Treatment of Depression & Nausea During Pregnancy & Lactation: Focus on Controversies in Care
Ashley Vincent, PharmD, BCACP, BCPS

Live Activity Handout
2 slides per page
Treatment of Depression & Nausea During Pregnancy & Lactation:
Focus on Controversies in Care

ACTIVITY DESCRIPTION
As medication use experts, pharmacists are often asked to provide recommendations for the "safest" treatment option during pregnancy and lactation. Often, little clinical data exist to guide these decisions and what data does exist may be somewhat contradictory or controversial. This activity aims to review the approach to assessing risks of medication during pregnancy and lactation based on available clinical information, while also examining guidelines related to the treatment of depression and nausea in pregnant and postpartum women. Participants will gain a clearer understanding of medications that are felt to be generally safe and unsafe for treatment of depression and nausea during pregnancy and while breast feeding through exploration of available literature.

TARGET AUDIENCE
The target audience for this activity is pharmacists and nurses in hospital, community, and retail pharmacy settings.

LEARNING OBJECTIVES
After completing this activity, the pharmacist will be able to:
- Assess the risk of medication use during pregnancy and lactation based on available labeling information
- Review recommendations for the treatment of nausea in pregnant women
- Describe strategies for the safe use of antidepressants in pregnant and breast feeding mothers

After completing this activity, the pharmacy technicians will be able to:
- Describe the potential risks of medication use during pregnancy
- Review recommendations for the treatment of nausea in pregnant women
- Recognize strategies for the safe use of antidepressants in pregnant and breast feeding mothers

ACCREDITATION
Pharmacy
PharmCon, Inc. is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Nursing
PharmCon, Inc. is approved by the California Board of Registered Nursing (Provider Number CEP 13649) and the Florida Board of Nursing (Provider Number 50-3515). Activities approved by the CA BRN and the FL BN are accepted by most State Boards of Nursing.

CE hours provided by PharmCon, Inc. meet the ANCC criteria for formally approved continuing education hours. The ACPE is listed by the AANP as an acceptable, accredited continuing education organization for applicants seeking renewal through continuing education credit. For additional information, please visit:
http://www.nursecredentialing.org/RenewalRequirements.aspx

Universal Activity No.: 0798-0000-17-041-L01-P
Credits: 1.0 contact hour (0.1 CEU)

Release Date: 02/01/2017
freeCE Expiration Date: 02/01/2020
ACPE Expiration Date: 02/01/2020

ACTIVITY TYPE
Knowledge-Based Live Webinar

FINANCIAL SUPPORT BY
Pharmaceutical Education Consultants, Inc.
ABOUT THE AUTHOR
Ashley H. Vincent, PharmD, BCACP, BCPS, is a Clinical Associate Professor of Pharmacy Practice, College of Pharmacy, Purdue University. She received her PharmD degree from the University of Pittsburgh and completed her PGY1 and PGY2 Ambulatory Care/Education residencies at the RL Roudebush VA Medical Center in Indianapolis, Indiana. Her practice for IU Health involves provision of disease state management services for an internal medicine clinic. Dr. Vincent’s research interests relate to qualitative and quantitative assessment of pharmacist provided services within the ambulatory care setting. Her teaching areas within the College of Pharmacy include hormonal contraceptives, medications in pregnancy and lactation, general women’s health, and concepts of ambulatory care pharmacy practice. In 2012, the Purdue University College of Pharmacy recognized Dr. Vincent’s work with the Innovation in Teaching and Learning Award.

FACULTY DISCLOSURE
It is the policy of PharmCon, Inc. to require the disclosure of the existence of any significant financial interest or any other relationship a faculty member or a sponsor has with the manufacturer of any commercial product(s) and/or service(s) discussed in an educational activity. Ashley Vincent reports no actual or potential conflict of interest in relation to this activity.

Peer review of the material in this CE activity was conducted to assess and resolve potential conflict of interest. Reviewers unanimously found that the activity is fair balanced and lacks commercial bias.

Please Note: PharmCon, Inc. does not view the existence of relationships as an implication of bias or that the value of the material is decreased. The content of the activity was planned to be balanced and objective. Occasionally, faculty may express opinions that represent their own viewpoint. Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not intended as a substitute for the participant’s own research, or for the participant’s own professional judgement or advice for a specific problem or situation. Conclusions drawn by participants should be derived from objective analysis of scientific data presented from this activity and other unrelated sources.

