred weak opioid for postoperative use in patients who are breastfeeding [81], because of its more predictable metabolism compared with codeine and wide experience of use after caesarean section, although the patient should be monitored for signs of significant adverse effects.

Tramadol: both parent drug and its active metabolite O-desmethyltramadol are excreted into breastmilk at low levels (relative child dose < 3%) [82]. There have been case reports of respiratory depression and death associated with the use of this medication. Despite a literature review finding no adverse events, the USFDA issued a statement in 2017 warning against taking tramadol while breastfeeding [76], citing similar potential risks to those seen with codeine ultrarapid metabolisers. The UKDILAS recommends that tramadol can be used short-term during breastfeeding with caution; however, the child should be observed for increased sleepiness, signs of respiratory depression, sedation and decreased alertness [83].

Oxycodone: has a metabolism that is similar to codeine: poor CYP2D6 metabolisers may have decreased clearance of oxycodone, and ultrarapid metabolisers higher concentrations of the more potent metabolite oxymorphone, leading to sedation. A breastfed child may receive >10% of a therapeutic dose of immediate release oxycodone [84]. For controlled release formulations, the estimated weight-adjusted child oxycodone dose is < 10% of the maternal dose [85]. Several case reports and studies have reported sedation, respiratory depression and difficulty feeding in children exposed to oxycodone via breastmilk, especially at doses > 30 mg per day [86]. As with any opioids, caution should be used when giving oxycodone as a single dose intra-operatively, and the child monitored for sedation after breastfeeding. Maternal excess effects may also feature. Repeated dosing of oxycodone should be avoided when breastfeeding.

Hydromorphone: a potent narcotic analgesic with limited data relating to breastfeeding. Hydromorphone has an oral bioavailability of 60%, plasma protein binding < 19% and inactive metabolites. However, there is a report that a 6-day-old neonate exposed to 4 mg every 4 h exhibited respiratory depression and needed to be treated with naloxone, after which it recovered [87]. This medication should be used with caution in patients who are breastfeeding.

Hydrocodone: has the active metabolite hydromorphone (see above). It is used for postnatal pain and to treat mastitis elsewhere in the world but is not used widely in the UK. It has a

plasma protein binding of 19–45%, and a relative child dose of 1.6% (range 0.2–9.0%) [88]. The use of doses > 40 mg for prolonged periods is not recommended due to possible neonatal sedation and respiratory depression.

Pethidine: has a half-life of 4 h but its active metabolite, norpethidine, has a half-life of up to 30 h. However, in neonates these figures are 13 h and 63 h, respectively [89]. Use of a pethidine PCA resulted in an accumulation of norpethidine in breastmilk resulting in drowsiness of a neonate [90]. As such, pethidine should not be used as an analgesic in patients who are breastfeeding.

Fentanyl/alfentanil: after a single dose of intravenous fentanyl, minimal amounts are detected in breastmilk [91, 92]. Bioavailability via the oral route is < 70%. When used epidurally or intravenously during labour or for a short time immediately postpartum, amounts of fentanyl ingested by the neonate are usually small and are not expected to cause any adverse effects in breastfed children [3]. No studies on more prolonged use (e.g. PCA) were found, and short-term use would appear acceptable. The child should be observed for drowsiness and the PCA discontinued as soon as possible with the mother transferred to oral analgesia. No waiting period or discarding of milk is required before resuming breastfeeding after fentanyl is used for short procedures (e.g. for endoscopy or investigative procedures) [93]. These recommendations can also be extrapolated to alfentanil [7].

Sufentanil: has a half-life of 2.7 h, protein binding of 91% and its oral bioavailability is poor. When given epidurally, sufentanil is excreted in colostrum and breastmilk in very small amounts and no problems have been observed in children [94]. However, intravenous administration of sufentanil via PCA after caesarean section may delay the onset of breastfeeding [95].

Remifentanil: there are no published data on the effect of remifentanil use on the breast-fed child. Remifentanil is rapidly metabolised by non-specific esterases. Remifentanil patient-controlled analgesia is used for labour analgesia in preference to other opioids, because of a short context sensitive half-life of < 10 min and minimal neonatal sedation [96, 97]; it can therefore be considered acceptable in patients who are breastfeeding.

Local anaesthetics

Local anaesthetics used commonly in the peri-operative period are lipid soluble, amino amide compounds (e.g. lidocaine, bupivacaine and ropivacaine) that may be secreted in small amounts in breastmilk. As local anaesthetics are used commonly during labour analgesia or obstetric anaesthesia, there has been extensive

investigation on possible neonatal effects secondary to direct placental transfer, with no evidence of harm [98]. Local anaesthetics can be used with no need to interrupt breastfeeding. It is important to follow guidance on maximal recommended doses of local anaesthesia for procedures.

Neuromuscular blocking drugs

Non-depolarising neuromuscular blocking drugs are quaternary ammonium compounds with poor lipid solubility and poor oral bioavailability. They are ionised at physiological pH and will not be present in breastmilk in significant amounts [10]. Suxamethonium is unlikely to be present in breastmilk in significant amounts as it is ionised at physiological pH and has poor oral absorption with rapid elimination from maternal circulation.

Neuromuscular blocking drug antagonists

Neostigmine: a quaternary ammonium compound with a half-life of 15–30 min. The amount transferred to breastmilk is probably too small to be harmful.

