OH BABY!
MY PATIENT IS PREGNANT

REPRODUCTIVE SAFETY OF PSYCHOTROPIC MEDICATIONS
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OBJECTIVES
• Identify risks of untreated maternal depression on the fetal and/or infant, child, family, relationships.
• Describe treatment options for perinatal depression and postpartum psychosis.
• List three risks to consider when treating pregnant and lactating women with psychotropic medications.

50% of pregnancies are UNPLANNED

“Are you sexually active?”
“What are you using for birth control?”
“Are you considering a pregnancy in the upcoming year?”

EFFECTS OF UNTREATED MATERNAL DEPRESSION

RISKS TO PREGNANCY AND FETUS
• Poor adherence to prenatal care
• Poor nutrition and self-care
• Substance use
• Increased fetal cortisol
• Preeclampsia
• Preterm labor
• Low birth weight

RISKS TO MOM, INFANT, CHILD, FAMILY
• Increased irritability/inconsolability of newborn
• Disturbed maternal-infant attachment
• Damaged stress responses
• Failure to thrive
• Behavior/learning/cognitive delay
• Stress on couples’ relationship –
  • (PPD risks to partners, as well)
  • Suicide/homicide

Myth #1

“______” COMES NATURALLY.
Fill in with any of the following childbearing tasks:
- Conception
- Carrying a pregnancy to term
- Birthing
- Breastfeeding
- Parenting

I had an epidural. Then I had a C-section. Then my baby wouldn’t nurse so I fed her from a bottle. And now I’m sitting here at the playground wondering what all the guilt was about because my kid is just as weird as yours.
sKIDmarking.com

THE STILL FACE EXPERIMENT – DR. EDWARD TRONICK

A mother denies her baby attention for a short period of time.

Prolonged lack of attention can move an infant from good socialization, to periods of bad but repairable socialization.

In “ugly” situations the child does not receive any chances to return to the good, and may become stuck.
POSTPARTUM DEPRESSION IS THE MOST COMMON COMPLICATION OF CHILDBIRTH

1 in 7 women suffers from PPD
Up to 50% of women with PPD are never detected
Women who have one episode of PPD have a 50% chance of recurrence in a subsequent pregnancy
Suicide accounts for ~20% of postpartum deaths
2nd most common cause of mortality in PP women

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"MOMMY BRAIN" aka NEUROPLASTICITY

• Oxytocin → Fall in LOVE
  • Brain derived neurotrophic factor (BDNF)
    • Triggers massive neuronal reorganization
    • Tons of brain cells need to be obliterated and replaced with new ones
    • Allows for erasing learned behavior and replacing it with new patterns
      - Learning to feed, protect, care for offspring
      - Store learned and emotional memories to recall potentially threatening behaviors
      - Affects our spatial learning — important for our ancestors to recall where food was located when foraging

Perinatal Mood and Anxiety Disorders

Postpartum Depression
Anxiety Disorder
OCD
PTSD

Genetics
Hormones
Neurotransmitters
Thinking Styles
LIFE STRESS
Scary Thoughts

BIOPSYCHOSOCIAL MODEL OF ANXIETY — CHILDBEARING

PERINATAL DEPRESSION SCREENING

"SCARY THOUGHTS" VS "PSYCHOSIS"

• The majority of both mothers (91%) and fathers (88%) report intrusive thoughts about their baby at some point following the baby’s birth (Kleinman, 2006)
• Message … you are telling the mother that to some extent you expect this level of distress and understand the internal struggle.

Thought of harming the infant in some way
WITHOUT THE INTENT TO DO SO
Are very common in postpartum anxiety


Postpartum "Baby Blues"
ASSESSING FOR POSTPARTUM PSYCHOSIS

- Personal or Family history of bipolar illness or psychosis?
- Talking or acting in a strange manner?
- Unusually quiet and withdrawn, or speaking rapidly w/ difficulty focusing or concentrating?
- Auditory or visual hallucinations – claiming to see or hear things that others do not?
- Suspicious or paranoid – others out to get her
- Decreased need for sleep or food
- High degree of confidence
- Exaggerated sense of capabilities or self-worth?
- Feel/appear abnormally hyperactive with racing thoughts and/or behaviors?

ADDRESS AND RULE OUT OTHER MEDICAL OR PSYCHOLOGICAL ETIOLOGY

- Bipolar disorder
- Psychotic illness/schizoaffective disorder
- Thyroid disorder
- Diabetes
- Autoimmune disorders
- Vitamin deficiencies (Vit D)

Rule out medical conditions that might precipitate psychosis:
- Toxicology screen
- CME/T
- TSH
- B12, Folate

TREATMENT STRATEGIES

- Cognitive Behavioral Therapy
- Exercise, Yoga, Mindfulness/Meditation
- Omega 3 Fatty Acids
- Acupuncture
- Complementary Alternative Medicine

“BUT…. WILL IT HURT MY BABY?”

