Medications and Mother’s Milk

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Outline

- Medication use during lactation
- Evidence to support medication use
- Factors to consider when selecting medications for use during lactation
  - Drug, maternal, fetal
- Suggested references

Conflict of interests – none to declare

Medication Use

- In Canada ~85% of women initiate breastfeeding
- >90% of women take meds in the 1st week postpartum

- Treatment for:
  - Problems related to lactation
  - Acute conditions
  - Chronic medical conditions
    - depression, diabetes, seizure conditions, GI conditions

Medication Use

- Women concerned about effects on infant
  - Want to do what’s best for infant

- Motherisk study
  - Recontacted 203 women who called about antibiotic use
    - 19 women did not take antibiotic
    - 7 weaned infant
  - Cohort study of 34 women on antiepileptics vs controls not on meds
    - Breastfeeding 50% vs. 85%

Medication Advice

“When in doubt, don’t breast feed”

- Not beneficial for women or infant
- Negative or conflicting information can lead to unnecessary interruption or discontinuation of breastfeeding
- Temporary interruptions increases likelihood of permanent weaning

- 1st source of information important

Lack of evidence

- Breastfeeding women excluded from clinical trials of new medications
  - “Gold standard” RCTs generally not available

- Manufacturers not required to study medication use in lactation
  - Product info from manufacturer usually insufficient (CPS, PDR, etc)
Evidence Sources

- Evidence comes from:
  - theoretical risks
  - case reports of ADRs
  - estimation of infant exposure
    - Milk/plasma ratio, relative infant dose
  - some epidemiologic studies (case-control, cohort)
  - expert opinion
    - Experts may not agree
- Difficult to develop consistent evidence based recommendations
  - HCP may provide conflicting advice / personal opinion
  - Recommendations vary between references

Factors to consider

1. Medication related
2. Maternal considerations
3. Infant factors

Methods of estimating infant drug exposure – M/P ratio

Maternal milk:plasma ratio

\[
\frac{[\text{Drug in mother’s milk}]}{[\text{Drug in mother’s plasma}]}
\]

- Index of the amount of maternal dose that will cross into the breast milk
  - Low transfer ratio < 1
  - High transfer ratio > 1
- Point estimate or AUC
- Dependent on timing of dose administration, sampling time of blood and breast milk
- Does not give any indication of effects on infant
- Little clinical utility

Methods of estimating infant drug exposure - RID

Relative Infant Dose

\[
\frac{\text{Infant dose (mg/kg/day)}}{\text{Maternal dose (mg/kg/day)}} \times 100\%
\]

- Estimate infant dose
  - Drug concentration in milk \times 150 \text{ mL/kg/day}
  - Can compare this to peds dosing, if available
- By convention RID < 10% RID considered safe
  - Most meds RID < 1-2%
- Infant absorption and metabolism not considered

Principles of Drug Transfer into Breast Milk

Absorption
Passive Diffusion

Medication → Maternal Plasma / Tissue → Breast Milk

Absorption:

More likely to transfer:
- Small molecule
- Low protein binding
- Un-ionized
- Lipid soluble

Metabolism

Elimination

Infant

Methods of estimating infant drug exposure

- Standard references do not agree on “safe” medication
- HCP may provide conflicting advice / personal opinion
- Recommendations vary between references
### Maternal factors to consider

- Are there non-drug treatments?
- Duration of treatment?
- Can treatment be delayed?
- Is the drug absorbed? If it is how does the mom metabolize the drug?

### Infant factors to consider

- Age of infant? Premature?
  - <6 months at highest risk of drug ADRs
  - 78% of ADRs reported in infants 2 months of age or younger
- Immature BBB in first year of life
  - Lipophilic drugs with CNS side effects are more likely to transfer into breastmilk and potentially cause CNS side effects in the infant
- Health status of the infant?
  - Premature? Major organ dysfunction?
- Exclusively breast fed? Formula or solid food?

### Drugs of concern during lactation

Some examples
- Chemotherapy
- Radiopharmaceuticals
  - May need to temporarily withhold breastfeeding
- Drugs of abuse – illicit and prescription
- Drugs that can decrease milk supply
  - Estrogens
  - Pseudoephedrine, amphetamines
  - Dopamine agonist (bromocriptine, cabergoline)

### Maternal factors to consider

- Timing
  - To minimize infant exposure breastfeeding before dose is due, take at HS
  - Colostrum in first 3 days of life more likely to contain meds but volume is low
- Will the drug affect milk supply?
  - ↓ dopamine agonists, high dose estrogens
  - ↑ dopamine antagonists – used therapeutically
    - Domperidone, metoclopramide

### Infant factors to consider

- Was the infant exposed in utero?
- Is the drug absorbed by the infant?
  - Still a risk of GI side effects if not absorbed
- Will the drug accumulate in the infant because of immature drug metabolic pathways?
  - Immature renal and hepatic function
    - Decreased drug clearance
    - 1/2 half-life >90 hrs in neonates vs 2.6 hrs in a 6 month old

### Infant factors to consider

- Is the drug used therapeutically in pediatrics?
  - Can extrapolate safety/harm from pediatrics data
- Are potential infant side effect easy to monitor?
  - Drowsiness, fussiness, diarrhea, etc
  - Are adverse effects undetectable?
  - Does the infant require blood work or monitoring by a health care professional?
Drugs reported to cause ADRs

- Cohort of 838 infants
  - 89% <4 months of age
- One or more maternal drugs
  - Analgesics 23.4%; antibiotics 19.8%; antihistamines 10.1%; sedatives 5%
- 11.2% reports of minor ADRs in infant
  - Diarrhea - antibiotics
  - Sedation - analgesics, narcotics*, sedatives, antidepressants
  - Irritability – antihistamines

*Codeine – high risk ultra-fast CYP 2D6 metabolizers (codeine → morphine)

Drugs in Pregnancy and Lactation

“Briggs”

- ++ use by pharmacists
- Not ideal for lactation
  - Better pregnancy resource
  - References retired AAP recommendations from 2001
  - Inconsistent pharmacodynamic info
    - Pantoprazole monograph – “unstable at acidic pH”
      - Not including in other PPI monographs
    - High molecular weight drugs (heparin, LMWH, mabs, protein based drugs)
      - Not all monographs mention “GI inactivation likely”

Medications and Mother’s Milk

“Hale’s”

- Recommended by experts in lactation
  - Rx, non-Rx, radioactive agents, drugs of abuse
  - Lactation risk category system:
    - L1 (safest) to L5 (hazardous)
    - All new drugs automatically L3 (probably compatible)
- Book published q2yrs $44.95
- Online $39.95 / year (individual)

LactMed

- Free website & app from the National Library of Medicine
  - Updated monthly
  - Peer reviewed monographs
  - Endorsed by the American Academy of Pediatrics

Conclusions

- Medication use during breastfeeding is common
- Almost all meds transfer in to breast milk to some degree
- Weak evidence for the safety/harms of medication use in breastfeeding - despite this:
  - many medications can be recommended
  - stopping breastfeeding may not be necessary
Conclusions

- Risk versus benefit decision
  - taking into account maternal and infant considerations
    - Mom needing treatment for URTI with a healthy 8 month old on some solids
  VERSUS
    - Mom with epilepsy and depression with a 1 month old infant born prematurely and exclusively breastfed
- Use LactMed or Hale’s

Questions?

Selected References: