

# ABM Clinical Protocol #15: Analgesia and Anesthesia for the Breastfeeding Mother, Revised 2017

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*A central goal of The Academy of Breastfeeding Medicine is the development of clinical protocols, free from commercial interest or influence, for managing common medical problems that may impact breastfeeding success. These protocols serve only as guidelines for the care of breastfeeding mothers and infants and do not delineate an exclusive course of treatment or serve as standards of medical care. Variations in treatment may be appropriate according to the needs of an individual patient.*

## Background

THERE IS LITTLE RIGOROUS INFORMATION in the scientific literature about anesthesia or procedural sedation in breastfeeding mothers. Recommendations in this area typically focus on pharmacologic properties of anesthetic agents, limited studies of milk levels, and rare infant effects. In addition to medication concerns, additional perioperative considerations may impact a breastfeeding dyad's continued breastfeeding success when a mother undergoes anesthesia or sedation. Despite the lack of controlled studies regarding outcomes of breastfeeding in mothers receiving anesthesia, multiple review articles conclude that most mothers may safely breastfeed immediately following anesthesia.<sup>1-8</sup> (IV) (Quality of evidence [levels of evidence IA, IB, IIA, IIB, III, and IV] is based on levels of evidence used for the National Guidelines Clearing House and is noted in parentheses.)<sup>9</sup> Most recommendations for breastfeeding in the perioperative setting come from expert opinion rather than from extensive studies or trials. Up-to-date information on specific medications can be found on the United States National Library of Medicine website LactMed,<sup>10</sup> with additional resources listed in Table 1.

Medication guidelines discussed in this protocol may be extended to mothers in the immediate postpartum period; however, specific considerations for this population are detailed in ABM Protocol #28, Peripartum Anesthesia and Analgesia for the Breastfeeding Mother. The focus of this protocol is on anesthesia and analgesia for breastfeeding mothers outside the postpartum period.

## Recommendations

### General principles

**Medications.** The implications of medications used in breastfeeding mothers depend on numerous factors, includ-

ing the amount of medication that passes into breast milk, the oral absorption of medication, the gestational and postpartum age of the child, and the potential for adverse effects on the breastfeeding infant.<sup>11</sup> Anesthetic agents cause little or no effects for older infants, but could potentially cause problems in neonates, particularly those who are preterm and/or suffer from preexisting apnea.

- Mothers with healthy term or older infants can generally resume breastfeeding as soon as they are awake, stable, and alert.<sup>1-8</sup> (IV) Resumption of normal mentation is a hallmark that medications have redistributed from the plasma compartment (and thus generally the milk compartment) and entered adipose and muscle tissue where they are slowly released.
- Infants at risk for apnea, hypotension, or hypotonia may benefit from a brief interruption of breastfeeding (6–12 hours) after maternal anesthesia. In this situation, mothers can express and store her milk in small amounts to be used when the infant is older, or it can be mixed with fresh milk containing no medications to dilute the milk with medications present.
- The most concerning class of medications used for anesthesia and analgesia in breastfeeding mothers is opioids, as these medications transfer into breast milk and may cause infant sedation or apnea. Judicious use of opioids for short periods is likely to be safe for most breastfeeding mothers and infants.<sup>6,12-14</sup> (IV)

**Brief procedures.** Mothers who have undergone dental extractions or other short procedures requiring the use of single doses of medication for sedation and analgesia can breastfeed as soon as they are awake and stable. Although shorter-acting agents such as fentanyl and midazolam may be

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TABLE 1. RESOURCES OF INFORMATION ABOUT MEDICATIONS

<i>Resource</i>	<i>Sponsor</i>	<i>Website and contact information</i>
LactMed E-Lactancia	U.S. National Library of Medicine Association for Promotion and Cultural and Scientific Research of Breastfeeding, Spain	<a href="https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm">https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm</a> <a href="http://www.e-lactancia.org">www.e-lactancia.org</a>
Infant Risk Center	Texas Tech University Health Sciences Center, TX	<a href="http://www.infantrisk.org">www.infantrisk.org</a> and +1 806-352-2519
Breastfeeding and Human Lactation Study Center	University of Rochester, NY	+1 585-275-0088
Mother to Baby	Organization of Teratology Information Specialists	<a href="https://mothertobaby.org">https://mothertobaby.org</a> and +1 866-626-6847
Motherisk	Hospital for Sick Children, Toronto Canada	<a href="http://www.motherisk.org">www.motherisk.org</a> and +1 877-439-2744

preferred, single doses of meperidine/pethidine or diazepam are unlikely to affect the breastfeeding infant.<sup>15</sup> (III) Local anesthetics given by injection or topical application are considered safe for breastfeeding mothers.<sup>2,3</sup> (IV)

**Regional anesthesia.** Regional anesthesia, including spinal, epidural, or peripheral nerve block, should be considered whenever possible, whether for intraoperative anesthesia or postoperative analgesia.<sup>3</sup> (IV) Regional anesthesia reduces the need for intraoperative medications and may also decrease the amount of pain medication needed postoperatively. In addition, the mother will be more awake and alert in the immediate postoperative period and will therefore be able to resume breastfeeding sooner.

