Anesthetic and Epidural Medications in Breastfeeding Mothers

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Drugs Commonly Used

- **Induction drugs**
  - Rapid transfer to surgical plane

- **Local Anesthetics**
  - Block nerve in periphery and centrally (epidural)

- **Opiates/Opioids**
  - Depress nerve action epidurally, subdurally, centrally
  - Reduce need for local anesthetics

- **Gases**
  - Provide muscle relaxation, sedation, analgesia(some)

Drugs Used for Induction

- Rapidly sedates patient into Surgical plane of anesthesia.
- Drugs Include:
  - Midazolam (Versed)
  - Etomidate
  - Propofol

- Produce profound sedation/analgesia, but of limited duration
  - In and Out quickly
  - Stored in adipose and muscle tissue...NOT plasma, Not breastmilk.

Redistribution

- Drug in plasma exits to peripheral compartments/ organs
- Redistribution from the vessel-rich tissues is responsible for termination of effect of many anesthetic drugs
- Wakening from thiopental, benzodiazepines (Versed) is not due to metabolism or clearance, but redistribution
Injection Phase of Typical Anesthetic Drugs

Redistribution Half-life

Valium 15 min
Versed 7 min
Propofol 2 min

Redistributes to other tissues in the periphery within minutes.

Thiopental Redistribution from Plasma Compartment

100%
% Of Dose

Plasma
Muscle
Fat

0.1 1.0 10 100 minutes

Epidural Injections
Clinical Use of Epidural Opioids Alone

- Benefit: Limited motor block
- Unfortunately, unreliable in advanced labor
- Water soluble (polar) drugs: Morphine
  - Inconsistent analgesia (50%) with delayed onset
  - Increased frequency of side effects (pruritus)
  - Increased frequency of neonatal complications
- Lipophilic drugs preferred:
  - Fentanyl, Sufentanil, Alfentanil
  - Slow onset (45 min), more potent analgesia, but shorter duration
  - More systemic absorption

Epidural Anesthesia

- Epidural Indwelling cannulas are often used today
  - Facilitate repeat dosing for increasing pain control.
- Addition of opioids to local anesthetics has dramatically changed obstetrical anesthesia
  - Adding opioids allowed reduce Local Anesthetic dose
  - Reduces Shivering
  - Reduces hypotension from local anesthetic
- Epinephrine increases analgesia but not duration
**Patient Controlled Epidural Analgesia (PCEA)**

- Infusion pump attached to catheter in Epidural Space
- Controlled by patient and infusion pump.
- Studies suggest total doses of local anesthetics and opioids are lower.
- OBs suggest that patient acceptance may be lower ??
  - Depends on institution !
  - Not really popular

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**Epidural Anesthesia**

- Fentanyl is most commonly used epidural opioid analgesic due to low cost and high potency.
- Sufentanil is an attractive alternative to fentanyl.
  - More rapid onset, more potent analgesia
  - Transfer of sufentanil to fetus is reported to be less significant, and without buildup like fentanyl.
  - Studies suggest neurobehavioral effects in infant are lowest.
- Bupivacaine or Ropivacaine are local anesthetic agents used

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**INTRATHECAL OR SUBARACHNOID**
Intrathecal Injection

Clinical Use of Intrathecal Opioids

- Advantages of intrathecal administration:
  - Rapid onset of analgesia
  - Limited motor blockade
  - Lower Doses of Opioids
  - Limitations of spinal opioids:
    - Not flexible for duration and intensity of labor
    - Unreliable for advanced labor and instrumental delivery

The Fate of Intrathecal Drugs

- Diffusion into the epidural space and then to systemic circulation
- Diffusion into the spinal cord and then systemic circulation
Combined Spinal-Epidural Analgesia
(nneedle-through-needle or walking epidural, CSE)

1st Step (infrathecal)
- 25 gauge spinal needle
- 16-18 gauge soft catheter

2nd Step (Epidural)
- Fentanyl or Bupivicaine

Combined Spinal-Epidural Anesthesia

Advantages of CSE analgesia and anesthesia:
- Rapid onset of intense analgesia
- Flexibility, you still have epidural catheter as labor progresses
- Benefit: Takes less time and effort to induce analgesia

Proposed Applications of CSE technique:
- Early labor (<4 cm)
- Advanced labor (>7-8 cm)
- Second stage

Maternal Complications and Side Effects

- Neurotoxicity
  - Some opioid drugs may cause neural tissue damage. Not well understood.
  - Intrathecal butorphanol may cause neural tissue damage

- Hypotension (local anesthetics)
  - BP falls by 20% in 14 – 50% parturient’s following spinal opioid
Spinal and Epidural Anesthesia

**Spinal**
- Higher incidence of hypotension
- Nausea, Vomiting, pruritus
- Dural puncture headache
- Limited duration of action

**Epidural**
- Higher complexity of technique
- Higher failure rate
- Slower onset
- Higher doses of medications
- Higher maternal/fetal drug exposure

