Episode 58: Medications For Neuraxial Anesthesia

On this episode: Dr. Jed Wolpaw With Dr. Dave Berman and Dr. Anh Nguyen.

In this episode, episode 58, I welcome our two OB Anesthesia fellows to the show, Dr. Dave Berman (email) and Dr. Anh Nguyen (email). We discuss the medications used for neuraxial anesthesia including local anesthetics, opioids, and adjuncts such as epinephrine, clonidine and more.

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Hyperlinks to section of notes.

Local anesthetics

- All have terminal amine group

1:57

- **Ionization**
  - All weak base with pKA > 7
  - If pH > pKa, molecule will be *ionized*
  - Diffuses across lipid bilayer, which do not like charged things. Thus we want local anesthetic pKa to be close to pH as possible (as non-ionized form)
  - PNB mepivacaine pKa 7.6 → faster onset than bupivacaine pKa 8.1
    - Exception: chloroprocaine pKa 8.7 but onset is fastest bc we give higher concentration as 3% vs others as 0.5% or 1%

8:45

- **Lipid** solubility
  - Higher lipid solubility → more **potent** because need less to achieve same clinical effect
  - Bupivacaine 0.125 - 0.75 % vs lidocaine 0.5 to 2%
  - Slower onset
- Termination by redistribution not metabolism
  - Protein bound will prevent from being redistributed into vessels. Associated with longer duration of action
- Metabolism
  - Amide: liver (impaired in liver disease)
  - Ester: esterase (impaired in deficiency)
  - exception: cocaine (ester) and hepatic metabolism
- Nerve structure
  - Myelinated and smaller = more easily blocked
    - Fewer molecules to block at node points
  - Sensory > motor in level and speed
  - Sympathetic even higher, easier
    - Aδ = fast
    - C = slow, not as fast
    - Sympathetic system found mostly thoracic, rather than lumbar

Amides

- **Amide** anesthetic *names have TWO i's*
- Commonly used in OB

9:52

  - **Bupivacaine**
    - Standard for labor analgesia and C-section
    - Long duration
    - Liver metabolized
    - Unique: predilection for sensory rather than motor blockade, which is significant for labor because don't want to hinder delivery
    - Common formulations: isobaric (slightly hyper) 0.5% and 0.75% (hyperbaric d/t dextrose)
    - Intravascular doses will cause *cardiovascular collapse* before *CNS toxicity*
      - Treat with IV intralipid + low dose epi + early airway support (lipidrescue.org)
  - **Ropivacaine**

        - Similar to bupivacaine but lower cardiotoxicity ml per ml
        - 40x less potent, more expensive
        - More volume / drug needed.
        - Margin of safety is controversial, thus not often used In OB.
    - Concentrations controversial.
        - Administering hyperbaric then positioning to supine → local will settle in thoracic kyphosis, giving T4-6 level ideal for c/s. If not ideal, may end up with gravity-dependent saddle block. Isobaric would be less sensitive to positioning, but difficult to get higher level
        - Baricity not as discussed in epidural bc not free flow space.
            - More volume = more spread. 0.5-1.5ml per dermatome

14:05

    - **Lidocaine**
        - Oldest, and go-to for rapid onset
        - Dense block, both motor/ sensory unlike bupivacaine
        - Spinal doses associated with **transient neurologic symptoms** (pain in buttocks, thighs, lower back. Not affect bowel/bladder function. Resolve in few days.
            - More associated with lithotomy and ambulatory surgery.
            - Pregnancy appears to be protective.
        - Loss of motor/bowel/bladder functions concerning for hematoma or abscess

16:07

    - **Mepivacaine**
        - Lowest pKa. Rapid onset. High sensory anesthesia. Short onset, good for spinal
        - Bupivacaine 120-150, mepivacaine 50-90. Less TNS than lido. Good for ambulatory, short procedures

Esters

- ONE I
- Metabolized by plasma esterases like pseudocholinesterase

17:22

- **Chloroprocaine**
    - fast, despite high pKa
    - Duration shortest (use limiting)
    - Less likely for LAST d/t metabolism
    - Limited fetal exposure
    - T1/2 ~30s at 2-3% concentration
    - Concern for neurotoxicity and decreased efficacy of long acting opioids (morphine) w/ chloroprocaine (found to be from **bisulfite** preservative)

Opioids

- μ, δ, K receptors in central nervous system

18:00

- Why use?
    - Increase block density, decrease amount of local
    - If need sympathectomy, will almost always get with just local anesthetic. If we give less local, then less sympathectomy so less side effects (hypotension)
- Quality important in neuraxial space = lipid solubility.
    - More lipid soluble = faster onset if IV, also faster offset.