**Perioperative considerations.** Breastfeeding mothers undergoing anesthesia or sedation should be scheduled as the first case of the day when possible to allow for minimal fasting times. Mothers should breastfeed or express milk immediately before surgery; a pump or help with hand expression must be available in the recovery room after surgery if infants are not allowed in this area. Hospital policies and procedures vary, but preventing engorgement and protecting a mother's milk supply and her confidence with breastfeeding should be prioritized. A more comprehensive perioperative breastfeeding plan is included at the end of this protocol.

### Information About Specific Agents Used for Anesthesia and Analgesia

#### Local anesthetics

Local anesthetics are given during a variety of procedures and are used in varying modalities. Medications may be used in spinal or epidural anesthesia, injected as a peripheral nerve block, infiltrated into the surgical field, or used as a topical application. Use of these medications typically helps minimize the need for additional systemic medications, and their use should be encouraged in breastfeeding mothers to decrease the need for opioids. Local anesthetics such as lidocaine, bupivacaine, and ropivacaine can be safely used in breastfeeding mothers. These and other local anesthetics are poorly absorbed orally and the large polarized molecules do not easily transfer into milk.<sup>2,3</sup> (IV)

#### Anesthetic agents

- Drugs used for anesthetic induction such as propofol, midazolam, etomidate, or thiopental enter the milk compartment only minimally, as they have very brief plasma distribution phases (only minutes), and hence their transport to milk is low to nil.<sup>16–19</sup> (III)
- Little or nothing has been reported about the use of anesthetic gases in breastfeeding mothers. However, they too have brief plasma distribution phases, and milk levels are likely to be nil. A series of case reports suggests that xenon maintenance after propofol induction allows for breastfeeding immediately after surgery.<sup>20</sup> (III)
- A study of low-dose ketamine for pain treatment after cesarean section has demonstrated no effects in the newborn, namely on the duration on breastfeeding.<sup>21</sup> (III) There is no information available on its use at anesthetic doses in breastfeeding mothers; it may be prudent to avoid large doses of this medication in breastfeeding mothers and monitor exposed infants afterward.<sup>22</sup> (IV)
- Dexmedetomidine is an alpha-2 agonist that acts centrally to reduce sympathetic outflow, producing sedation and analgesia. It has low oral availability and is usually administered through the intravenous route. A single study of milk levels following infusion used during cesarean delivery determined that a breastfeeding infant would receive a relative infant dose (RID) of 0.04–0.098%.<sup>23</sup> (III)
- The United States Federal Drug Administration (FDA) in 2016 issued a Drug Safety Communication warning of the risk of using general anesthesia and some sedative medications in young children and pregnant women.<sup>24</sup> This advisory focused on the risk of possible effects on brain development when these agents are used repeatedly or for more than 3 hours. Note that there is no evidence to suggest a similar concern over use of anesthetic agents and medications in a breastfeeding mother.
- Neuromuscular blocking agents are safe for the breastfeeding infant, as they have low lipid solubility and are largely distributed in the extracellular fluid volume.<sup>3</sup> Although there are no data on the pharmacokinetics of these drugs in breast milk, based on their

physical characteristics and their poor oral availability, they are considered safe for use in the breastfeeding mother. (IV)

- Reversal agents and anticholinergics used together to act against neuromuscular blockers appear to be generally safe for use, although there are no data on breast milk pharmacokinetics related to pyridostigmine or edrophonium. The anticholinesterase neostigmine could not be found in the breast milk of a mother with myasthenia whose infant appeared to have abdominal cramps after administration of the drug to the mother.<sup>25</sup> (III) Pyridostigmine was found in a very small amount in breast milk of mothers receiving the drug for treatment of myasthenia gravis, and was considered safe for the infant.<sup>26</sup> (III) Sugammadex is known to be excreted in small concentrations in breast milk in animal studies, although there are no studies in humans.<sup>27–29</sup> (III) Oral absorption of cyclodextrins in general is low and no effect on the breastfeeding child is anticipated. Of the anticholinergic agents, atropine is found in trace amounts in breast milk. Glycopyrrolate is not expected to be found in breast milk and is poorly absorbed through the gastrointestinal tract.<sup>5</sup>
- Antiemetics are used commonly in the perioperative period, and most of these medications are considered safe during breastfeeding. Ondansetron, dexamethasone, and metoclopramide may be preferred because of their lack of sedating side effects.<sup>3</sup> (IV) Prochlorperazine, promethazine, and scopolamine are likely safe, but may lead to maternal sedation; promethazine and scopolamine may also adversely affect milk supply if given repeatedly.<sup>30–32</sup> (III)

