Episode 46: Obstetric Pharmacology and Fetal Assessment

On this episode: Dr. Jed Wolpaw With Dr. Mike Hofkamp

In this episode, episode 46, I welcome back Dr. Mike Hofkamp to discuss obstetric pharmacology and fetal assessment.

Book recommendation: The Undoing Project about heuristics

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Hyperlinks to section of notes.

Inhalational agents

3:27

- Rapid transfer across placenta
- Associated with low Apgar scores, especially with longer induction times
- **Key point:**
    - Minimize exposure during c-section or general anesthesia. Don't start until cord about to be cut
- Effects on uterine tone?
    - In general, relaxation, which can be helpful in some scenarios like if uterine inversion or getting fetus out. But problematic if trying to get uterus to contract after baby out
- Nitrous Oxide
    - Supplemental or analgesia.
    - Can cause diffusion hypoxia in infant. Thus neonate should have supplemental O2 after delivery.
    - How?
        - Neonate breathing out transferred nitrous oxide will crowd out oxygen causing hypoxemia

Benzodiazepines

5:54

- Not typically given
- Diazepam is lipophilic = cross readily
- Midazolam (more often used) = polar so less crossing

Opioids

7:16

- i.e., meperidine, associated with neonatal CNS and respiratory depression. More for shivering
- Morphine and fentanyl rapidly cross placenta.
- Remifentanil rapidly metabolized by esterase, thus ideal for induction for c-section. Safer
- Mixed μ agonist antagonists like butorphanol and nalbuphine, given for laboring patients
- Downside to fetus in non-delivering pregnant patient? Probably not

Propofol

8:59

- Lipophilic = cross placenta
- Apgar higher in thiopental than propofol
- In non-delivering OB surgeries, inhaled and propofol effects on fetus are short lived and not significant

Teratogenic effects

Versed

10:03

- Theoretical risk of teratogenicity

NSAIDs

10:42

- Not teratogenic, but implications for term delivery with heart problems, especially fetal PDA

Acetaminophen

11:26

- Not teratogenic. Perhaps theoretical

Local anesthetics

12:08

- More sensitive.
- Pregnancy → ↓ α-glycoprotein levels → ↑ concentration of free lidocaine = more potent
- IV Dosing not adjusted

Oxytoxic drug

13:52

- Cause uterine contraction. Produced by hypothalamus or exogenous
- Induce labor and contract uterus to decrease blood loss
- Oxytocin is by protocol
- Too much can cause hyperstimulation and interrupt fetal blood flow → stop oxytocin and give something like **terbutaline** (β agonist) to stop contractions – can cause pulmonary **edema**, hyperglycemia, hyperkalemia

Methylergotamine

16:10

- Uterotonic. Reserved for significant PPH.
- IM only. So potent that never given as IV
- Contraindicated in preeclampsia because risk of intracerebral hemorrhage

Prostaglandins

17:20

- ProstaglandinF2α (Hemabate)
- Good for preeclampsia.
- Bad for asthma because can cause bronchoconstriction

Tocolytics

Magnesium sulfate

18:43

- Can be tocolytic. Usually preeclamptic to prevent seizures
- Potentiates nondepolarizing neuromuscular blockers
- ↓ MAC.
- Monitor signs of toxicity. First see loss of reflexes ~4-8mg/dl, then respiratory, then cardiac depression
- Neuroprotective for preterm fetus, stopped immediately after delivery
- Also use calcium channel blockers (eg, nifedpine)

Anti-seizure drugs

- Generally not safe, often involves multidisciplinary discussion

Phenytoin

23:15

- Competitive inhibitor of vit K, thus avoid especially during first trimester because can cause fetal anticonvulsant syndrome (oral, facial, cardiovascular, digital abnormalities) and fetal hydantoin syndrome (more minor abnormalities)

Carbamazepine

24:45

- Treats all but petit mal epilepsy.
- Can cause craniofacial defects, fetal developmental delays, spina bifida - avoid

Phenobarbital

25:06

- Partial generalized tonic-clonic seizures
- Bad side effects

Valproic acid

25:18

- Risk of spina bifida
- Fetal valproate syndrome – epicanthal folds, shallow orbit, low set ears

Mechanisms of placental transfer

26:20

- Don’t cross
    - Ionized, polarized, big
    - Glycopyrrolate, heparin, succinylcholine, non-depolarizing agents
- Do cross

    - Anything that cross BBB, < 1000 Daltons, more non-ionized form
    - Atropine, scopolamine, diazepam, midazolam, etc
- Ion trapping
    - Unionized on maternal side, cross via gradient into more acidic placental environment.
    - If pKa closer to physiologic level crosses, will likely be protonated / ionized – "trapped" , like lidocaine
- Protein binding
    - Free unbound is available to cross
- Fetus liver metabolize doesn't happen until third trimester.