**Neonatal Sedation and Outcome following epidurals**
- Often difficult to distinguish between effects of medications...and the delivery itself
- Many professionals complain that infants delivered of medicated mothers are generally
  - less alert
  - Have poorer muscle tone
  - feed poorly initially

**Literature on Neonatal Sedation and Outcome**
- Murray (1981) found no effect of labor meds compared to “non-medicated” controls using the Neonatal Behavioral Assessment Scale.
- Rosenblatt (1981) found poorer orienting behavior, more tremors and startles at 6 weeks of age.
- Septsiki (1992) found epidurals were related to poorer behavioral outcomes and recovery for the first 30 days of life (NBAS).
- Less alertness, poorer orientation, depressed performance
- Lufhus (1995) found more sedation and poorer NACS scores in fentanyl+bupivacaine group at 24 hrs.
- Helbo-Hansen (1993) found lower NACS scores with Fentanyl + bupivacaine epidurals, but none with sufentanil.
- Dewey found in 268 mothers that labor anestheisa was correlated with longer labor, higher C-section rates, and excess weight loss.
Neonatal Sedation and Outcome

- Nissen (1997) found depressed sucking behavior
  - Following 100 mg dose Pethidine/meperidine.
  - 1.1-5.3 hours after dose.
  - Poor lip-mouth movements
  - 6 of 13 infants did not suckle
- Ransjo-Arvidson (2001) found pethidine or bupivacaine or others may interfere with spontaneous:
  - Breast-seeking behavior.
  - Suckling
  - Also, increased newborn temperature and crying

Maternal Epidurals Complications

- Hypotension is the most common complication
- Inadvertent dural puncture and headache
- Duration of labor may or may not increase
- Limiting epidurals in nulliparous labor and delaying its placement until 5 cm cervical dilation may reduce risks
- Increased risk of chronic back pain does not occur.
- New studies show good outcomes and high breastfeeding rates in mothers with epidural fentanyl.

Obstetrical Hypotension

- Generally occurs due to higher blocks
- Risk of reduced uterine perfusion is major complication
- Must be detected early following monitoring every minute during and after infusion for at least 10 min.
- Occurs commonly:
  - 51% within 3 minutes (n=147 women)
  - 80% within 5 minutes
Drugs Used During Anesthesia

Local Anesthetics
Bupivacaine (Marcaine)
- Local Anesthetic agent preferred in parturients.
- Blocks local nerve impulses.
  - Systemic absorption leads to fetal depression, maternal hypotension.
- Long half-life anesthetic = 3-7 hours
- Highly protein bound which would decrease milk absorption (84-95% protein binding)
- Ropivacaine use is increasing due to less hypotension.

Pethidine / Meperidine
- Weak opioid
- Strong Sedative
- Metabolized to Active Metabolite
  - Normeperidine
    - Good convulsant
    - 73 hour half-life in neonates
    - Not reversed by Narcotic blockers (Narcan)
- Being banned from numerous hospitals
**Meperidine inhibits initial breastfeeding.**

- N=72 newborns
- 40 of 72 mothers had received pethidine (meperidine).
- 25 out of the 40 did not suck at all.
- Author suggested no one use pethidine.


**Meperidine Complications**

- Depresses fetal muscular activity, aortic blood flow, heart rate, oxygen saturation
- It exacerbates acidosis, reduces Apgar scores, reduces respiration and neurobehavioural scores, and suckling.
- Rooting reflex significantly reduced at 2 hours.
- CNS excitation:
  - Mild nervousness, tremors, twitches, multifocal myoclonus, grand mal seizures.
- Use of narcotic antagonists may actually aggravate seizures (does not displace normeperidine).
- Do not use in patients on SSRIs. several reported cases of serotonin syndrome (seizures)

**PCA Meperidine Vs Morphine (postpartum)**

- Among nursing parturients after cesarean delivery, intravenous patient-controlled analgesia (PCA) with meperidine is associated with significantly more neonatal neurobehavioural depression than PCA with morphine. Wittels B et.al. Anesth Analg 1997 Sep; 85(3):600-6
Reported Milk Levels

- Following dose of 50-400 µg fentanyl IV during labor, the concentration of fentanyl in milk was generally below the level of detection (<0.05 ng/mL).
- Oral Bioavailability is low (25-75%)
- Volume of Distribution is high (3-8 L/kg)
- Peak colostrum concentrations occurred at 45 minutes following intravenous administration and averaged 1.4 µg/L.
- Colosurem levels dropped rapidly and were undetectable after 10 hours.
- In another study of chronic exposure to fentanyl (transdermal patch 30 µg/hour).
  - At 27 days, the infants blood was negative for both fentanyl and its metabolite norfentanyl.
  - The mother’s milk contained 6.4 ng/mL fentanyl and 6.2 ng/mL norfentanyl.

Reference:
Egan TD. Anesthiology 79:881, 1993

T1/2 = 317-956 min.