#### Analgesics

Opioid analgesics. Opioids are frequently used during surgery as part of a balanced anesthetic technique, and they may be continued postoperatively for pain. All opioids transfer into breast milk in varying amounts, and differences in breast milk concentration along with variation in oral availability make certain types of these medications more or less safe for a breastfeeding mother. In general, opioids of any type should be used with caution and for the shortest reasonable course in a breastfeeding mother.<sup>12,13</sup>

Opioids are given intravenously during surgery and may be administered as oral pain medications once mothers are tolerating oral intake postoperatively. Two specific medications used frequently during the perioperative period, morphine and hydromorphone, may be given through the intravenous or oral route. Because their oral availability is rather poor, the American Academy of Pediatrics (AAP) has identified them as possible safer choices for breastfeeding mothers over other opioids.<sup>11</sup> Intravenous opioids used during surgery are generally considered safe for immediate resumption of breastfeeding as soon as mothers are awake in the recovery room.

#### Intravenous medications

- Morphine. Morphine is still considered a reasonable option for breastfeeding mothers due to its limited transport to milk and its poor oral availability.<sup>11,33,34</sup> (III) It may be given through the intravenous or oral route.

- Fentanyl. Fentanyl levels in breast milk have been studied and are extremely low after 2 hours and generally below the limit of detection.<sup>35,36</sup> (III) Fentanyl also demonstrates very low oral availability and it is unlikely to cause any appreciable effects by its low levels in breast milk. Its use is typically restricted in the hospital to the operating room, emergency department, or critical care areas because of its potency and rapid onset of action.
- Hydromorphone. There are two reports available regarding hydromorphone and breastfeeding, neither of which evaluates its use through the intravenous route. One study evaluating a single intranasal dose of hydromorphone 2 mg found that infants would receive an RID of 0.67%.<sup>37</sup> A more recent single case report discusses the course of a 6-day-old infant who presented to the emergency room with sedation and poor feeding, and who required naloxone after episodes of apnea and bradycardia. Mother had been receiving hydromorphone 4 mg orally every 4 hours around the clock since her cesarean delivery 6 days before.<sup>38</sup> (III)
- Remifentanyl. Although there are no published data on remifentanyl, this esterase-metabolized opioid has a brief half-life even in infants (<10 minutes) and has been documented to produce no fetal sedation even in utero. Although its duration of action is limited, it could be used safely and indeed may be ideal in breastfeeding mothers for short painful procedures.
- Sufentanil. Sufentanil transfer into milk has not been published, but its safety profile is likely similar to fentanyl.<sup>36</sup> This opioid is most commonly used during general anesthesia, or as an additive in epidural anesthesia and analgesia.
- Meperidine. The transfer of meperidine/pethidine into breast milk is low (1.7–3.5% of maternal weight-adjusted dose). However, meperidine/pethidine and its metabolite (normeperidine) are consistently associated with dose-related neonatal sedation. Transfer into milk and neonatal sedation have been documented for even up to 36 hours after a single dose.<sup>33</sup> (III) Infants of mothers who have been exposed to repeated doses of meperidine/pethidine should be closely monitored for sedation, cyanosis, bradycardia, and possibly seizures, and the AAP recommends against its use in breastfeeding mothers.<sup>11</sup> (IV)
- Nalbuphine and butorphanol. Nalbuphine and butorphanol are partial opioid agonists, with nalbuphine administered intravenously and butorphanol usually through the nasal route. Levels of both these medications in breast milk are very low, although they are not typically used as part of perioperative analgesic regimens. However, the AAP has recommended butorphanol as a reasonable choice if opioid analgesics are required for a breastfeeding mother.<sup>11</sup> (IV)

*Oral medications* given for postoperative pain. All oral opioids used for postoperative pain should be limited to the shortest reasonable course, and infants should be watched closely for sedation when mothers require these medications. Analgesic effects from codeine and tramadol derive from metabolites that are dependent upon the CYP2D6 activity. Interindividual variation in the CYP2D6 activity may cause

ultrapid metabolizers to receive excessively high amounts of active metabolites, leading to potential for sedation or respiratory depression from typical dosing. Although hydrocodone and oxycodone also partially undergo metabolism by CYP2D6 to more potent metabolites, the parent drug also exerts an analgesic effect and there is less concern over the clinical effects of variation in metabolism.