- No decision during pregnancy is risk free
- Consider both pharm and non-pharm to options
- Psychotherapy in addition to pharmacotherapy and/or as an alternative when clinically appropriate

BUT... WILL IT HURT MY BABY?

“The safest medication in pregnancy is the one that allows for full remission of symptoms of anxiety/depression.”

BALANCING THE RISKS

UNTREATED DEPRESSION IN PREGNANCY
- Postpartum depression affects 1 in 8 births
  - Pre-eclampsia
  - 50% increased risk of developmental delay at 18 months
  - Poor self care
  - Impaired bonding with baby

ANTIDEPRESSANT USE IN PREGNANCY
- Women with a history of depression of the newborns (PPHN) – low absolute risk
  - Premature birth
  - Truncated maternal withdrawal
  - Long term developmental delay – data mostly reassuring
- Majority of evidence does not suggest association of increased risk of birth defects above the baseline

METABOLISM OF PSYCHOTROPIC MDS IN PREGNANCY AND LACTATION

- Lower psychotrophic drug levels
- Decreased clinical effectiveness
- Increased drug elimination

- Sex steroids increase CYP450 activity
- Plasma volume changes in protein binding
- Slower gastric emptying
- Renal blood flow
Women trying to conceive - history of MDD:
- Encourage period of euthymia
- Sustained remission - may consider tapering and discontinuing
- More recently depressed or with symptoms: consider remaining on medication, optimizing medication

Mild - moderate MDD - psychotherapy first line tx
- Lifestyle components - nutrition, weight management, prenatal care, childbirth education
- Treatment for substance abuse
- Document all exposures dating back to conception

Pregnant women with severe MDD: medication first-line

Pregnant women on antidepressants during pregnancy:
- take into account patient preferences, previous course of illness
- Medication selection should be based on known safety information

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Does this make the patient or prescriber feel better???
- Discontinuation of antidepressants near conception
- Using a lower antidepressant dose in pregnancy
- Switching to sertraline in pregnancy/postpartum
- Try supplements or alternative therapies

Antidepressant risks maternal/fetal risks to consider
- SSRIs as a group do not increase risk of congenital malformations above baseline risk of 2-4%
- Gestational age decreased by ~4-7 days, SGA, lower birth weight
- similar risks for exposure to untreated vs. meds
- Miscarriage
- SSRI related ventricular outflow defects, craniosynostosis, omphalocele
- extremely small risk
- not replicated in other studies

Does this make the patient or prescriber feel better???
- Stop breastfeeding or defer antidepressant treatment
- Counseling mothers to pump and dump
- Use of non-benzodiazepine sedative hypnotics

Perinatal sleep strategies
- Make sleep a priority
- Establish a sleep plan in pregnancy - Postpartum Planning (DONA)
- Enlist the entire family
- Treat mood and anxiety disorders
- SSRIs - generally very safe overall as a class
- TCA's are very best line for severe anxiety
- Mood stabilizers:
- Stabilize mood by preventing the highs and lows of the disorder
- Depakote and Tegretol - safe for BF but NOT during pregnancy
- Antipsychotic meds:
- Used to treat psychotic illness, bipolar disorder, and sometimes to tx severe depression or treatment-resistant OCD. Haldol can be used in BF mothers when necessary
- Zyprexa, Seroquel, Abilify have been used in pregnancy and BF, but R/B need to be weighed carefully.
- Anti-anxiety: benzodiazepines quickly relieve symptoms. Should be used temporarily and primarily when the antidepressant is taking effect
- Sleep Meds: Ambien, Trazodone, low dose clonazepam - safe in BF and short term use.
- Prenatal benzodiazepine exposure increased the risk of oral cleft, although no studies have confirmed it.
DOES THIS MAKE THE PATIENT OR PRESCRIBER FEEL BETTER?? – change to a “category B label” drug

PREGNANCY:
Dosing
Impact on fetus
Registry information

LACTATION:
Amount of drug in breast milk
Potential effects, if any

FEMALES AND MALES OF REPRODUCTIVE POTENTIAL:
Pregnancy testing
Contraception
Fertility related to the drug

MARIJUANA USE IN PREGNANCY

- Number of Americans age 12 or older who regularly used marijuana:
  - 5.8% in 2007
  - 17.3% in 2012
- Younger/socioeconomically disadvantaged women: 15-28%
- Estimated that half of female marijuana users continue using during pregnancy

LIMITATIONS OF RESEARCH

- Retrospective studies
- Confounding biases
- Correlation does not equal "causation"

FDA Labeling of Drugs
- A, B, C, D, X

OPIATE USE DISORDER IN PREGNANCY

- Medication metabolism rate increases as pregnancy progresses
  - Split methadone dosing from once to twice daily
- Metabolism is accelerated in pregnancy = Larger clearance of medication
  - Factors to consider in treatment plan if pregnant women returns to substance use:
    - Environmental/social support/basic needs/personal safety factors
    - Stage of pregnancy – pharmacokinetics
    - Potential interactions changing metabolism of the opioid contributing to relapse

PREGNANCY AND BIPOLAR DISORDER

MED MANAGEMENT GUIDELINES

- Folate supplementation is advised
- Medication should be avoided if clinically feasible
- Avoid abrupt discontinuation
- Comprehensive antepartum counseling should begin at least 3 months before pregnancy
  - Comprehensive antepartum counseling should begin before and be continued throughout pregnancy, replacing
  - Comprehensive postpartum counseling
  - Avoid changing effective medications unless there is significant safety or clinical advantage
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DISCONTINUE MEDS OR MOOD RELAPSE ??