FDA categories

30:20

- Category A = adequate RCT showing no risk
- Category B = animal studies show no risk and NO human studies; or animal studies show risk and human studies do not (conflict or just + animal)
- Category C = animal studies show some risk or no data exists (no known harmful human data)
- Category D = evidence of human risk but benefits may outweigh risk (?anticonvulsants?)
- Category X = absolute contraindication (isotretinoin, warfarin)

Amniotic fluid

34:25

- Fetal urine, lung fluid, skin, transudate, water
- Electrolytes, proteins, desquamated fetal cells
- Amniocentesis = sampling to measure lecithin, sphingomyelin to assess lung maturity
- Bacteria, karyotyping, alpha fetal protein levels correlating w neural tube defects
- Risk of spontaneous abortion = 0.25-1%, usually 20-22G needle.

Oligohydramnios

37:03

- UP insufficiency or ↑ artery resistance
- "less cushion" → more room for cord issues
- If post-date, screened 2x week for oligo
- Some come from fetal urination, so also can be from decreased fetal kidney function

Polyhydramnios

38:15

- Excess fluid in sac
- 1% of pregnancies
- Can be from diabetes: hyperglycemia → fetal polyuria
- Impaired swallowing: tracheoesophageal fistula
- Maternal renal/cardiac issues

Antepartum fetal assessment

Ultrasound

39:33

- Transabdominal (when fetus displaced towards chest) vs transvaginal (1st trimester bc easier to visualize)
- Basic: number of fetuses, viability, position, gestational age, growth malformations, placenta, os, fluid volume, masses
- Targeted/comprehensive: detailed structure, fetal malformation
- Limited: can be from fetal lie

Fetal heart rate

41:33

- Animal studies correlated to humans roughly approximate fetal heart rate
- Internal: more accurate
- FHR superimposed to contractions to see

Decelerations

42:20

- Early: not ominous fetal hypoxia
- Late: after apex of contraction: non-reassuring. Uteroplacental insufficiency
- Variable: cord compression, eg more likely in oligohydramnios
- **Mnemonic**: think of order of fetus coming out:
    - Head: early
    - Next is cord (variable)
    - Last: placenta

FHR variability

43:20

- Want to see sinusoidal pattern indicative of intact neurologic system and represents fetal wellbeing
- "Roadtracks"
    - Tracing is flat. Non-reassuring.

44:25

- These are subjective studies with limited benefits
- Prospective studies show ↓ Apgar scores < 4 and ↓ neonatal seizure but thinking is that damage is already done before onset of labor

Nonstress test

45:55

- Fetus on monitor and watch for 30-40 min
- Baseline FHR, variability, change in pattern of time

Contraction stress test

46:36

- Induce contraction (minimum of 3 in 10 min) to monitor fetal response
- Patient stimulated to produce oxytocin → contraction
- Negative test: no decelerations or contractions
- Positive test: severe decelerations
- Indicated to assess fetal wellbeing, eg if non-reassuring nonstress test

Biophysical profile

49:06

- Sonographic scoring system over 30-40 min to assess wellbeing
- Perfect = 10. For each, normal = 2 points, abnormal = 0
    - Breathing
    - Reactivity
    - Amniotic fluid volume
    - Tone
    - Movement

Antepartum therapy

Corticosteroids

50:52

- Betamethasone or dexamethasone
- Prevent fetal respiratory distress syndrome by inducing type 2 pneumocytes to produce surfactant
- Less intraventricular hemorrhage, necroenterocolitis
- Used in setting of prematurity, so try to hold off delivery day or two with tocolytics

Fetal surgery

51:50

- Possible to repair life-threatening malformations prior to delivery
- Fetal with normal karyotypes do better
- Best time to operate is prior to viability (before 24 wks)
- Patient must understand risks/benefits! Especially given not strong data

Did we miss anything important? What do you keep in mind when you use these medications?

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