- **Hydrocodone.** Hydrocodone has been used frequently in breastfeeding mothers. Occasional cases of neonatal sedation have been documented, but these are rare and generally dose related.<sup>39,40</sup> Doses in breastfeeding mothers should be limited to 30 mg per day.<sup>40</sup> (III)
- **Oxycodone.** Oxycodone levels in milk have been studied, with a range of 5–226 µg/L (RID up to 8%).<sup>41</sup> One retrospective study showed that one in five breastfed infants with mothers taking oxycodone experienced central nervous system depression. The strong concordance between maternal and infant symptoms may be used to identify infants at higher risk. It is important to monitor these infants carefully for drowsiness.<sup>42</sup> (III) LactMed recommends a maximum total daily dose of 30 mg,<sup>43</sup> and the AAP advises against the use of the medication in breastfeeding mothers.<sup>11</sup> (IV)
- **Codeine.** A report of a neonatal death following the maternal use of codeine suggests that the use of codeine in breastfeeding mothers should be limited.<sup>44</sup> Although rare, rapid metabolizers of codeine exist, and levels of morphine following the use of codeine may be unexpectedly and significantly elevated, thus putting a breastfeeding infant at risk. The FDA in 2017 issued an advisory against the use of the medication in breastfeeding mothers in the United States<sup>45</sup>; (IV) it continues to be prescribed in other areas of the world, but other medications are preferred when available.<sup>12,46</sup>
- **Tramadol.** Tramadol is a weak opioid with an additional activity at central norepinephrine and serotonin receptors. Like codeine, it needs to be metabolized by CYP2D6 to an active metabolite to exert its analgesic effects. With an RID of <1% of the active metabolite and no reported effects in breastfed infants, it has previously been considered a safe choice for breastfeeding mothers.<sup>47–49</sup> However, the FDA has advised against the use of this medication in breastfeeding mothers in the United States.<sup>45</sup> (IV)

Regardless of the opioid chosen, the dose needs to be carefully considered. Virtually any opioid may be used transiently, but infants should be monitored for sedation,<sup>13</sup> especially when these medications are used for more than 4 days.<sup>6</sup> Note that mothers on chronic opioid therapy may be using exceedingly high doses of hydrocodone, oxycodone, methadone, and other opioid analgesics that were started before or during pregnancy. Safety of breastfeeding for these patients should be considered on an individual basis.

**Nonsteroidal anti-inflammatory drug analgesics.** Use of nonsteroidal anti-inflammatory drugs (NSAIDs) alone or in combination with opioids after surgery can improve pain control due to their anti-inflammatory properties. NSAIDs are

generally safe for breastfeeding and can help minimize the total dose of opioid needed to control pain.<sup>50,51</sup> (III) In addition, due to their low lipid solubility and high protein binding, NSAIDs have limited transfer into breast milk (milk to plasma ratios <1).<sup>52</sup> While transfer of NSAIDs to breast milk is low, this class of medications should be avoided in mothers with infants who have ductal-dependent cardiac lesions.<sup>11</sup>

- **Ibuprofen.** Ibuprofen is considered an ideal, moderately effective analgesic. Its transfer to milk is low to nil.<sup>53</sup> (III)
- **Ketorolac.** Ketorolac is a potent analgesic in breastfeeding mothers and increasingly popular when used postoperatively. Its primary benefit is excellent analgesia, with no sedative properties. In addition, the transfer of ketorolac into milk is extremely low.<sup>54</sup> However, its use in postsurgical patients with hemorrhage may be risky as it inhibits platelet function, although this is somewhat controversial. It should not be used in patients with a history of gastritis, aspirin allergy, or renal insufficiency. If there is no risk of hemorrhage, it carries few complications for breastfeeding mothers and their infants. (III)
- **Celecoxib.** Celecoxib transfer into milk is extraordinarily low (<0.3% of the weight-adjusted maternal dose).<sup>55</sup> Its short-term use is safe in breastfeeding mothers. (III)
- **Naproxen.** Naproxen transfer into milk is low, but gastrointestinal disturbances have been reported in some infants following prolonged therapy. Short-term use (1 week) is likely to be safe.<sup>56</sup> (III)

