ABM Clinical Protocol #15: Analgesia and Anesthesia for the Breastfeeding Mother, Revised 2012

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A central goal of The Academy of Breastfeeding Medicine is the development of clinical protocols 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

LABOR, BIRTH, AND BREASTFEEDING initiation compose a normal, continuous process. Oxytocin, endorphins, and adrenaline produced in response to the normal pain of labor may play significant roles in maternal and neonatal responses to birth and early breastfeeding.[1] Use of pharmacologic agents for pain relief in labor and postpartum may improve outcomes by relieving suffering during labor and allowing mothers to recover from birth, especially cesarean birth, with minimal interference from pain. However, these methods may also affect the course of labor and the neurobehavioral state of the neonate and have adverse effects on breastfeeding initiation. Unfortunately, the literature in this area has not addressed this issue as a whole, integrated process.

In the setting of labor and childbirth, we will use the following definitions throughout this protocol:

- Analgesia: modification of painful stimuli so that they, while still experienced, are not painful.
- Anesthesia: total loss of sensation.
- Epidural analgesia: use of epidural anesthetics and opioids to reduce the painful experience of labor.
- Epidural anesthesia: use of epidural anesthetics to eliminate sensation, as for cesarean section.

Very few studies directly address the impact of various approaches to labor pain management on breastfeeding outcomes. Although there are some older trials in which women were randomized to analgesia versus no analgesia in labor, these studies are limited by both crossover and confounding. At present, such trials would not be considered ethical, so we will not anticipate randomized controlled trials comparing breastfeeding outcomes for analgesia versus no analgesia in labor. We do have a few recent trials looking at breastfeeding outcomes with different techniques and dosages for epidural analgesia; these trials used a case-control design to compare patients who received an epidural with those who had no analgesia. The technology of epidural anesthesia, in particular, is evolving quickly, so studies that are even a few years old may not reflect current practices. This protocol will ex-amine the evidence currently available and make recommendations for prudent practice.

There is even less information in the scientific literature about anesthesia for surgery in breastfeeding mothers. Recommendations in this area focus on pharmacologic properties of anesthetic agents and limited studies of milk levels and infant effects.

Quality of evidence for each recommendation, as defined by the U.S. Preventive Task Force, is noted in parentheses (I, II-1, II-2, and III).

Analgesia and Anesthesia for Labor

1. Maternity care providers should initiate an informed consent discussion for pain management in labor during the prenatal period, well before the onset of labor. Risk discussion should include what is known about the effects of various modalities on the progress of labor, risk of instrumented and cesarean delivery, effects on the newborn, and possible breastfeeding effects. (III)

2. Unmedicated, spontaneous vaginal birth with immediate, uninterrupted skin-to-skin contact leads to the highest likelihood of baby-led breastfeeding initiation.[2,3] Longer labors, instrumented deliveries, cesarean section, and separation of mother and infant after birth may lead to higher risk of difficulty with breastfeeding initiation.[4–6] Labor pain management strategies may affect these birth outcomes and secondarily affect breastfeeding initiation in addition to any direct effects of the medications themselves.[7] (II-1; II-2)

3. Women have differing levels of pain tolerance. Labor pain may exceed a woman's ability to cope or be magnified by fear and anxiety. Suffering in labor may lead to dysfunctional labors, poorer psychologic outcomes, and increased risk of postpartum depression, all of which may have a negative effect on breastfeeding.[8,9] Severe maternal physiologic stress in labor also causes physiologic stress for babies, which may affect their readiness to breastfeed at birth.[10] (III)

4. Continuous support in labor, ideally by a trained doula, reduces the need for pharmacologic pain management in labor and decreases the rates of instrumented delivery and cesarean section. An earlier meta-analysis suggested that doulas also improve breastfeeding outcomes both in the immediate postpartum period and several weeks after birth, but an update to this meta-analysis did not find statistical differences in breastfeeding outcomes.[11] (I)

5. Nonpharmacologic methods for pain management in labor such as hypnosis and acupuncture have been found effective in reducing labor pain.[12] (I) Other methods that are used in some but not all countries such as psychoprophylaxis (e.g., Lamaze), intradermal and/or subcutaneous water injections for back pain, etc., appear to be safe and have no known adverse neonatal effects. These methods may reduce the need for pharmacologic interventions. Additional study of breastfeeding outcomes is needed for these modalities.[13]

6. Evidence suggests that breastfeeding success is affected by the behavior of the newborn. Depressed or delayed suckling, which can be caused by medications given to mothers, can lead to delayed or suppressed lactogenesis and risk of excess infant weight loss.[14,15] (II-2)