Neither freeCE/PharmCon nor any content provider intends to or should be considered to be rendering medical, pharmaceutical, or other professional advice. While freeCE/PharmCon and its content providers have exercised care in providing information, no guarantee of it’s accuracy, timeliness or applicability can be or is made. You assume all risks and responsibilities with respect to any decisions or advice made or given as a result of the use of the content of this activity.
Learning Objectives

• Assess the risk of medication use during pregnancy and lactation based on available labeling information
• Review recommendations for the treatment of nausea in pregnant women
• Describe strategies for the safe use of antidepressants in pregnant and breast feeding mothers
Medication Use During Pregnancy & Lactation

• > 80% of women use at least 1 medication during pregnancy
• Average of 2.6 medications in 1st trimester
  • 27% take ≥ 4 medications
• Limited data on use during lactation


Pharmacokinetic Changes in Pregnancy

• Absorption
  • Slower gastric emptying
• Distribution
  • Increased plasma volume, change in protein binding, lower ratio of lean muscle to adipose tissue
• Metabolism
  • Changes in phase 1 and phase 2 metabolism enzymes, in part due to sex hormones
    • e.g. CYP 2C19 activity reduced ~50%
    • e.g. CYP 3A4 activity increased
• Elimination
  • Increased renal and hepatic blood flow

Risks of Medication Use During Pregnancy

- Teratogen = agent that can cause fetal malformation
- Birth defects / malformations
  - 20-25% genetic factors
  - 10% environmental factors
  - 60-65% unknown factors
- Pregnancy loss
- Prematurity
- Infant death
- Developmental disabilities
- Neonatal withdrawal

Timing of Medication Exposure

Stages of human fetal development

https://stock.adobe.com/search?f=fetal+development&filters%5Bcontent_type%5D=1&filters%5Bcontent_type%3Avideo%5D=1&filters%5Bcontent_type%3Aillustration%5D=1&filters%5Bcontent_type%3Azip_vector%5D=1
Risk Categories - Traditional

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
</table>
| A        | Adequate and well-controlled studies  
          | No demonstrable risk to fetus in first trimester  
          | Examples: folic acid, magnesium sulfate, levothyroxine |
| B        | No adequate and well-controlled studies in human  
          | Animal studies fail to show risks  
          | Examples: metformin, amoxicillin, pantoprazole |
| C        | Animal reproduction studies show adverse effects  
          | No adequate and well-controlled studies in human  
          | Examples: fluconazole (single-dose), sertraline, amlodipine |
| D        | Evidence of human fetal risk  
          | Potential benefit may warrant use  
          | Examples: paroxetine, lithium, phenytoin |
| X        | Studies show fetal abnormalities, evidence of human fetal risk  
          | Risks >> benefits  
          | Examples: atorvastatin, warfarin, istotretinoin (Accutane) |

Assessing Medication Use

Prescription Drug Labeling Sections 8.1 – 8.3 USE IN SPECIFIC POPULATIONS

**CURRENT LABELING**

- 8.1 Pregnancy
- 8.2 Labor and Delivery
- 8.3 Nursing Mothers

**NEW LABELING** (effective June 30, 2015)

- 8.1 Pregnancy includes Labor and Delivery
- 8.2 Lactation includes Nursing Mothers
- NEW 8.3 Females and Males of Reproductive Potential

Risk Categories

- Pregnancy (Label section 8.1)
  - Pregnancy Exposure Registry contact information
  - Risk Summary
  - Clinical Considerations
    - Maternal and fetal risks
    - Dose adjustments during pregnancy and postpartum
    - Maternal and fetal adverse reactions
    - Labor or delivery
  - Data
    - Human data
    - Animal data

Risk Categories

- Lactation (Label section 8.2)
  - Risk Summary
    - Presence in human milk
    - Effects on breastfed child
    - Effects on milk production
  - Clinical Considerations
    - Counseling information
    - Minimizing exposure
    - Monitoring reactions
  - Data
Risk Categories

- Females and Males of Reproductive Potential (Label section 8.3)
  - Pregnancy Testing
    - Recommendations
    - Requirements
  - Contraception
    - Before, during, or after therapy
  - Infertility
    - Human and/or animal data on effects on fertility

Medication Transfer from Mother to Infant – Lactation

1. Orally available to mother
2. Absorbed into mother’s bloodstream
3. Able to cross into breastmilk
4. Orally available to infant
5. Absorbed into infant’s bloodstream
Relative Infant Doses