#### Other analgesics.

- **Acetaminophen/paracetamol.** Acetaminophen/paracetamol has been used for postoperative analgesia as well as maternal fever. Transfer into the milk is low and appears to be less than the usual dosage given to infants. One study showed that infants would only receive a maximum of 2% of the maternal weight-adjusted dose.<sup>57</sup> Hepatotoxicity is thought to be less common in newborns given the low levels of specific cytochrome P-450 enzymes that convert the drug to its toxic metabolites.<sup>11</sup>
- **Gabapentin.** Gabapentin is one of the first-line drugs for treatment of neuropathic pain and is also used as part of a multimodal analgesia regimen in the perioperative period. Limited studies indicate low serum concentrations in infants of mothers taking up to 2 g a day.<sup>58–60</sup> (III) It is suggested to monitor the infant for weight gain and drowsiness. Gabapentin is likely safe, especially in single or short-term doses.<sup>61</sup>
- **Pregabalin.** Pregabalin is also used in the treatment of neuropathic and postoperative pain. There is limited information about the passage of this medication into the breast milk, but the RID is 7–8%.<sup>62</sup> (III) LactMed recommends monitoring infants for drowsiness and suggests using possible alternative medications if available.<sup>63</sup>

#### Perioperative Breastfeeding Plan

##### *Preoperatively*

- Consider postponing elective procedures until child is older and milk supply and breastfeeding relationship are well established.

- Breastfeeding mothers should be encouraged to express milk ahead of the surgical date, to have milk available for their child in case of extended separation at the time of surgery.
- A responsible adult other than the mother should be identified to care for and observe the child postoperatively if opioids are required for postoperative pain.
- Breastfeeding mothers should be scheduled for first case or early in the day to minimize fasting times, and may use a 2-hour window for clear fluids if there are no risk factors for aspiration.
- Mothers should breastfeed or express milk just before the start of the procedure.

#### Intraoperatively

- Consider regional anesthetic technique to minimize use of systemic sedative medications.
- Aggressive postoperative nausea and vomiting prophylaxis should be utilized.
- Fluid management strategies should focus on maintaining euvoolemia without overhydration that may cause edema.
- Employ multimodal pain management strategies to minimize need for opioids.

#### Postoperatively

- Mothers with term, healthy children may breastfeed as soon as they are awake in the recovery room.
- If children are not allowed in the recovery room, a breast pump or assistance with hand expression must be available for mothers immediately after surgery.
- For vulnerable infants who should be protected by a brief interruption from breastfeeding postoperatively, milk should be expressed as soon as the mother is awake. The milk does not necessarily need to be discarded. It can be frozen for use when the child is at lower risk in the future. Alternatively, the milk can be used diluted with other breast milk not containing anesthetic (expressed either before or 1 day after the procedure).
  - The mother should be encouraged to express during the interruption from breastfeeding, at least as often as she would normally breastfeed to maintain supply (around every 2–4 hours depending on child's age).
- Opioids should be used judiciously, at the lowest dose and for the shortest period of time that provides adequate analgesia. The breastfed child should be cared for and observed by an adult other than the mother, when opioids are used.

#### Recommendations for Future Research

More study of specific breastfeeding outcomes after surgical anesthesia in breastfeeding mothers is needed. Common-sense recommendations to avoid prolonged fasting times in breastfeeding mothers and encourage frequent expressing or breastfeeding in the immediate perioperative period have not been rigorously explored in controlled settings. The effect of fluid management strategies and hemodynamic variation and need for vasoactive medications on milk supply should be investigated. In addition, breastfeeding-friendly policies in hospitals and outpatient surgery centers should be

prioritized and studied, and may be reasonable options for quality improvement processes.

As is the case for many medications used during breastfeeding, more information on medication transfer into breast milk and infant effects is urgently needed. Case reports of negative outcomes may help to delineate where significant concern is warranted, but reports of single dyads or small series with apparently uneventful breastfeeding courses do not necessarily assure safety. More study in particular is required of the special needs of premature and unstable infants, including how their ability to clear maternal anesthetic and analgesic drugs may differ from healthy, term newborns. In addition, thoughtful investigation into the implications of maternal anesthesia on neurobehavioral outcomes in breastfeeding infants may help allay concerns over this theoretical small risk.<sup>64</sup>

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ABM protocols expire 5 years from the date of publication. Content of this protocol is up-to-date at the time of publication. Evidence based revisions are made within 5 years or sooner if there are significant changes in the evidence.

The 2012 edition of this protocol was authored by Anne Montgomery and Thomas W. Hale.

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