- In neuraxial space, already at site of action so cause rapid dissociation/offset
- Less lipid soluble = already in space so onset not sig diff. but tend to remain longer

18:59

- **Fentanyl**
  - Rapid onset, high margin of safety in neuraxial.
  - Lipophilic = duration short ~1-2hrs
  - Synergistic w locals and ↑ density of block.
  - Main drawback:
    - Pruritis, common in all but more in fentanyl because rapid onset, which lasts longer than analgesic effects.
  - Intrathecal 10-25µg. Shown that higher doses not ↑ analgesia, but ↑ in pruritis
  - Traditionally thought neuraxial opioid beneficial because steady stream into blood stream as CNS opioid. However low systemic dose at a typical rate of bupivacaine 0.125% with 2µg fentanyl over 8ml/hr, which equates to 16µg over 1 hour

21:54

- **Morphine**
  - Gold standard for post-c/s analgesia.
  - Moms can ambulate without motor weakness while benefits of significant analgesia and decrease postop opioid requirements
  - Morphine = 2 peaks.
    - CSF flow: brain → ventricles → spinal space → reabsorbed, recirculates into brain
    - **1st peak**: spinal space, acting on spinal receptors (1-3 hrs long) → reabsorbed → rostral spread to brain →
    - **2nd peak**: (6-8 hrs after administration, duration up to 36hrs) acting on periaqueductal gray, thus significant risk of respiratory depression especially in those with sleep disorder breathing at baseline (thus caution in morbid obesity, sleep apnea, or other opioid therapies).
  - 50-250 µg spinal or 1-4mg epidural appears to not lower opioid requirements, but increases pruritis and delayed respiratory depression

Labor analgesia

24:08

- Goal is to be comfortable with preserved motor function
- Dilute bupivacaine (sensory > motor) + low dose fentantyl
- PCEA
- Reduce amount of local required to decrease side effects, namely hypotension from sympathectomy as well as significant motor weakness.
- Local only allows for less pruritis.
- Recent data shows intermittent bolus tends to ↑ pain scores relative to continuous infusion, but drawback is the technology: pump needs reprogramming for intermittent bolus which may be cost prohibitive. Improved pain scores modest at best. Controversial

Cesarean section analgesia

26:40

- Spinal more dense coverage, evenly covered, more reliable.
- If c/s longer than expected, need to supplement.
- Practice: if high risk or morbid obese, combine bupivacaine and fentanyl in spinal dose. Typically, 10-15mg bupivacaine with 10-25µg fentanyl. For postop pain, morphine in spinal or

place epidural, or use continuous spinal epidural technique, especially if concerned for delayed resp depression, worrisome pruritis, or on high opioid therapy.

Adjuvants

29:00

- Why?
  - Mitigate side effects of opioids
- Synergistic – denser block or decrease requirements

30:37

- **Epinephrine**
  - ↑ block density, ↓ reabsorption of anesthetic → prolong duration
  - β3 receptors in adipose tissue, but no concerning function in CNS
  - α1 vasoconstriction → limits systemic uptake
  - α2 analgesia
  - Commonly 1:400,000(2.5µ/ml)-1:200,000 (5µ/ml) in epidural or 100-200 µg in spinal
    - Rule of thumb: divide 1million by denominator to get dose in µg
  - Epinephrine 5µg nearly doubles duration. 3.3µg shown not to have effects on fetus. 5µ/ml of bupivacaine has no effect as well
  - Studies have shown not strong significance of adding epinephrine into bupivacaine (epidural). Conflicting evidence in spinal solutions
  - if local more lipid soluble, advantage of epinephrine is less significant
  - Lidocaine and ropivacaine have lipid:water ratio ~2.7. Bupivacaine's ratio is 10x → epi works better with lidocaine / ropivacaine
  - Be aware of uterine and cardiovascular effects
    - Intravenous epinephrine → hypertension thus ↑ systolic to diastolic ratio. More concerning for patients with preeclampsia