7. Intrapartum intravenous fluids are often given in larger quantities when pharmacologic pain relief methods such as epidural analgesia or anesthesia are used. These fluids can potentially lead to maternal engorgement, affect birth weight and newborn weight loss,[16] and cause neonatal hyperglycemia and rebound hyperinsulinemia. (II-2)

8. Parenteral (intravenous, intramuscular) opiates used for labor may block the newborn's normal reflexes to suckle at the breast within the first hour after birth.[17,18]

   a. If opiates are used, shorter-acting opiates such as fentanyl or sufentanil are preferred. Remifentanil is potent and has rapid onset and offset but can be associated with a high incidence of maternal apnea, requiring increased monitoring. Its transfer in utero to the fetus is minimal.

   b. Meperidine/pethidine/morphine should generally not be used except in small doses less than 1 hour or more than 4 hours prior to anticipated delivery because of greater incidence and duration of respiratory depression, cyanosis, and bradycardia in neonates.

   c. Nalbuphine, butorphanol, and pentazocine may be used for patients with certain opioid allergies or at increased risk of difficult airway management or respiratory depression. These medications may, however, interfere with fetal heart rate monitoring interpretation. Observe the mother and infant for psychotomimetic reactions (3%).

   d. Both the dosing (especially multiple doses) and the timing of parenteral analgesics may lead to greater neonatal effects. For example, fentanyl administration within 1 hour of delivery or meperidine/pethidine administration between 1 and 4 hours prior to delivery is associated with more profound neonatal effects.[19]

   e. When a mother has received intravenous or intramuscular narcotics for labor, mother and infant should be given more skin-to-skin time to encourage early breastfeeding.[18] (III)

9. Although many studies have shown that epidural analgesia affects infant behavior,[20] the effect of epidural analgesia on breastfeeding continues to be controversial. Older case-control and cohort studies suggested that breastfeeding rates were lower after epidural analgesia, and another observational study found decreased breastfeeding rates with higher doses of fentanyl.[21] However, because these studies were not randomized, they also raise the question as to whether women who choose epidural analgesia may be less likely to continue breastfeeding.[22] Hormonally, epidural analgesia has been shown to decrease oxytocin levels during labor and to affect oxytocin and prolactin levels on Day 2 postpartum.[23] Practically, use of epidural analgesia may affect labor outcomes such as an increased use of instrumented delivery and postpartum separation of mother and infant related to birth outcomes that may secondarily affect breastfeeding.

Several recent trials have shown no differences in breastfeeding rates in women with epidural analgesia. These trials randomized women to different techniques of epidural analgesia but used a case-control design to compare them with women who did not have any analgesia for labor. One trial done in New York randomized 177 multiparas who had previously breastfed to different doses of epidural analgesia and compared them to a selected group of women with no analgesia. All of these women had vaginal births. There were no differences in breastfeeding rates except in the group who received >150 mcg of fentanyl.[24] A larger trial done in the United Kingdom randomized 1,054 primiparas to different techniques of epidural analgesia and compared them to a selected group. These groups differed in that the epidural groups included more women with cesarean and instrumented deliveries. There was no statistically significant difference in breastfeeding initiation or continuation in these groups except that the "control" women who had received intravenous pethidine had lower rates of breastfeeding initiation.[25] Another well-designed prospective cohort study also showed no differences in breastfeeding rates after epidural analgesia in a population with high breastfeeding rates and good breastfeeding support.[26]

In summary, epidural analgesia has subtle effects on infant behavior. Women who choose epidural analgesia may differ from women who do not with respect to breastfeeding plans. Higher or repeated doses of medication in the epidural space may make a difference. Like many other aspects of breastfeeding, epidural analgesia likely has almost no effect on women who are determined to breastfeed and have good support but may be one more subtle challenge to women whose intention to breastfeed is more vulnerable.

   a. If epidural analgesia is chosen, methods that minimize the dose of medication and minimize motor block should be used. Doses of fentanyl >150 μg should be avoided.[23] Longer durations and repeated administration of epidural analgesia should be

avoided if possible, to minimize effect on labor outcomes that may secondarily affect breastfeeding. Combined spinal-epidural analgesia and patient-controlled epidural analgesia may be preferable.[27] (I; II-2)

    b. When epidural analgesia has been used for labor, particular care to provide mothers with good breastfeeding support and close follow-up after postpartum hospitalization should be taken. (II-2)

10. There are minimal data concerning the effects on the neonate of other labor anesthesia, including inhaled nitrous oxide, paracervical block, pudendal block, and local perineal anesthesia.[28] These modalities do not usually expose the infant to significant quantities of medication. In some situations, these may serve as alternatives to intravenous narcotics or epidural analgesia for labor. Their use, however, is limited by several factors. These include lack of efficacy, technical difficulties in performing, and a high rate of complications.

