Balancing Risk-Benefit See-Saw: Choosing Medication for the Pregnant or Lactating Perianesthesia Patient

Melanie Chichester, BSN, RNC-OB
Labor & Delivery, Christiana Care Health System, Newark, Delaware

92% of pregnant women take over-the-counter medications
95% of pregnant patients receive prescription medications
45% use herbal medications during pregnancy

Potential harm to the fetus or nursing infant is probably what worries you the most
Is there a potential harm to the mother if the drug is withheld?
Bottom line: Does the benefit of the drug outweigh its risks?

U.S. Food and Drug Administration (FDA) classification for pregnancy and lactation labeling.
Revised - More detailed, comprehensible, and practical information about the use and effects of drugs during pregnancy and lactation

“Old” Drug Categories
A – Substance fails to demonstrate a risk to the fetus in the first trimester and there is not evidence of risk in later trimesters.
B- Either animal studies have no demonstrated a fetal risk but there are no controlled studies in pregnant women or animal reproduction studies have shown an adverse effect that was not confirmed in controlled studies in women in the first trimester with no evidence of a risk in later trimesters.
C- Either studies in animals have revealed adverse effects on the fetus and there are no controlled studies in women or studies in women and animals are not available. Drugs should be given only if potential benefit justifies potential risk to the fetus.
D-There is positive evidence of human fetal risk but the benefits from use in pregnant women may be acceptable despite the risk.
X- Studies in animals or humans have demonstrated fetal abnormalities. The risk of the use of the drug in pregnant women clearly outweighs any possible benefit.
The drug is contraindicated.

“New” categorization
Proposed by FDA in 2008
“Finalized” in 2011
Still being put into place
Detailed information about risks of medications
  Removes categories from all drugs.
  Pregnancy and lactation sections have three components:
    risk summary
    clinical considerations
    data section
Pregnancy exposure registries
  Contact information about how to enroll.
General statement about background risk
  All pregnancies have some risk of birth defects, loss, or other adverse outcome regardless of drug exposure.
**Teratogen**
Substance that produces an increase in the incidence of a specific defect more frequently than in spontaneous population.
1/33 babies is born with an anomaly.
Teratogen must be given at the critical time
Embryo most vulnerable to major organ defects from 4-8 weeks

**Physiologic Changes of Pregnancy**
Cardiovascular
- plasma volume ^ 50%, CO ^ 50%

Renal/GU
- GFR 50% higher = Lower circulating concentrations
- Increased body fat
  - Changed distribution of fat-soluble drugs
- Decreased plasma albumin
  - distribution of protein bound drugs
- Delayed gastric emptying
  - Delayed onset for PO meds

Molecular weight of drugs affects how medications cross the placenta
- Large molecules do not cross (insulin, heparin)

**Conundrum**
Does medication use benefit outweigh risk in most circumstances?
Does medication use risk outweigh benefit in most circumstances?
*Most fall in the middle somewhere*

**Pain medication**
Acetaminophen B/B/B
NSAIDS B/B/D

*NSAIDS should not be used in pregnancy because of the risk of premature closure of the ductus arteriosis*
This is a relative contraindication
- 400 mg ibuprofen for a headache at 18 wks OK
- ATC NSAID at 33 wks is NOT

Common issues which might require pain management during pregnancy/lactation
- Migraine
- Appendicitis/Cholecystitis/Renal lithiasis
- Trauma
- Cesarean delivery

Decreased functional residual capacity/increased minute ventilation and oxygen consumption
Increased susceptibility to hypoxia
Tylenol always OK
Opioids really are OK in pregnancy
- Class C/D (neonatal effects of prolonged use)
  - Morphine
  - Fentanyl
  - Hydromorphone

NSAIDs are acceptable for adjunct pain management after cesarean deliver.
Considered safe during lactation
PONV
Most common post-procedure complication
After cesarean delivery: relaxed pyloric sphincter, hypotension, exteriorization of the uterus, visceral stimulation, and use of neuraxial opioids