• Can be used to calculate potential exposure
• If range, use highest number
• Examples
  • Ranitidine 1.3 – 4.6%
  • Codeine 8.1%
  • Enalapril 0.2%
  • Propranolol 0.3 – 0.5%
  • Aspirin 2.5 – 10.8%
  • Lorazepam 2.5%
  • Tetracycline 0.6%
  • Doxycycline 4.2 – 13.3%

Relative Infant Dose – Example

• Mom is receiving ampicillin 2000 mg IV q4h
  • How much is the baby getting via breastmilk?
• Ampicillin RID = 0.2 – 1.5%; Mom weighs 70 kg
• RID = (infant dose in mg/kg/day) / (mom’s dose in mg/kg/day)

1. Weight adjust mom’s dose:
   2000 mg x 6 doses = (12000 mg/day)/(70 kg) = 171 mg/kg/day

2. Solve for infant dose:
   0.015 = (x mg/kg/day)/(171 mg/kg/day)
   X = 2.6 mg/kg/day
What does RID Tell Us?

<table>
<thead>
<tr>
<th>RID RANGE</th>
<th>PRESENCE IN BREASTMILK</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2%</td>
<td>Minimal transfer to milk</td>
</tr>
<tr>
<td>2 – 5%</td>
<td>Small amount of transfer to milk</td>
</tr>
<tr>
<td>5 – 10%</td>
<td>Moderate amount of transfer to milk</td>
</tr>
<tr>
<td>&gt; 10%</td>
<td>Large amount of transfer to milk</td>
</tr>
<tr>
<td></td>
<td>Risk of effects in infant exists</td>
</tr>
</tbody>
</table>

Infant Considerations

- Age
- Weight
- Preterm vs. term
- Other health conditions
- Percentage of diet composed of breastmilk
Hale’s Lactation Risk Categories

• L1: Safest (i.e.: acetaminophen, amoxicillin)
• L2: Safer (i.e.: diphenhydramine, fluoxetine)
• L3: Moderately safe (i.e.: pseudoephedrine, hydrocodone)
• L4: Possibly hazardous (i.e.: colchicine, dapsone)
• L5: Contraindicated (i.e.: amiodarone, chemotherapy agents)

Poll Question Opening
Poll Question Closing

Management of Nausea in Pregnancy
“Morning” Sickness

- Nausea & vomiting of pregnancy (NVP)
- Hyperemesis gravidarum: persistent vomiting leading to weight loss, electrolyte disturbances and fluid loss
  - > 50,000 hospitalizations / year¹
- Usually presents by week 9 and stops at end of 1st trimester
- Most common pregnancy complaint – up to 80%²


NVP – Potential Mechanisms

- Psychological predisposition¹
- Evolutionary adaptation²
- Human chorionic gonadotropin (hCG)³
- Estrogen⁴,⁵

NVP Treatment – Nonpharmacologic

- Prenatal vitamins for 3 months before conception
- Avoid triggers
  - Smells, foods, motion
- Eat small, frequent, low-fat meals
- Drink chilled beverages
- Ginger

NVP Treatment – Pharmacologic

1ST LINE
- Pyridoxine (Vitamin B₆) ±
- Doxylamine

LAST LINE
- Glucocorticoids

ST LINE
- Pyridoxine (Vitamin B₆) ±
- Doxylamine
- Antihistamines
- Phenothiazines
- Anticholinergics
- Dopamine antagonist
- Serotonin inhibitors

NVP Treatment – Glucocorticoids

• Methylprednisolone 16 mg TID x 3 days then 2-week taper
• Confirmed association with oral clefts
  • First trimester exposure
  • 1-2 cases/1000 treated women
• Use with caution
• Avoid before 10 weeks gestation
• Stop if no response in 3 days

NVP Treatment – Serotonin Inhibitors

• Ondansetron 4-8 mg q6h
• Conflicting efficacy
  • Similar to metoclopramide with fewer side effects\(^1\)
  • Better at controlling severe vomiting than metoclopramide\(^2\)
  • Improved symptoms compared to pyridoxine/doxylamine\(^3\)
• Safety concerns
  • QT interval prolongation (maternal)
  • Cleft palate
  • Fetal cardiac anomalies