Anesthesia for Cesarean Section

1. Regional anesthesia (epidural or intrathecal/spinal) is preferred over general anesthesia. Separation of a mother and her infant should be minimized, and breastfeeding should be initiated as soon as feasible.[29] In fact, the infant may go to the breast in the operating room during abdominal closure with assistance to support the infant on the mother's chest. If breastfeeding is initiated in the recovery room, there is the added advantage that the incision is often still under the influence of the anesthetic. (III)

2. A mother who has had general anesthesia may breastfeed postoperatively as soon as she is alert enough to hold the infant and is not overly sedated. (III)

Postpartum Analgesia

1. Non-opioid analgesics should generally be the first choice for pain management in breastfeeding postpartum women, as they do not impact maternal or infant alertness. (III)

    a. Acetaminophen/paracetamol and ibuprofen are safe and effective for analgesia in postpartum mothers.

    b. Ketorolac is commonly used for postpartum analgesia, especially after cesarean section, despite a Food and Drug Administration black box warning (in the United States) against the use of this medicine for breastfeeding women.[30] Milk levels after oral administration are quite low, but levels have not been measured after parenteral administration.

    c. Diclofenac suppositories are available in some countries and commonly used for postpartum analgesia. Milk levels are extremely low.

    d. Cyclooxygenase-2 inhibitors such as celecoxib may have some theoretical advantages if maternal bleeding is a concern; this must be balanced with higher cost and possible cardiovascular risks, which should be minimal with short-term use in healthy young women.[19]

2. Both pain and opioid analgesia can have a negative impact on breastfeeding outcomes; thus mothers should be encouraged to control their pain with the lowest medication dose that is fully effective. Opioid analgesia postpartum may affect babies' alertness and suckling vigor. However, when maternal pain is adequately treated, breastfeeding outcomes improve.[31,32] Mothers should be encouraged to adequately control their pain, especially after cesarean birth or severe perineal trauma requiring repair. (II-2)

    a. Parenteral medications (may be intravenous or intramuscular)

      i. Meperidine/pethidine should be avoided due to reported neonatal sedation when given to breastfeeding mothers postpartum,[33] in addition to the concerns of cyanosis, bradycardia, and the risk of apnea that have been noted with intrapartum administration.[34,35]

      ii. The administration of moderate to low doses of intravenous or intramuscular morphine is preferred to meperidine/pethidine as passage to milk and oral bioavailability are least with this agent.[33,36]

      iii. When patient-controlled intravenous analgesia (PCA) is chosen after cesarean section, morphine or fentanyl is preferred over meperidine/pethidine.[32,37]

      iv. Levels of butorphanol in human milk have been reported with approximately 0.5% of the weight-adjusted maternal dose* transferred into human milk. These appear minimal and probably are of no concern to a breastfeeding neonate in the first week postpartum. The use of butorphanol during labor has been reported to produce sinusoidal fetal heart rate patterns and irritability in newborns.

      v. Levels of nalbuphine in human milk are quite low. In one study the levels of nalbuphine in milk average only 42 μg/L with an estimated weight-adjusted relative infant dose (RID) of 0.59%.[38]

      vi. Hydromorphone (approximately seven to 11 times as potent as morphine) is sometimes used for extreme pain in a PCA, intramuscularly, intravenously, or orally. Following a 2 mg intranasal dose, levels in milk were quite low with a weight-adjusted RID of about 0.67%.[39] This correlates with about 2.2 μg/day via milk. This dose is probably too low to affect a breastfeeding infant, but this is a strong opioid, and some caution is recommended.

    b. Oral medications

      i. Hydrocodone has been used frequently in breastfeeding mothers worldwide. Less than 3.7% of the weight-adjusted maternal dose (RID) reaches the infant per day. Higher doses (10 mg of hydrocodone) and/or more frequent administration may lead to neonatal sedation and should be used with great caution.

      ii. Recent cases have raised concern about the use of codeine. Some mothers may rapidly metabolize