Risks of alternative treatment
- Failure to respond to emergency Rx
- Neurodevelopmental risks
- Congenital malformation
- More severe mood relapse
- Impulsive behavior
- Substance use
- Poor care (inpatient)
- Difficulty bonding
- Hospitalization

Risks of continuing mood stabilizer
- More mood relapse
- More severe mood relapse
- Impulsive behavior
- Substance use
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- Hospitalization
DISCONTINUATION OF LITHIUM DURING PREGNANCY?

- Lithium 0.05 – 0.1% Ebstein’s anomaly w/ 1st trimester exposure

Mood stabilizer considerations

- Preconception: 3 months prior - folic acid supplementation
- Valproic acid – 1-4% rate of NTD, high rate of impaired neurocognitive development
- Carbamazepine: 1% risk of NTD
- Lamotrigine: no risk of congenital anomalies after antenatal exposure
- Conflicting reports on oral cleft defects

ANTIEPILEPTICS AND MOOD STABILIZERS

LITHIUM
- May be associated with a small increase in congenital cardiac malformations
- Physiologic alterations of pregnancy may affect pharmacokinetics of lithium

DEPABAKTE
- Risk of fetal anomalies, neural tube defects, fetal valproate syndrome, and long-term adverse neurocognitive effects.
- Avoid in pregnancy, if possible, especially during the first trimester

LAMICITAL
- Overall risk for malformations with lamotrigine = 2.7% across several studies
- Potential maintenance therapy option for pregnant women with bipolar disorder
- Pregnancy increases lamotrigine clearance by 50%

TEGRETOL
- Associated with fetal carbamazepine syndrome. Risk of neural tube defect
- Avoid in pregnancy, if possible, especially during the first trimester

BREASTFEEDING CONSIDERATIONS AND MEDS

- Most SSRIs and TCAs have not been associated with health problems for breastfeeding infants
- Fluoxetine has been reported to accumulate in infants (longer half-life)
- Consider alternatives as a 1st line treatment unless the patient has a history of good response to this drug

ADHD PSYCHOSTIMULANT USE IN PREGNANCY AND LACTATION

- If discontinuing a psychostimulant:
  - Evaluate the severity of impact on executive functioning skills.
- If continuing a psychostimulant:
  - Discuss the possible risk of intrauterine growth restriction.
  - Measure growth by third trimester ultrasound.
- If one changes to a “safer” med (TCA, bupropion), and the medication is NOT therapeutically managing the mother’s symptoms:
  - Re-evaluate
  - Is it worth it to stay on that alternative med for the remainder of the pregnancy?
SCHIZOPHRENIA

Nearly double the risk of perinatal complications to that of general population:
- Higher rate of operative delivery, NICU admission, neonatal morbidity
- Marked impairments in multiple areas
- Serious/Disabling PMD symptoms
- Social Support system

Considerations: metabolic effects, blood dyscrasias, movement disorders

High potency 1st generation antipsychotics preferred to low potency

2nd generation antipsychotics less studied
- Overall no increased risk of congenital anomalies
- Considerations: metabolic effects, blood dyscrasias, movement disorders

INTEGRATIVE CARE MODELS

addresses barriers related to

Szego
Fear of losing parental rights

Lack of obstetric provider training in clinical aspects of depression care and communication skills

Lack of standardized processes for depression care

Lack of specialized reproductive psych providers

Lack of specialized referral networks

Inadequate capacity for follow-up and care coordination

KEY POINTS:
PHARMACOLOGICAL TREATMENT OF PERINATAL WOMEN

1. Avoid discontinuing meds that provide psychiatric stability
2. Previously effective meds
3. Carefully substitute less teratogenic agents if necessary
4. Dose requirements may be higher in the second half of pregnancy

MOTHER-BABY MENTAL HEALTH
INTENSIVE OUTPATIENT PROGRAMS

- Program or Placebo (up to 1-3 yrs)
- Serious/Disabling PMD symptoms
- Marked impairments in multiple areas
- Not imminently dangerous to self/other
- Can function outside of 24/7 care
- Social Support system
- Readiness for change (reluctant participants in program)

QUESTIONS?

REFERENCES


American Academy of Child Psychiatry, 17, 568.