Sugammadex: no information is available on the clinical use of sugammadex during breastfeeding. As sugammadex is a large, highly polar molecule, the amount in breastmilk is likely to be very low and oral absorption by the child is unlikely [99]. Sugammadex is therefore acceptable to use during breastfeeding. However, administration of sugammadex reduces the effectiveness of hormonal contraception and patients taking oral or non-oral hormonal contraception should be given advice use alternative barrier contraceptive methods for seven days after receiving sugammadex [100].

Anti-emetics

5-HT₃ antagonists: ondansetron should be safe and presents a low risk to the breastfeeding child as levels in breastmilk are very minimal [101]. In addition, ondansetron has a licence for use in children from 6 months of age; the exposure of the child through breastmilk will be lower than when it is administered directly. There are no data available on the transfer of granisetron into human milk, but levels are likely to be low.

Cyclizine: there are no reports of levels entering breastmilk or data on which to base conclusions. This is unlikely to produce adverse effects if used short term.

Prochlorperazine: oral bioavailability is low due to high first-pass metabolism. It is compatible with short-term use during breastfeeding.

Dexamethasone: no data are available on the transfer of dexamethasone into human milk. Other corticosteroids (e.g. prednisolone) have been used

extensively during breastfeeding with no evidence of any adverse effects [102].

Metoclopramide: also used as a galactagogue, so may increase milk supply. It may be used in patients who are breastfeeding but should be avoided if lactation has stopped recently e.g. for cancer treatment.

Domperidone: when taken orally levels in milk are low due to first-pass hepatic and intestinal metabolism. It can be used as a galactagogue, so may increase milk supply; ensure that patients have access to a breast pump if there is any delay in feeding. Domperidone should be avoided if the patient has stopped lactation recently e.g. for cancer treatment.

Droperidol: may be used in children as an anti-emetic. There are no studies on passage into breastmilk. It has a plasma protein binding of 85–90% and a half-life of 2.2 h [5]. The use of a single dose use during surgery is unlikely to affect the breastfed child.

Cardiovascular medicines

Atropine: a tertiary amine, rapidly absorbed from the gastrointestinal tract and found in trace concentrations in breastmilk; may have antimuscarinic effects in the child. Lactation may be inhibited due to reduction of prolactin. Compatible with breastfeeding.

Glycopyrronium: a quaternary ammonium compound which does not readily cross the central nervous system membranes barriers. Poor bioavailability and short plasma half-life make it the preferred antimuscarinic. Compatible with breastfeeding.

Ephedrine: although excreted in breastmilk [103], limited acute intra-operative use is not likely to harm a breastfeeding child.

Phenylephrine: due to its poor oral bioavailability of 38%, phenylephrine is not likely to produce clinical effects in a breastfed child. There are theoretical concerns of it reducing milk supply based on pseudoephedrine as an oral nasal decongestant.

Antibiotics

Short courses of antibiotics are commonly used peri-operatively. There is no evidence of harmful effects in patients who are breastfeeding. For detailed information please consult LactMed [3] or sources in online Supporting Information Appendix S2.

Other medicines used in anaesthesia

Dantrolene: in one case report a mother received intravenous dantrolene over 72 h for symptoms of malignant hyperthermia [104]. Concentrations of

dantrolene in breastmilk ranged from 1.2 $\mu\text{g.l}^{-1}$ on day 2 to 0.05 $\mu\text{g.l}^{-1}$ on day 4. The relative child dose was calculated as 7.9%. The highest concentration in breastmilk was detected 36 h after the first bolus of dantrolene. Based on the elimination half-life determined in this study (9 h), the authors suggested that breastfeeding is safe 2 days after discontinuation of intravenous dantrolene administration.

Intralipid: no data on passage into breastmilk but expert sources suggest that the risk is low [105].

Discussion

Given the relative paucity of published data on the transfer of anaesthetic medicines into breastmilk, the peri-operative management of a patient who is breastfeeding is often a source of uncertainty and worry, for both healthcare professionals and the patient themselves. This guideline aims to support both patients and healthcare providers with pragmatic recommendations for the peri-operative management of the patient who is breastfeeding to ensure that breastfeeding is not interrupted unnecessarily and that the child is exposed to minimal risk. While many of the recommendations relate to specific medicines, the benefits of supporting breastfeeding during the peri-operative period through logistical interventions should not be underestimated.

The limitations of these recommendations are due largely to the very limited evidence base. Studies to date are predominantly case reports or very small retrospective studies with the potential for bias. This precluded the use of GRADE recommendations. The working party recognises that the evidence in this field continues to evolve and that new medicines will be introduced into clinical practice over time; therefore, these guidelines are only valid at the time of publication and continuously updated online information sources should be used in conjunction with this document.

This pragmatic, multidisciplinary guideline aims to facilitate the peri-operative management of patients who are breastfeeding. It is hoped that these will be of value to both clinicians and patients in determining the optimal anaesthetic management strategy to support breastfeeding and ensure minimal risk to the breastfed child.

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Supporting Information

Additional supporting information may be found online via the journal website.

Appendix S1. Example of a peri-operative breastfeeding pathway.

Appendix S2. Resources for professionals and patients.

Appendix S3. Sample patient information leaflet.

Appendix S4. Pharmacokinetic information for anaesthetics and other medicines.

Appendix S5. Pharmacokinetic terms and implications.