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*An important concept when discussing the risk of maternal medications to the breastfeeding infant is that of the relative infant dose. It is imperative to understand that this is a value that is calculated by dividing the infant's dose from the milk in mg/kg/day by the mother's dose in mg/kg/day. In this manner of calculation, a weight-normalized dose is determined that the baby may receive, which is more accurate than when one does not take the weight of the mother and the baby into account.

codeine to morphine, which can lead to toxic levels of morphine in the infant. Codeine should be used with caution, although it is probably safe in the majority of breastfeeding mothers.[40]

   iii. Several studies now suggest that oxycodone may be useful in some patients postpartum. Less than 3.5% of the weight-adjusted maternal dose (RID) transfers into human milk. Prolonged and frequent administration may lead to neonatal sedation.[41] There is also the rare mother who is an ultrarapid metabolizer, whose babies are at higher risk for central nervous system depression [see Analgesics 1(i) below].

   iv. Several recent studies of buprenorphine suggest that approximately 1.9% of the weight-adjusted maternal dose is transferred to the infant daily. Buprenorphine has a long half-life and should be used with some caution in infants who have not been previously exposed to the drug. Mothers treated continually for addiction may continue to breastfeed using this medication as long as the infant is tolerant to the current dose.[42]

  c. Epidural/spinal medications

   i. Single-dose opioid medications (e.g., neuraxial morphine) should have minimal effects on breast-feeding because of negligible maternal plasma levels achieved. Extremely low doses of morphine are effective.

   ii. Continuous post-cesarean epidural infusion may be an effective form of pain relief that minimizes opioid exposure. A randomized study that compared spinal anesthesia for elective cesarean with or without the use of postoperative extradural continuous bupivacaine found that the continuous group had lower pain scores and a higher volume of milk fed to their infants.[31]

Anesthesia/Sedation for Surgery in Breastfeeding Mothers

1. The implications of drugs used in anesthesia in post-partum mothers depend on numerous factors, including the age of the infant, the stability of the infant, the length of lactation, and the ability of the infant to clear small quantities of anesthetic medications.[43] Anesthetic agents will have little or no effect on older infants but could potentially cause problems in newborn infants, particularly those who are premature or suffer from apnea. (III)

2. Mothers with normal term or older infants can generally resume breastfeeding as soon as they are awake, stable, and alert. Resumption of normal mentation is a hallmark that these medications have redistributed from the plasma compartment (and thus generally the milk compartment) and entered adipose and muscle tissue where they are slowly released. The exception could be a drug that is highly lipid soluble, in which breast tissue may function as a fat compartment, acting as a drug reservoir. For women who undergo post-partum tubal ligation, interruption of breastfeeding is not indicated as the volume of colostrum is small; hence the dose to the infant is low as well.[44] In addition, the levels of medication in the maternal plasma and milk

are low once mothers resume normal mentation. For maternal safety, regional anesthesia is recommended for this procedure in preference to general anesthetic. (III)

3. Mothers who have undergone dental extractions or other 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 preferred, single doses of meperidine/pethidine or dia-zepam are unlikely to affect the breastfeeding infant.[42] (III)

4. Mothers who have undergone plastic surgery, such as liposuction, where large doses of local anesthetics (lidocaine/xylocaine or lignocaine) have been used should probably pump and discard their milk for 12 hours prior to resuming breastfeeding. (III)

5. The maternal dose and the ability of the infant to clear small amounts of medications that can cause cardiore-spiratory effects is of primary concern before returning to breastfeeding. Infants subject to apnea, hypotension, or hypotonia should probably be protected by a few more hours of interruption from breastfeeding (12–24 hours) prior to resuming nursing. (III)

Information About Specific Agents Used for Anesthesia and Analgesia

Anesthetic agents

1. Drugs used for anesthetic induction such as propofol, midazolam, etomidate, or thiopental enter the milk compartment only minimally, as they have extraordinarily brief plasma distribution phases (only minutes), and hence their transport to milk is low to nil.[45–48]

2. 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 nil. A recent series of case reports suggests that xenon maintenance after propofol induction allows for breastfeeding immediately after surgery.[49]

3. The use of ketamine in breastfeeding mothers is unreported. Following the use of ketamine, many adult patients may exhibit dissociative anesthetic effects. This is often suppressed with the addition of midazolam or other benzodiazepines. The emergent reactions are apparently age-dependent and appear to occur more frequently in adults (30–50%) and less frequently in children (5–15%).[50]

4. For specific local anesthetics for epidural use (such as bupivacaine and ropivacaine), see general comments about epidural analgesia/anesthesia. These and other local anesthetics are poorly absorbed orally so should be safe in postpartum breastfeeding mothers. Milk levels of bupivacaine and ropivacaine[51] are exceedingly low.