## Ondansetron – Maternal QT Prolongation

### Contraindicated Medications

<table>
<thead>
<tr>
<th>Group</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihistamines (hydroxyzine)</td>
<td>Macrolide antibiotics (erythromycin, azithromycin)</td>
</tr>
<tr>
<td>Analgesics / sedatives (methadone, oxycodone)</td>
<td>Trazodone</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Fluoxetine</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>Antimalarials (chloroquine, quinine)</td>
</tr>
<tr>
<td>Antiarrhythmics (amiodarone, sotalol, quinidine)</td>
<td>Metronidazole</td>
</tr>
<tr>
<td>Antipsychotics (haloperidol, chlorpromazine)</td>
<td>HIV protease inhibitors</td>
</tr>
<tr>
<td>Tricyclic / tetracyclic antidepressants (amitriptyline, imipramine)</td>
<td></td>
</tr>
</tbody>
</table>

## Ondansetron – Fetal Safety Concerns

### Cardiac Anomalies

### Cleft Palate

### No Risk

*Abstract only.*
Ondansetron – Cardiac Anomalies

• Swedish Medical Birth Register + Swedish Register of Prescribed Drugs; 1998 – 2012
• n = 1349 exposed infants
  • Majority exposed at 7 + weeks gestation

<table>
<thead>
<tr>
<th>Malformation Type</th>
<th># of Occurrences with Ondansetron</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any malformation</td>
<td>49</td>
<td>0.95 (0.72-1.26)</td>
</tr>
<tr>
<td>Cardiovascular defect</td>
<td>19</td>
<td>1.62 (1.04-2.14)</td>
</tr>
<tr>
<td>Septum defect</td>
<td>17</td>
<td>2.05 (1.19-3.28)</td>
</tr>
</tbody>
</table>


Ondansetron – Cardiac Anomalies

• Denmark; 1997 – 2010
• n = 1248 exposed infants
  • First trimester exposure
• Results
  • Major malformation – OR: 1.3 (1.0 – 1.7)
  • Heart defect – OR: 2.0 (1.3 – 3.1)

Ondansetron – Cleft Palate

• United States; National Birth Defects Prevention Study; 1997 – 2004
• 11 of 55 cases of cleft palate had ondansetron exposure
• Results
  • Cleft palate – OR: 2.37 (1.18 – 4.76)


Ondansetron – No Risk

• Denmark Medical Birth Registry + National Patient Register; 2004 – 2011
• n = 1970 exposed infants
  • Median first prescription fill at 70 days gestation

<table>
<thead>
<tr>
<th>Adverse Outcome</th>
<th>Number of Occurrences (%)</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous abortion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 prescription</td>
<td>22 (12)</td>
<td>0.68 (0.41 – 1.13)</td>
</tr>
<tr>
<td>≥ 2 prescriptions</td>
<td>10 (0.9)</td>
<td>0.30 (0.06 – 1.53)</td>
</tr>
<tr>
<td>Any major birth defect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 prescription</td>
<td>14 (3.8)</td>
<td>1.41 (0.75 – 2.62)</td>
</tr>
<tr>
<td>≥ 2 prescriptions</td>
<td>22 (2.5)</td>
<td>0.98 (0.56 – 1.72)</td>
</tr>
<tr>
<td>Low birth weight</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 prescription</td>
<td>24 (3.8)</td>
<td>0.75 (0.46 – 1.24)</td>
</tr>
<tr>
<td>≥ 2 prescriptions</td>
<td>49 (4.2)</td>
<td>0.77 (0.49 – 1.19)</td>
</tr>
</tbody>
</table>

Ondansetron – No Risk

- Western Australia; all births with ondansetron dispensed under Australian Pharmaceutical Benefits Scheme; 2002 – 2005
- n = 263
  - 211 had 1st trimester exposure

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number (%)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any birth defect</td>
<td>16 (6.1)</td>
<td>1.3 (0.8 – 2.1)</td>
</tr>
<tr>
<td>Any major birth defect</td>
<td>12 (4.6)</td>
<td>1.1 (0.6 – 2.0)</td>
</tr>
<tr>
<td>Any major birth defect 1st trimester exposure</td>
<td>10 (4.7)</td>
<td>1.2 (0.6 – 2.2)</td>
</tr>
</tbody>
</table>


Ondansetron – Considerations

- Study design leading to identification of concerns
  - Retrospective cohort design
- Confounding maternal variables that increase risk
- Risks of medication exposure vs. risks of uncontrolled NVP
- Timing of medication exposure
- Animal studies do not support teratogenicity
Ondansetron – Role in NVP

Nonpharmacologic treatment

Pyridoxine

Pyridoxine + doxylamine

Consider ondansetron

Poll Question Opening
Poll Question Closing

Management of Depression in Pregnancy & Lactation
Depression

• Prevalence
  • Depression in women: 9.5%
  • Depression during pregnancy: 14-23%
  • Depression after pregnancy: 10-15%

• Burden of disease
  • A leading cause of disability in adults
  • Postpartum depression affects the mother and the child

Consequences of Maternal Depression

• Paternal depression
• Growth effects
• Preterm delivery
• Neonatal effects
• Delayed expressive communication
• Higher rate of emergency department visits

Screening Recommendations

- United States Preventative Services Task Force (USPSTF)
  - Depression screenings for adults, including pregnant and postpartum women

- National Institute for Health and Care Excellence (NICE)
  - Assess for depression at first contact with primary care and early in postnatal period

Screening Tool

- Edinburgh Postnatal Depression Scale (EPDS)
  - Designed specifically for use in pregnant or postpartum women

I have blamed myself unnecessarily when things went wrong.

- Yes, most of the time
- Yes, some of the time
- Not very often
- No, never
Treatment Options

- Cognitive Behavioral Therapy (CBT)
- Medication Therapy
- Electroconvulsive Therapy (ECT)


Treatment Considerations

- Previous medication therapy
- Severity of depression symptoms
- Possible adverse effects of medication
- Potential harms of not treating
- Trimester of pregnancy
- Changes in pharmacokinetics
- Plans for breastfeeding
- Patient preference

Antidepressant Use in Pregnancy – Risk of Cardiac Defects

• 2005: FDA reclassified paroxetine from pregnancy category C to D due to potentially increased risk of cardiac malformations

• Right ventricular outflow tract obstructions associated with paroxetine

• Ventricular septal defects associated with sertraline

Antidepressant Use

• 949,504 eligible pregnancies identified
  • 1st trimester antidepressant use (6.8%)

<table>
<thead>
<tr>
<th>Class or Medication</th>
<th>Use during 1st trimester (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective Serotonin Reuptake Inhibitor (SSRI)</td>
<td>4.9</td>
</tr>
<tr>
<td>Tricyclic Antidepressant (TCA)</td>
<td>0.6</td>
</tr>
<tr>
<td>Selective Norepinephrine Reuptake Inhibitor (SNRI)</td>
<td>0.7</td>
</tr>
<tr>
<td>Bupropion</td>
<td>0.9</td>
</tr>
<tr>
<td>Other Antidepressants</td>
<td>0.7</td>
</tr>
</tbody>
</table>

## Results

- **Rate of cardiac malformations**
  - 1st trimester exposure: 90.1 per 10,000 infants (0.901%)
  - No exposure: 72.3 per 10,000 infants (0.723%)

- **Relative risk (95% confidence interval)**
  - SSRI: 1.06 (0.93 to 1.22)
  - TCA: 0.77 (0.52 to 1.14)
  - SNRI: 1.20 (0.91 to 1.57)
  - Bupropion: 0.92 (0.69 to 1.22)
  - Other antidepressants: 1.21 (0.91 to 1.60)

---

### Selective Serotonin Reuptake Inhibitors (SSRIs) During Pregnancy

<table>
<thead>
<tr>
<th>Article</th>
<th>Location</th>
<th>Sample</th>
<th>Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davis et al, 2007</td>
<td>USA</td>
<td>SSRI, n = 805</td>
<td>Stratified by health system, maternal age, birth season</td>
<td>One or more malformation risk: SSRI (RR=0.97; 95% CI, 0.81-1.16)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unexposed, n = 49,031</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Källén et al, 2007</td>
<td>Sweden</td>
<td>SSRI, n = 6,555</td>
<td>Adjusted for birth year, maternal age, parity, smoking, previous miscarriages</td>
<td>Congenital malformations: SSRI (AOR=0.89; 95% CI, 0.79-1.07)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unexposed, n = 873,876</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pedersen et al, 2009</td>
<td>Denmark</td>
<td>SSRI, n = 1,370</td>
<td>Adjusted for age, year, income, marital status, smoking</td>
<td>Major malformations: SSRI (AOR=1.21; 95% CI, 0.91-1.62)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unexposed, n = 493,113</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Tricyclic Antidepressants (TCAs) During Pregnancy

<table>
<thead>
<tr>
<th>Article</th>
<th>Location</th>
<th>Sample</th>
<th>Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davis et al, 2007</td>
<td>USA</td>
<td>TCA, n = 167 Unexposed, n = 49,669</td>
<td>Stratified by health system, maternal age birth season</td>
<td>One or more malformation risk: TCA (RR=0.86; 95% CI, 0.57-1.30)</td>
</tr>
<tr>
<td>Simon et al, 2002</td>
<td>USA</td>
<td>TCA, n = 209 Unexposed, n = 209</td>
<td>Matched for maternal age, year, history of antidepressant use, psych treatment history</td>
<td>Major malformations: TCA (OR=0.82; 95% CI, 0.35-1.95) Cardiac malformations: TCA (OR=0.50; 95% CI, 0.05-5.53)</td>
</tr>
</tbody>
</table>