Antiemetics
Diphenhydramine/Benadryl
  Pregnancy class B
5-HT₃ receptor agonists/-setrons
  Pregnancy class B
Metoclopramide
  Pregnancy class B
Dexamethasone
  Pregnancy class C
  Caution for diabetic mothers
Promethazine
  Pregnancy class C
Aprepitant/Emend
  Pregnancy class B
Cochrane review
  “There were insufficient data to demonstrate any class of intervention was superior to another”

Antimicrobials
Up to 30% of women will take antimicrobials during pregnancy
β-lactams
  Class B
  Penicillin G, Penicillin V, Amoxicillin
Macrolides
  Erythromycin, Azithromycin/Zithromax
  Class B
Cephalosporins
  Class B
  Cefazolin, cephalaxin, cefotetan
Clindamycin
  Class B
Vancomycin
  Class B
Aminoglycosides
  Class C/D
  Gentamycin
Rifampin
  Class C
  TB
  Unlikely risks/benefit to mother outweighs risks
Fluoroquinolones/Cipro, Levofloxacin
  Class C
  Possibility of bone/cartilage damage in fetus
  Benefit must outweigh risk
  Used for strain resistant to lactam & macrolides
Tetracycline/Doxycycline
Class D
May cause permanent staining of adult teeth when used in pregnancy or lactation

Etc…
Metronidazole/Flagyl - Class B
BV, trich, Giardiasis
Nitrofurantoin/Macrodantin - Class B
UTI
Sulfanomides
Trimethoprim & sulfamethoxazole/Bactrim
Category C
Increased risk of birth defects
Also hyperbilirubinemia in newborn

Ahhh…Flu season
Special populations, like pregnant women, are considered at increased risk of morbidity/mortality
CDC and the American College of Obstetricians & Gynecologists (ACOG) both recommend vaccination in pregnant women

M2 ion channel inhibitors
Amantadine
Rimantadine
Neuraminidase inhibitors
Oseltamivir
Zanamivir
Pregnancy Category C
“No evidence of an association between antepartum antiviral exposure and adverse outcomes”

Antimicrobial prophylaxis
EBP: Use antibiotics within 60 minutes of the start of the cesarean delivery

**Thromboembolic disease**
Leading cause of maternal death in the USA
Increased risk (4-5x) of venous thromboembolus in pregnancy (0.5-3/1000)
Remember Virchow’s triad?: hypercoagulation, vascular damage, and venous stasis
Risk equally high all trimesters
Even higher postpartum (20x higher)
Compression boots recommended for all women for cesarean delivery
PE more common postpartum
Dyspnea, tachycardia
Venous doppler studies of LE
Spiral CT scan SAFE, even in pregnancy
Benefit (saving maternal life!) outweighs risk
Less radiation than V/Q scan
Anticoagulants
Heparin- safe in pregnancy
LWWH- safe in pregnancy (neither cross placenta)
LMWH has become first choice
Safe in breastfeeding- minimal expression in breast milk
Warfarin- NOT (cranio-facial defects)
   Acceptable in lactation
New onset DVT/PE > IV heparin
   When stable > LMWH for duration of pregnancy
Convert LMWH > heparin @ 36 weeks
   (12 hrs wait vs 6 hr wait)
Best recommendation immed PP:
   Resume anticoagulation 6-12 hours after vaginal delivery or 12-24 hours after cesarean delivery
At 2 weeks PP, bridge to warfarin if long term therapy
   If only for 6 weeks, may stay on LMWH

Hypertension
HTN complicates ~1/10 pregnancies
   Chronic (up to 5%)
   Gestational hypertension
   Pre-eclampsia
   Superimposed pre-eclampsia (30% of CHTN)

Antihypertensives
Aldomet
   Class B
   Alpha adrenergic agonist
Labetalol
   Beta blocker
   Class C
Hydralazine
   Class C
Nifedipine (long acting)
   Class C
Diuretics- generally avoided, but…
   Hydrochlorothiazide
      Class B/D
   Furosemide
      Class C
   Spironolactone
      Not recommended

Others…
ACE inhibitors are class X in pregnancy
ARBs also
   CAN use when breastfeeding (risk/benefit)
Nitroprusside metabolites > cyanide
   Last resort due to fetal exposure

Anticonvulsant
Magnesium sulfate is used to prevent or treat eclampsia/NOT an antihypertensive
4-6 gm IV bolus over 20 minutes/2 gm/hr infusion
Monitor VS, reflexes, breath sounds, I & O, labs
Upper GI distress
Heartburn
Aluminum hydroxide/Maalox
   Pregnancy class B
Calcium carbonate/TUMS
   Pregnancy class C
Simethicone/Mylicon
   Pregnancy Class C
Ranitidine/Zantac
   Pregnancy class B
Famotidine/Pepcid
   Pregnancy class B
Cimetidine/Tagamet
   Pregnancy class B
Proton pump inhibitors
   Pregnancy class C
   Omeprazole (Prilosec)
   Lansoprazole (Prevacid)
   Pantoprazole (Protonix)
   Esomeprazole (Nexium)

Epilepsy
500,000 women of childbearing age have epilepsy
One in every 250 pregnant women (~0.5%) takes an anticonvulsant drug
Not just for breakfast anymore…
   Prescribed for bipolar mood disorders, migraine, and neuropathic pain syndrome.
Seizure history 9-12 months pre-pregnancy reasonably predictive for during pregnancy
Pregnancy does not increase seizure risk
Adverse effects during pregnancy identified
   Cardiac defects
   Cleft lip/palate
   Neural tube defects/ IQ deficits can be seen
   Growth restriction/limb hypoplasia
   Hypospadias
   Effects vary for individual drugs
Discontinuing or inadequate treatment of epilepsy may be more dangerous than effective anticonvulsant therapy.
   Use the fewest number of drugs and the lowest dose possible
Phenytoin/Dilantin
   Pregnancy class D
Carbamazepine/Tegretol
   Pregnancy class D
Phenobarbital
   Pregnancy class D
Valproate compounds
   Pregnancy class D
The next generation
Keppra/Levetiracetam
  Pregnancy class C
Lamotrigine/Lamictal
  Pregnancy class C
  May have an increased risk of preeclampsia or PP bleeding*
Topiramate/Topamax
  Pregnancy class D
Oxcarbazepine/Trileptal
  Pregnancy class C

Epilepsy: general thoughts
Optimize meds preconception
Minimize exposure:
  polypharmacy > single agent
  single agent > careful observation
Use best med for seizure type & lowest dose
Add folic acid supplements
Watch newborns for bleeding problems

Breastfeeding/lactation
Breast-feeding good for mom & baby
Most medications do cross into breast milk
Most of the time, insufficient information
Rarely are studies done on drug amounts in breast milk
Dose varies
  Amount excreted into breast milk
  Volume of milk ingested
  Plasma concentration in mother
Generally, breast is best
Always consider what is being prescribed during lactation

If your PACU patient has had a baby within the past year,
ask if she is still breastfeeding!
Does she need to pump pre/post-procedure?

More thoughts on breast feeding...
Most drugs are excreted in breast milk
  Dose dependent- lower dose, less drug
  Time dependent- take drug immed after feeding
Most antibiotics OK (except tetracycline family)
Can now use ACE/ARB for hypertension
Can now use Coumadin/warfarin for DVT/PE/A-fib
Iodine & gadolinium contrast materials OK?
  But mom may want to pump & dump for her own peace of mind
Radiology Dept may counsel against breastfeeding for 24-48 hrs
Bottom line…
“Potential harm to the fetus or nursing infant is paramount among these factors. Equally important is assessment of the potential harm to the mother that withholding a drug can cause. The decision, then, typically comes down to, ‘Does the benefit of the drug outweigh its risks?’

Resources Online

http://www.aafp.org/afp/20030615/2517.html

http://www.obfocus.com/high-risk/meds1.htm

http://www.cdc.gov/ncbddd/meds/

http://content.nejm.org/cgi/content/full/338/16/1128

When do you call the OB dept?
**Anytime you have a question about a pregnant patient!**
Can be good source of information if you are unsure about giving a medication!

References


Mchichester@christianacare.org