36:08

- **Sodium bicarbonate**
  - Speeds onset. Block quality via alkalization as nonionized form
  - Studies have shown can improve onset by 10 min, but now controversial
  - Alkalization more pronounced in epinephrine because these solutions are more acidic (pH ~ 3.2-4.2)
  - Must use immediately after mixing because may precipitate. More often in bupivacaine than lidocaine
  - Fast onset → watch for fast sympathectomy aka hypotension
  - 1mEq/mL per 10ml local. Mainly with lidocaine

38:38

- **Clonidine**
  - More often in caudals
  - α2 agonist – analgesia without affect sensory/motor block
  - Prolong duration. ↑ segmental spread of blockade
  - Hypotension (preganglionic adrenergic neurons)/bradycardia.
  - Sedation (locus coeruleus)
  - α2 receptors on primary afferent terminals of cord, substantia gelatinosa in brainstem.
    - ↑ potassium → ↓ release of substance P.
  - **Black box warning** of hemodynamic instability, thus not popular in OB and in the US.
  - Useful if other drugs contraindicated or breakthrough pain.
  - 75µg not associated hypotension.
  - Intrathecally. 15-30µg can be added

- Chestnut: 75-150µg in epidural
- Caudals for intrauterine procedures ~ 20µg

41:50

- **Dexmedetomidine**
  - 7x more selective for α2.
  - 7-10µg intrathecal. Epidural 1µg/kg
  - Higher incidence of bradycardia.
  - Superior to clonidine but not widely used

43:03

- **Neostigmine**
  - ↓ breaks down acetylcholine in cord. Muscarinic effect releases GABA →analgesia
    - Lots of evidence this causes PONV with spinal.
    - More effective with **somatic pain**.
    - Larger doses may reduce uteroplacental flow via CNS and direct inhibition of uterine contractions.
    - Post c/s, 75-300µg epidurally but increased sedation.
    - Not FDA approved for epidural

44:50

- **Ketamine**
  - NMDA antagonist (and adrenergic, cholinergic, etc)
  - Potentiate local anesthetic via faster onset of sensory / motor.
  - ↑ duration of action and extends motor block.
  - Caudal 0.5mg/kg for children undergoing lower abdominal surgery shows prolonged analgesic duration, concerns for neurotoxicity

46:00

- **Magnesium**
  - NMDA antagonist. Block voltage-gated calcium channels.
  - Prolong motor/sensory block up to 3-27 hrs in ortho and GYN procedures.
  - Prolong spinal when coadministered.
  - Dose 25-100mg used with opioids ± local
  - Epidural showed rapid onset of sensory block in thoracic/ortho, lower incidence of postop shivering, PONV.
  - Faster onset, longer duration, ↓ breakthrough pain with no significant side effects of fetal outcome.
  - Bradycardia, hypotension, sedation, headaches, disorientation, periumbilical burning pain.
  - Note that study population not in pregnant women because of unknown risks to mother and baby.

48:06

- **Dexamethasone**
  - Steroid, potent anti-inflammatory
  - ONE Study showed 8mg of standard hyperbaric 0.5% bupivacaine intrathecal in ortho cases prolong duration without significant side effects.
  - Epidural 4-8mg has been investigated

49:10

- **NSAIDS**
  - Parecoxib, lornoxicam - recent studies
  - Prolong effects as epidural, but lornoxicam shows histopathologic signs of neurotoxicity

49:40

- **Midazolam**
  - Acts on benzodiazepine receptor of gray matter in cord
  - Analgesia from spinal suppression of sensory receptors
  - Nociceptive effects via GABAergic and opioid mechanisms
  - Intrathecal 1-2.5 mg. prolong postop analgesia
  - Epidural 50µg/kg potentiates effects of bupivacaine in upper abdominal surgery
  - Again, not investigated in OB.

PSA Be very careful with mixing your drugs! Don't do something you've never done by yourself! Be very careful of your conversions with epinephrine!

How are you using adjuvants?

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