# Other Antidepressants During Pregnancy

<table>
<thead>
<tr>
<th>Article</th>
<th>Location</th>
<th>Sample</th>
<th>Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Einarson et al, 2001</td>
<td>Canada, USA, Brazil, Italy</td>
<td>Venlafaxine, n = 105 Unexposed, n = 105</td>
<td>No differences reported for age, alcohol use, and smoking</td>
<td>Major malformations: venlafaxine 1.6% vs. unexposed 0.7% (OR=2.21; 95% CI, 0.20-24.69)</td>
</tr>
<tr>
<td>Chun-Fai-Chan et al, 2005</td>
<td>Canada, USA, UK</td>
<td>Bupropion, n = 91 Unexposed, n = 89</td>
<td>Matched for age, alcohol use, and smoking</td>
<td>Major malformations: bupropion 0% vs. unexposed 2.2%</td>
</tr>
<tr>
<td>Djulus et al, 2006</td>
<td>Canada, USA, UK, Italy, Israel, Australia</td>
<td>Mirtazapine, n = 104 Unexposed, n = 104</td>
<td>Matched for age, alcohol use, chronic conditions, smoking, gestational age</td>
<td>Major malformations: mirtazapine 1.9% vs. unexposed 1.9%</td>
</tr>
</tbody>
</table>
Depression Recommendations – Pregnancy

Screen all pregnant women

- EPDS score ≥ 10
- Previous or current antidepressant use
- Consider agent continuation ± CBT

- EPDS score < 10
- No history of depression treatment
- Consider CBT ± sertraline
- Monitor, reassess next visit

Depression and Breastfeeding

- Antidepressants are 1st line for moderate to severe postpartum depression
- All antidepressants pass into breast milk
- Maternal milk/plasma (M/P) ratio and relative infant dose (RID) can be used to help determine safety in breastfeeding
  - M/P < 1
  - RID < 10%
- Lactation risk category (L1-L5)

Selective Serotonin Reuptake Inhibitors (SSRIs) & Breastfeeding

• Breast milk concentrations
  - Higher RID: fluoxetine (6.8%), citalopram (3.5-3.6%)
  - Lower RID: sertraline (0.4-2.2%), paroxetine (1.2-2.8%)

• Maternal adverse effects:
  - Delayed milk secretion
  - Gastrointestinal distress
  - Headache
  - Sexual dysfunction

• Infant adverse effects:
  - Irritability or agitation
  - Excessive crying
  - Sedation

Tricyclic Antidepressants (TCAs) & Breastfeeding

• Nortriptyline is typically undetectable in infants with no adverse events reported (RID 0.53%)

• Maternal adverse effects:
  - Hypotension
  - Sedation
  - Dry mouth
  - Constipation

• Infant adverse effects:
  - Poor feeding or emesis
  - Sedation
Other Antidepressants & Breastfeeding

- Venlafaxine
  - Drug and metabolite detectable in infant serum (RID 6.8-8.1%)
  - Monitor for sedation and adequate weight gain
- Bupropion
  - Limited infant data (RID 0.2-1.98%)
  - Possible risk of irritability and seizures
- Mirtazapine
  - Limited infant data (RID 1.6-2.8%)
  - No adverse effects reported

Depression Recommendations – Lactation

Screen women during the 1st postpartum year

- EPDS score ≥ 10
  - Previous or current antidepressant use
  - Fluoxetine, venlafaxine, citalopram
  - Change to another antidepressant ± CBT

- EPDS score < 10
  - No history of depression treatment
  - Consider starting CBT ± sertraline

- Monitor, reassess at future visit
Take Home Points

- Product labeling contains important clinical information about safety of medication during vulnerable times

- Nausea
  - Pyridoxine ± doxylamine is first line
  - Ondansetron appears to be safe and effective
  - Corticosteroids should be avoided / reserved as last line due to documented harm

- Depression
  - Pregnancy
    - Continue current treatment
    - Consider sertraline if pharmacotherapy started
  - Lactation
    - Fluoxetine, venlafaxine or citalopram should be avoided
    - Sertraline appears to be safe