Kappa Analgesics

- Butorphanol (Stadol)
  - 17% Oral bioavailability
  - RID = 0.52 %
  - Probably minimal risk.
- Nalbuphine (Nubain)
  - More selective for kappa receptor (than mu)
  - RID = 0.76% or 2.3 µg per day.
  - Psychotomimetic effect occurs in approximately 3% of patients. (patient floating on the bed)

Midazolam (Versed)

- Rapid but short acting T1/2 = 1.9 hours
  - Milk/Plasma ratio = 0.15
  - Milk level = 9 µg/liter
  - RID = 0.004% to 0.6%
  - Undetectable in milk after 4 hours

Propofol (Diprivan)

- Rapid anesthesia
- Rapid recovery (2-8 min)
- Breastmilk levels low
- RID = 4.4%
  - Milk concentrations
    - 0.04 - 0.74 mg/L during induction phase
    - Colostrum levels= 0.12-0.97 mg/L
- No reported problems
**Ketamine**

- Ketamine is a strong anesthetic agent that is used intranasally, intravenously, intramuscularly, and orally.
- Rapid acting anesthetic/analgesic
- Rapid Redistribution phase (4.68 minutes)
- Dissociative effect or emergence reaction common
- No levels reported in milk
- Some caution recommended.
- T1/2 = 3 hours
- Oral bioavailability = 20-30%
- MW = 274

**Morphine**

- Poor oral bioavailability = 26%
  - after two epidural doses (4 mg each), milk concentration = 82 ug/mL
  - RID = 9.1%
  - M:P ratio = 1.1 - 3.6
  - Considered best choice for breastfeeding mothers for severe pain

**Meperidine (Demerol)**

- Two hours after 50 mg IM, breastmilk levels = 0.13 mg/L
- Normeperidine levels were still detectable in milk for 56 after administration (8.1 ng/mL)...may lead to buildup in infant.
- RID = 1.4 – 13.9%
- Neurobehavioral delay has been reported via milk.
- Probably safe in older infants and after SINGLE use for dental extraction, etc.
Hydrocodone
- RID is moderate to low: 2.4% - 3.7% which is about 0.7% of the therapeutic dose in OLDER infants.
- Do not use more than 30 mg/day.
- Moms on continuous therapy prenatally, it is still probably safe as the infant may already be tolerant.
  - Evaluate the individual mom for dose and length of prior exposure.

Remifentanil
- Potent opioid, but brief half-life (< 10-20 minutes)
- Easily metabolized by infant as well as adult.
- No breastfeed data. No prenatal data.
- Probably safe

Lidocaine and Bupivacaine
- Lidocaine (maternal = 965 mg over 7 hours)
  - RID = 0.5 – 3.1%
  - daily intake for infant 2 mg/day
- Epidural Study of 27 women.
  - Received 183 mg lidocaine, and 82 mg bupivacaine (epidural)
  - Average milk levels over 12 hours were 0.5 and 0.07 mg/L respectively.
- In another study bupivacaine epidurals
  - Breast milk levels were too low to detect, < 0.02 mg/L at 2 to 48 hours.
  - RID = 0.9%
Gases

- **Nitrous Oxide**
  - plasma T1/2 < 3 min

- **Halothane**
  - after 3 hours exposure only 2 ppm was detected in milk
  - oral bioavailability unknown but probably low
  - Newest data show treatment with isoflurane was as effective as Electroconvulsive therapy for treatment of depression.

Gases in Recovery areas.

Maternal Risk?

- Concentrations of nitrous oxide, sevoflurane, and desflurane in operating room and recovery suites are dependent on ventilation of these spaces.
- Exposure levels to staff are generally low but may be higher than recommended for pregnant women.
- Volatile anesthetics are:
  - Rapidly excreted
  - Low oral bioavailability
  - Produce minimal levels in most operating suites (due to scavenging systems.
- Probably safe environments for breastfeeding mothers.

Oxytocin

- Oxytocin used during delivery;
  - May decrease endogenous oxytocin levels dose-dependently.
  - The more oxytocin used, the less oxytocin released during breastfeeding.
  - Oxytocin infusions reduced overall prolactin levels postpartum.
- But this was done on day 2 postpartum.

References:
Methylergonovine

- Ergot alkaloid used as a uterotonic agent to reduce postpartum hemorrhage.
- New data suggests it significantly reduces prolactin levels
  - About 50%
- May suppress lactation. First 6 days, went from 880 ml/d to 563 ml/d.
- Probably safe, but be observant, and don’t use too long.
- Alternative:
  - Misoprostol


In Conclusion

- No study thus far conclusively proves that epidurals reduce breastfeeding success. All are conflicted.
- Effect of opioids on infants is multifactorial, depending on dose used, parity, and duration of exposure.
- Fentanyl doses < 150 µg seem less likely to interrupt breastfeeding. Higher doses may increase breastfeeding failure rates.
- Pethidine/Meperidine should be avoided if at all possible.
- Transfer of anesthetic drugs to breast milk is apparently low and is not of major concern in normal full term infants.
  - Wait until mother is awake and alert to breastfeed.