Analgesics

1. Opioid analgesics

  a. Morphine is still considered an ideal analgesic for breastfeeding mothers due to its limited transport to milk and its poor oral bioavailability in infants.[33,37]

  b. 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.[33] Meperidine/pethidine should be avoided during labor and in postpartum analgesia (except, perhaps, within 1 hour prior to delivery). Infants of mothers who have been exposed to repeated doses of meperidine/pethidine should be closely monitored for sedation, cyanosis, bradycardia, and possibly seizures.

c. Although there are no published data on remifentanil, 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.

d. Fentanyl levels in breastmilk have been studied and are extremely low after 2 hours and generally below the limit of detection.[52,53]

e. Sufentanil transfer into milk has not been published, but it should be similar to that of fentanyl.

f. Nalbuphine and butorphanol levels in breastmilk are very low. At this time they would only be indicated in the specific situations mentioned previously. If these agents are used, observe the mother and infant for psychotomimetic reactions (3%).

g. Hydrocodone has been used frequently in breastfeeding mothers. Occasional cases of neonatal sedation have been documented, but these are rare and generally dose related. Doses in breastfeeding mothers should be kept at the minimum necessary to control pain. Frequent dosing throughout the day may lead to sedative effects in the breastfed infant.

h. A recent report of a neonatal death following the use of codeine suggests that the use of codeine in breastfeeding mothers should be monitored closely.[54] Although rare, rapid metabolizers of codeine are known, and levels of morphine following the use of codeine may be significantly elevated thus putting the infant at risk. Use caution with codeine in breastfeeding mothers.

i. Oxycodone levels in milk are known and average approximately 58 μg/L (range, 7–130 μg/L) (RID = 1.5–3.5%). Oxycodone may not be significantly safer for the rare mother who is an ultrarapid metabolizer, as it is also a substrate for CYP2D6. A recent retrospective study showed that one in five breastfed infants with mothers medicated with oxycodone experienced central nervous system depression. The strong concordance between maternal and infant symptoms may be used to identify babies at higher risk. It is important to follow these infants carefully for drowsiness.[55]

j. Regardless of the opioid, always consider the dose used. Many mothers undergoing chronic pain therapy in various pain clinics may use exceedingly high doses of hydrocodone, oxycodone, methadone, and other opioid analgesics. Those infants of mothers with exceedingly high doses should be closely monitored for sedation and apnea. If the infants are exposed in utero, the risk, initially, is probably somewhat less because of tolerance of the infant.

2. Non-steroidal anti-inflammatory drug analgesics
Use of non-steroidal anti-inflammatory drugs (NSAIDs) alone after vaginal birth or in combination with opioids after cesarean birth can improve pain control by assisting with some of the pain due to uterine cramping. NSAIDs are generally safe for breastfeeding and can help minimize the total dose of opioid needed to control pain.[32] (III)

a. Ibuprofen is considered an ideal, moderately effective analgesic. Its transfer to milk is low to nil.[56]

b. Ketorolac is a potent analgesic in breastfeeding mothers and is increasingly popular when used postpartum. Its primary benefit is excellent analgesia, with no sedative properties. In addition, the transfer of ketorolac into milk is extremely low.[57] However, its use in postsurgical patients with hemorrhage may be somewhat 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. However, the Food and Drug Administration now has a black box warning against use of ketorolac in breastfeeding women.[30]

c. Celecoxib transfer into milk is extraordinarily low ($<0.3\%$ of the weight-adjusted maternal dose).[58] Its short-term use is safe.

d. Naproxen transfer into milk is low, but gastrointestinal disturbances have been reported in some infants following prolonged therapy. Short-term use (1 week) is probably safe.[59]

Recommendations for Future Research

1. Studies of labor analgesia and anesthesia for cesarean section should specifically study breastfeeding outcomes. Although randomization of analgesia versus no analgesia is not possible, good prospective study designs should allow appropriate comparisons and should help describe appropriate support for breastfeeding mothers and infants who have been exposed to labor analgesia.

2. More study of specific breastfeeding outcomes after surgical anesthesia in breastfeeding mothers is needed.

3. More data on the use of ketorolac as it has gained in popularity in the postpartum period are needed.

4. More study is required of the special needs of premature and unstable babies including how their ability to clear maternal anesthetic and analgesic drugs may differ from healthy, term babies.

Acknowledgments

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