Depression In Pregnancy and Postpartum: Screening, Diagnosis, Consequences of Untreated Illness, Engagement, and Traveling the Road to Recovery

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Case: Mary

- 29 year old single woman 2 weeks after the birth of her third child
- She had one prior severe depressive episode that started while she was pregnant with her 2\textsuperscript{nd} child. She also has a diagnosis of GAD
- No prior hospitalizations or suicide attempts, but she does have a history of SI
- Family History: bipolar in aunts and several cousins
- Prior medication trials: bupropion, fluoxetine, and clonazepam
• Today you note the following:
  – Mood, irritable, sad, anhedonic, stressed, can’t relax, racing thoughts, hopelessness, overwhelmed, poor sleep, fleeting thoughts she would be better off dead

• She notes that she stopped the medication because, “I’m good. I don’t need it anymore.” She goes on to state, "I am scared the medications will harm by baby".
Key Point #1

When treating maternal illness in pregnancy or postpartum there is the mother and the baby to consider.
Risk-Benefit Ratio

Risk of Untreated Illness

Risk of Untreated Illness

NO RISK-FREE ZONE!!!
Outline

• Brief Review of Common Mood and Anxiety Disorders
• Consequences of Untreated/Under-treated Depression and Anxiety
• Screening and Treatment Options
• Helping Families Recover
• Issues Around Engagement in Treatment
What are the Most Common Perinatal Mood and Anxiety Disorders?
What are Potential Consequences if Left Untreated?
Mood Disorders

• Most often occur during developmental and hormonal transitions:
  – Adolescence
  – Premenstrual
  – Peripartum
  – Perimenopause

• Hypotheses:
  – Increased sex-steroid sensitivity as a susceptibility factor?
  – Women with postpartum depression increased sensitivity to estrogen signaling

Postpartum Blues

- 50-85% of all new mothers
- Labile mood
- Emotional hypersensitivity
- Tearful
- Mild sleep disturbance
- No major change in functioning

- Generally responds to support and reassurance
- No treatment necessary, except if severe and >14 days
- Begins 2-4 days after birth
- Resolves 12-14 days later

Postpartum Depression

• Begins a little later ~ a few weeks
• 10-15%
• Often not detected until much later
• Symptoms: sleep disturbance, anhedonia, hopelessness, worthlessness, energy changes, appetite changes, concentration difficulties, and SI/HI/SIB.

Postpartum Psychosis

- 0.1 - 0.2%
- 1-2 per 1,000 births
- Rate is 100 times higher in women with BP or a previous history of postpartum psychosis
- Extremely disturbed mood
- Highly agitated
- Severely disturbed sleep
- Delusions/hallucinations
- Suicidal thoughts
- Major loss of functioning
- Rapid decline over 1-2 weeks

**Psychiatric emergency**

Don’t Forget About The Fathers

• More than 10% of fathers suffer from psychiatric morbidity in the postnatal period.

• Depression amongst fathers is associated with:
  – having depressed partners
  – having an unsupportive relationship
  – being unemployed.

Perinatal Anxiety and OCD

• GAD:
  – Most common anxiety disorder in perinatal period
  – 8.5% to 10.5% of pregnant and postpartum women meet criteria (5.2% general population)

• OCD: <1% in pregnancy; 3-4% postpartum (<2% in general population)

• Panic Disorder: 1-2% (general population)

• Key symptom: Scary thoughts – negative, unwanted, repetitive, and/or intrusive thoughts/images

Perinatal Anxiety and OCD

• Obsessive thoughts 91%
• Intrusive memories of birth 15-37%
• Excessive worry 15-37%
• Rumination
• Catastrophic misinterpretation of bodily sensations

Scary Thoughts of Harming the Baby

- >90% of postpartum women have intrusive thoughts of accidental harm to their babies (illness, fall abduction, suffocation)
- 50% of postpartum mothers have intrusive thoughts about intentionally harming their baby

<table>
<thead>
<tr>
<th>OCD</th>
<th>Psychosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrusive thoughts cause distress (ego dystonic)</td>
<td>Not associated with distress (ego syntonic)</td>
</tr>
<tr>
<td>Fear of acting on intrusive thoughts, avoidance behaviors/rituals</td>
<td>Other associated symptoms of psychosis (confused, agitated, hallucinations, loss of reality)</td>
</tr>
<tr>
<td>Low likelihood to act; mom otherwise in touch with reality</td>
<td>Increased likelihood that mother may act on thoughts</td>
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</tbody>
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Trauma and PTSD

- Obstetric/labor trauma
  - 20% of women

- Interpersonal trauma
  - 28% have been sexually abused in childhood
  - 20% experience intimate partner violence
  - 4-8% are abused during pregnancy

- Peripartum PTSD
  - 12.3% - PTSD lifetime
  - 2-7% PTSD in pregnancy and postpartum
  - 1.5-3% new onset PTSD after birth trauma

Time To Relapse of Depression

N = 201.
Consequence of Untreated Depression and Anxiety

• Pregnancy:
  – Inadequate weight gain
  – Risk for preeclampsia
  – Pre-term birth
  – Low birth weight
  – Small for gestational age
  – Increased uterine artery resistance
  – Elevated maternal perinatal cortisol and neonatal cortisol

Consequences of Untreated Depression and Anxiety

• Postpartum
  – Difficult infant temperament
  – Increased risk for later child behavior problems
  – Negative effects on child cognition
  – Impaired mother-infant interaction
  – Prenatal effects moderated by mother-infant attachment

“The potential effectiveness of screening for Postpartum Depression appears to be related to the availability of systems to ensure adequate follow-up of women with positive results.”

When to Screen?

- OB visit and at 6 weeks
- Pediatrician well-baby visits up to 6 months
- Continuously when engaged in a treatment relationship
- Postpartum depression presents within the first weeks, but peaks around 3-6 months
- Screening took easily available (EPDS, PHQ-2, PHQ-9)
- Only 5% of screen-positive women receive adequate treatment.
- Screening alone in OB does not yield higher rates of treatment engagement, need for collaborative care models:
  - Barriers: low rates of referrals, off-site mental health, stigma, undertreatment, low access to a variety of personalized treatment options, treatment delivery in a timely fashion
Screening Measures

- **EPDS**
  - Sensitivity = 0.86; Specificity 0.78
  - For positive screen >10
  - Take 5-10 minutes, self administered, could be self-scored

- **PHQ-2**
  - Sensitivity = 0.83; Specificity = 0.92
  - For positive screen >3
  - Takes Less than 1 minutes, self administered and can be asked

- **PHQ-9**
  - Sensitivity = 0.88; Specificity = 0.88
  - For positive screen >10
  - Takes 5-10 minutes, self administered, could be self-scored

• Mild or moderate depression but no personal or family history
  – START WITH THERAPY such as
    – Self-help strategies (support groups, yoga, mindfulness)
    – Counseling (IPT, CBT)

• Moderate depression and personal or family history of depression, or active severe depressive episode
  – Start THERAPY AND MEDICATIONS at once

• Treatment-resistant depression
  – Consider augmenting with mood stabilizer/antipsychotics or ECT

ACOG = American College of Obstetricians and Gynecologists; APA = American Psychiatric Association; IPT = interpersonal psychotherapy; CBT = cognitive-behavioral therapy.
Treatment Options

MentalHealthHumor.com

You know, just 30 minutes of exercise a day can reduce depression by 50%.

By: Chato B. Stewart

JUST GIVE ME THE DRUGS!

Reduce Depression
Psychotherapies

- Interpersonal psychotherapy (IPT)
- Cognitive-behavioral therapy (CBT)
- Behavioral activation (BA)
- Dyadic relational/attachment interventions
- Home based interventions

Antidepressants vs. CBT Vs. Placebo for Moderated to Severe Depression

Placebo (n = 60)  ADM (n = 120)  CT (n = 60)

8 Weeks
25%  50%  43%

16 Weeks
10%  46%  40%

ADM = antidepressant medication; CT = cognitive therapy.
Complementary and Alternative Treatments

- Light therapy
- Exercise
- Mindfulness
- Yoga
- Omega 3 Fatty Acids
- SAM-e
  - 1600mg/day → 70% in depression over 30 days in women with postpartum depression
- St. John’s wort (mild depression)
- N-acetylcysteine
- Vitamin D (treat if deficient)
- Vitamin B12 (treat if deficient)

ADM = antidepressant medication; CT = cognitive therapy.
Not the primary treatment for mood disorders.
More research necessary.
Severe depression, bipolar disorder, and treatment resistant depression require antidepressants, mood stabilizers, and atypical antipsychotics.
Mary is No Getting Better

- Mary is now 2 months postpartum.
- She has met with her therapist a couple of times but she is getting more depressed and dysfunctional
- She and her husband are now worried about postpartum depression given her prior history
- She agrees to start medicine now
- She still desires to breastfeed?
- Prior medication trials: sertraline, bupropion, clonazepam, fluoxetine (remission), venlafaxine (remission)

How do you address the risk-benefit discussion?
Key Point #3

• Use what worked in the past!
• Encourage families to be open
• Encourage families to reflect on family history
Consult with Doctor

- We can use antidepressants and mood stabilizers during pregnancy and in post-partum.
- Always important to weight risks and benefits
Breastfeeding

• All medications transferred to breast milk, but concentrations are far less than in utero exposure.

• Drug transfer to the breast milk and to baby is variable by medication but ranging from <1-20% - Least likely to transfer: paroxetine, sertraline, TCAs

• Avoid drugs with a long half-life; possibility of accumulation in breast milk

• Check baby for adverse effects: drowsiness, poor feeding, monitor CBC, comp, TSH.

ECT

- Safe application in pregnancy
- No teratogenic effects
- No intrauterine growth restriction
- No neurodevelopmental toxicity
- Some adverse effect on neonate: cyanotic, low muscle tone
- 2nd and 3rd trimester: Women should be positioned slightly toward left side with support under the right hip to prevent vena cava compression syndrome
Practical “Take Aways”

- Always balance the risks of medication and reoccurrence of illness
  - Aiming to minimize fetal/neonate exposure to both maternal mental illness and medication
- Avoid polypharmacy
- Non-pharmacological interventions should be a key component of the treatment plan.
- Use lowest effective dose BUT dose adequately
- Use medications with the lowest teratogenic risk
- History of previous treatment response should help guide decisions
- Provide written materials to explain the risks
- Document in your notes that you discussed and they voiced understanding
Road to Recovery and Treatment Engagement

“One small crack does not mean that you are broken, it means that you were put to the test and you didn’t fall apart” – Linda Poindexter
Road to Recovery

• Acceptance
  – Mental Illness is REAL
  – It cannot be ignored
  – Sooner you accept; the easier recovery will be
  – Remove judgement and negative emotion
  – Mental Illness does not define you
Road to Recovery

• Overcoming Fear
  – Fear, embarrassment, guilt are often preventing people from getting help
  – Educate, Educate, Educate!
  – Increase support
    • Groups, therapist, other providers, family, friends
Road to Recovery

• Being Patient
  – Every step is putting you closer to the goal of recovery
  – Some frustration is Normal
  – Recognize the old you returning
  – Engage family members
  – Keep note of initial symptoms of relapse
  – Recovery is not always “perfect”
  – There is not always a right way
Road to Recovery

- Encourage “positive thinking”
- “Be kind to yourself”
- Celebrate success!
- Stay in the present
- Empower them to be their own advocate
- Review Distress Tolerance Skills
- Use Motivational Interviewing
What can you do

• Talk to them
  – Express concern and support
  – Opportunity to provide information, support, and guidance
  – Improved recognition of early signs
  – Earlier treatment
  – Greater understanding and compassion

• Connect them to other supports
  – School counselor, primary care provider, spiritual leader, etc
• Offer to help with every day tasks
• Including your friend or family member in your plans:
  – Continue to invite him or her without being overbearing
  – Continue to invite them even if they resists your invitations
• Educate other people so they understand the facts about mental health and do not discriminate
• Treat people with respect, compassion, and empathy

www.mentalhealth.gov
Other things that are helpful?

- Know how to connect people to help
- Communicate in a straightforward manner
- Speak at a level appropriate to a person’s age and developmental level
- Discuss the topic when and where the person feels safe and comfortable
- Watch for reactions during the discussion and slow down or back up if the person becomes confused or looks upset.
• Cold vs. Flu
• Management of High Cholesterol
• Management of Diabetes

“Just like people need to take medicine and get professional help for physical conditions, someone with a mental health problem may need to take a medicine and/or participate in therapy to get better”
Key Point #4

Building a Good Relationship is Key?
(Think about Your Favorite Teacher or Favorite Boss)
Risk Factors

• Biopsychosocial Risk Factors
  – Hopelessness
  – Impulsive and/or aggressive tendencies
  – History of trauma or abuse
  – Family history of suicide
  – Past behavior
    – Alcohol and other substance use disorders

• Environmental Risk Factors
  – Relational or social loss
  – Easy access to lethal means
  – Local clusters of suicide that have a contagious influence

• Sociocultural Risk Factors
  – Lack of social support and sense of isolation
  – Stigma associated with help-seeking behavior
  – Certain cultural and religions beliefs
  – Barriers to assessing substance abuse health care treatment
TREATMENT ENGAGEMENT

We should no longer whisper about mental illness
Key Point #5

Do not forget about yourself!
Take Care of Yourself

- Eating right
- Sleep well
- Exercise
- Take breaks when necessary
- It is okay to ask for help
- Do things you enjoy
- Use coping techniques
- Talk to someone
- Do things you enjoy!
Thank you

• Michigan Home Visiting Conference Organizers
• Dr. Muzik and Dr. Rosenblum
• Mary Ludtke
• Thank you to my patients! (Always teaching me about how to be a better clinician and how to improve mental wellness).
Questions?
IF YOU ARE INTERESTING IN LEARNING MORE ABOUT MEDICATION MANAGEMENT
What Do You Have to Consider When Treating with Medications?

• Teratogenicity (congenital malformations)
• Toxicity for pregnancy/fetal outcomes
  – SA
  – PTB
  – LBW
  – SGA
• Neonatal syndrome
• Neurobehavioral/developmental effects

SA = spontaneous abortion; PTB = preterm birth; LBW = low birth weight; SGA = small for gestational age.
• Baseline population risk for any malformation is 2-4% among healthy, unexposed women

• Thus, any medicine risk must be measured against this baseline risk
FDA Pregnancy Categories

• Are not enough information and misleading

A  Well controlled studies in human pregnancy show no increased risk (<1% of medications)
B  Animal studies show no risk OR
   While animal data show risk well controlled human studies do not
C  Animal studies show risk and no well controlled human studies available
   OR
   There are no animal or well controlled human studies (66% of medications)
D  Human data show risk OR
   Benefits may outweigh known risk
X  Animal or human data show fetal risk positive; the risk clearly outweighs the benefit
Problems with Studies

- Confounding factors are not taken into account in studies
  - Maternal age
  - Other prescription and non-prescription drugs
  - Nutrition
  - ETOH/cigarettes
  - Genetic influences
  - Effects of mental illness or comorbid health conditions
  - Environmental toxins
  - Stress
  - Socioeconomic status
  - Method of delivery
Teratogenicity

- TCA overall risk is low
- SSRIs overall risk is low
- Other antidepressants less data but assuring
  - Bupropion: cardiac malformation risk minimal (2/1000)
  - Venlafaxine, duloxetine, mirtazapine: no malformation risk

TCA = tricyclic antidepressant; SSRI = selective serotonin reuptake inhibitor.
The “Paxil” Story

• In 2005 GlaxoSmithKline analyzed own data on N = 815 exposed infants, and found that these infants had 1.5- to twofold increased risk for heart defects, specifically atrial and ventricular septal defects → paroxetine became FDA Category D

• Since 2005 many contradicting studies. Some found...
  – Increased risk for unspecific malformations
  – Increased risk for specific cardiac malformations
  – No risk for malformation (risk .7%)
  – Risk is dose-dependent(>25 mg/day) and only when exposed in first trimester

Most Recent Study on Paroxetine

- Large, population-based cohort study b/w 2000 to 2007
- Participants: 949,504 pregnant women who were enrolled in Medicaid during the period from 3 months before the last menstrual period through 1 month after delivery and their live born infants
- How many exposed? 64,389 women (6.8%) used ADs during the first trimester
- Finding: RR for cardiac malformation was 1.06 (95% CI, .93-1.22) in the fully adjusted analysis restricted to women with depression
- Conclusion: no substantiated risk between AD (in particular sertraline and paroxetine) and cardiac risk

Funded by the Agency for Healthcare Research and Quality and the National Institutes of Health

AD = antidepressant; RR = relative risk
• NAS in 25-30% for SSRIs and more common TCAs
  – With 2nd (?) or 3rd trimester exposure
  – Jitteriness, irritability, difficulty with feeding, breathing, hypotonia, temperature instability, seizure
  – Long-term effect (19 months): no developmental effect
  – Does not typically require NICU admission, transient ~2 weeks
  – One study showed no difference in NAS rates with stopping medication 2 weeks prior to delivery (retrospective registry study)

NAS = neonatal abstinence syndrome; NICU = neonatal intensive-care unit.
Neonatal Syndromes (continued)

- **Persistent pulmonary hypertension**
  - At birth the normative closure of ductus arteriosus and foramen ovale does not happen and they stay open leading to a left-to-right shunting of blood causing
    - Hypoxia in neonatal organism
    - If chronic: \(\rightarrow\) right ventricle failure

- **Base rate:** 2/1000
- **Absolute risk with exposure to SSRIs** 6 x higher but still rare
- **Other possible risk variables:** C-section, BMI, race
- **Revised FDA communication in 2012** noting that earlier the risk was overestimated

Spontaneous Abortion

• Antidepressant-related to increased risk for SA
  – N = 3567 12.4% on antidepressants vs 8.7% off
  – No difference between various classes of antidepressants
  – None of the studies took confounders into consideration such as
    – Poor health habits, psychiatric illness, smoking, etc
    – This reduces the clinical utility of findings

• Bupropion appears to have higher risk for SA than SSRIs

• Antidepressant-related to near-term PTB (defined as birth >35 weeks but <37 weeks)
  
  – Gestational age dependent on duration of exposure to antidepressant; longer exposure related to shorter gestation

• Antidepressant-related to increased risk for SGA

• Antidepressant exposure related to LBW; effect is minimal (~75 g less) and disappears when control group are untreated depressed mothers

Neurobehavioral Toxicity

• TCA or fluoxetine exposure—no global IQ, language, or behavioral problems at 15 months and 7 years of age (N = 219; N = 122)

• No effects on motor performance and attention/learning tasks in 6-month-old babies who were SSRI exposed; but, babies exposed to antipsychotics did worse on neurological motor tasks

• Minor motor developmental delay in toddlers exposed to SSRIs

Neurobehavioral Toxicity (continued)

- Two large population-based case-control studies hint at association between SSRI use and ASD in offspring
  - However, while significant SSRI explain only .6% of cases with ASD
- A study of nearly 1000 mother-child dyads suggested that boys are significantly more at risk for ASD than girls if their mothers took an SSRI during pregnancy, especially during the first trimester
- Recent review concludes that exposure during the first trimester may increase the risk of ASD, however confounders were not assessed

ASD = autism spectrum disorder.
Case: Mary

- Mary and her husband agree that she will start an antidepressant
- Which one?
- Past trials: sertraline, fluoxetine, bupropion XL, venlafaxine
Use what has worked in the past
(Single exception: valproate in pregnancy)
Case: Mary

- Previously euthymic on fluoxetine 40 mg
- Plan: restart fluoxetine 10 mg x 5 days, then 20 mg and titrate to 40 mg

“START LOW, GO SLOW, KEEP GOING”

“I am so anxious that I am crawling out of my skin!”

“Every time I increase the dose, I get more anxious and my sleep is even worse for a few days.”
Are anxiety meds safe?

- No evidence of congenital malformation
  - Initial concern cleft lip/palate, disproven

- Lorazepam and clonazepam preferred
  - Less likely to accumulate in fetus/neonate
  - Alprazolam rapid on/off = unknown fetal effects

- 550 infants with normal development to 4 yo

• 70% of pregnant women report poor sleep
• Women with poor sleep have higher EPDS score ≥10 (39% vs 20% HC; \( P < .01 \))
• Women with sleep <6 hours/night compared to 7-9 hours/night have more depressive symptoms (60% vs 31%, \( P = .03 \))
• 45% of pregnant and 55% of postpartum women with depressive symptoms also report clinical insomnia
• Sleep disturbances in the 2nd trimester predict significant depressive symptoms in the 3rd trimester
• Sleep disturbances during pregnancy predict significant depressive symptoms postpartum

Clinical Pearl: Insomnia x 4 Nights = Red Flag

Treatment in Pregnancy

- **Stress reduction**
  - Massage, relaxation, and meditation techniques

- **Sleep hygiene**
  - Warm bath 1 hr before bed raises core temp and stimulates sleep response

- **CBT-I or medications**
  - Diphenhydramine
  - Zolpidem
  - Trazodone
  - Tranquillizer

Treatment while Breastfeeding

- **Stress reduction**
  - Massage, relaxation, and meditation techniques

- **Sleep hygiene**
  - Warm bath 1 hr before bed raises core temp and stimulates sleep response
  - Help w/ infant care and feeding
  - Minimize use of alcohol (paradoxical effects)

- **If ≥ 4 days**
  - CBT-I or medications

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Sleep Medications

• Benzodiazepines
  – Teratogenity: 1st trimester—possible cleft lip malformation (old data) but this has not been replicated in later studies
  – 3rd trimester—floppy baby syndrome, withdrawal symptoms and restlessness in neonates, PTB, LBW

• Trazodone
  – No malformations

• Zolpidem
  – Possibly some increased risk for PTB, SGA, LBW—but clinically low significance; low risk for malformation

Valproic Acid

- Teratogenicity: 10%, particularly if exposure in 1st trimester
  - Risk is dose dependent (>1000 mg/day)
  - Midface hypoplasia and other facial anomalies
  - Cardiac anomalies
  - Folate supplementation up to 5 mg daily may reduce risk
- Intrauterine growth restriction
- Mental retardation—Independent of which trimester exposure
- Neonatal toxicity
  - Irritable, jittery, hypotone, feeding difficulties, liver toxicity
  - Hypoglycemia
- Single dosing causes higher peaks
  - Mostly exposure in unplanned pregnancy end of 1st trimester

Lamotrigine

- Teratogenicity
  - 3 out of 4 registries report no more than baseline population risk for malformations (2-4%)
  - 1 out of the 4 registries suggested increase in RR for midline facial clefts with 1st trimester exposure; but absolute risk is very low (4:1000)
- Neonatal toxicity
  - Transient liver toxicity
  - Watch skin rash
- Increased excretion in pregnancy → need to increase dose in later gestation

• **Teratogenicity**
  – Risk for cardiac malformation—Ebstein’s anomaly (tricuspidal displacement/right ventricle hypoplasia)
  – Initial risk was overstated in the 1970s
  – Population risk is: 1 : 20,000 (.00005%)
  – Lithium-exposed risk is: 1-2 : 1,000 (.001-.002%)
  – Therefore, while the RR is increased by 20- to 40-fold, the absolute risk for Ebstein’s anomaly is still extremely low when on lithium

• **Risk for neonatal toxicity**
  – Floppy baby, cyanose, hypotone, hypothyroidism, nephrogenic diabetes insipidus
  – Clearance is increased in late pregnancy—dose increase!

Carbamazepine

- Teratogenicity: 2.6% same as general population
  - Neural tube exposure 1st trimester, dose related-spina bifida: risk 2.6x higher than the general population rate of 1:1000 births—so absolute risk rate still small
  - Craniofacial and other facial anomalies not confirmed higher risk
  - Oxcarbazepine safe
  - Screening: maternal α-fetoprotein (blood) and 2D or 3D ultrasound weeks 16-20
  - Vitamin K prophylaxis: start week 36 to prevent hemorrhagic disease in the newborn (carbamazepine induces cytochrome P450 enzyme which degrades Vitamin K)

- Intrauterine growth restriction

- Neonatal toxicity
  - Transient liver toxicity
  - Neonatal bleeding, administer Vitamin K 1 mg to baby

- Mostly exposure in unplanned pregnancies or epilepsy patients

First-Generation Antipsychotics

• Exposure to phenothiazines during pregnancy (N = 1309)
  – No differences were found in rates of congenital malformations, perinatal mortality rate, birth weight as compared to the population

• Pregnancy exposure to haloperidol (N = 215)
  – No increase risk for major malformations

• Increased incidence of PTB and neonatal adaptation but not malformation compared to unexposed

Second-Generation Antipsychotics

- Limited data on exposed children!
- **Manufacturers’ registries:** olanzapine = 242, clozapine = 523, quetiapine = 446, risperidone = 250
- **Case reports:** clozapine = 74, olanzapine = 69, quetiapine = 3, risperidone = 12
- **Prospective comparative study**
  - 151 women were followed exposed to following drugs
  - Olanzapine = 60, risperidone = 49, quetiapine = 36, clozapine = 6
  - The researchers found no teratogenic effects
- 570 women in Swedish database were exposed to SGA: slight increased risk for major malformations (OR 1.5)
- Increased incidence of PTB and neonatal adaptation but not malformation compared to unexposed

Second-Generation Antipsychotics (continued)

• Neurobehavioral development
  – Single study from Hong Kong
  – Exposed = schizophrenia, 50% clozapine
  – Control = no mental illness
  – Exposed with significant delays at 2 to 4 months but caught up on all measures by 1 yo

• Aripiprazole: 3 case reports

• Ziprasidone: 3 case reports

• Overall: increased risk for EPS in neonate with antipsychotics

• 2011 FDA drug safety communication (EPS)

Case: Mary

• Mary had an uneventful vaginal delivery at 39 weeks

• She experienced some worsening mood and disrupted sleep in the first week postpartum

• She wants to breastfeed and mild ejection is slow; this has been stressful. She is also concerned

  “I want to breastfeed my baby”

  “Is it safe for my baby to be on clonazepam and fluoxetine?”
• All medications transferred to breast milk, but concentrations are far less than *in utero* exposure

• <10% of maternal serum plasma is considered compatible with breastfeeding
  
  – Fluoxetine: 5-9% of maternal dose
  
  – Other SSRIs: range from 1-20%
  
  – Carbamazepine: <1%
  
  – Lorazepam, clonazepam: <1%

• Avoid drugs with a long half-life: possibility of accumulation in breast milk

• Check baby for adverse effects: drowsiness, poor feeding, monitor CBC, comp, TSH, CAVE: premies

Breastfeeding

- Antidepressants

- Breastfeeding OK, drug transfer to breast milk and to baby variable by medication but ranging from <1-20%

- Least likely to transfer: paroxetine, sertraline, TCAs

- Rule: continue the medicine used in pregnancy or start agent that was effective in prior medication trials

• Benzodiazepines

  – Breastfeeding OK as minimal excreted in breast milk (clonazepam, lorazepam OK)

Breastfeeding (continued)

- Lithium
  - Breastfeeding not recommended as baby vulnerable for dehydration and lithium toxicity
  - If mother insists, need to perform blood draws in first weeks to check how much lithium transferred via milk; transfer is variable up to 30%

Breastfeeding (continued)

• Valproic acid
  – Breastfeeding OK, infant serum level 6% of mom, no adverse effects

• Carbamazepine
  – Breastfeeding OK, infant serum 6-65% of mom, no adverse effects

• Lamotrigine
  – Breastfeeding OK, 30% mom dose, no adverse effects

ECT

- Safe application in pregnancy

- No teratogenic effects, no intrauterine growth restriction, no neurodevelopmental toxicity

- Some adverse effect on neonate: cyanotic, floppy, hypotone

- 2nd and 3rd trimester: women should be positioned slightly toward their left side with support under the right hip when receiving ECT to prevent a vena cava compression syndrome

1. Treatment of perinatal mood disorders aims to minimize fetal/neonatal exposure to both maternal mental illness and medication

2. Nonpharmacologic interventions should be a key component of the treatment plan

3. Use what has worked in the past (Single exception: valproate in pregnancy)
Resources

• Pregnancy
  – www.reprotox.org
  – www.motherisk.org

• Lactation
  – www.medsmilk.com
Questions?