UNIVERSITY of WASHINGTON
PSYCHIATRY & BEHAVIORAL SCIENCES
School of Medicine

PSYCHOPHARMACOLOGY FOR DEPRESSION DURING PREGNANCY AND POSTPARTUM

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Neuropsychotropic Drug Therapy
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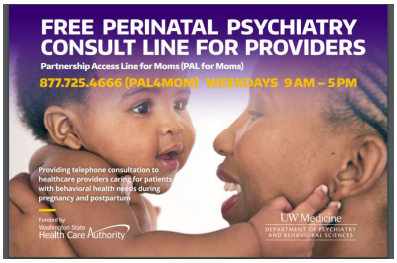
DISCLOSURES



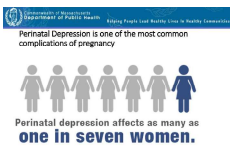
OUTLINE

- Overview of perinatal depression
- Principles of prescribing antidepressants in the perinatal period
- Pharmacological treatment of perinatal depression

Perinatal Depression

PREVALENCE

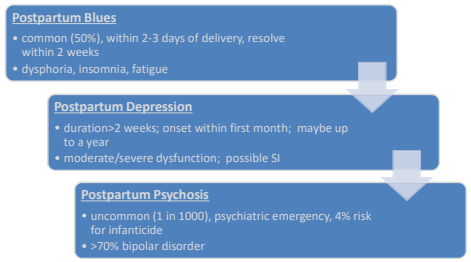
- Depression during pregnancy - 7-13 %
- Postpartum depression (PPD) - up to 20%
- Less than 20% receive treatment



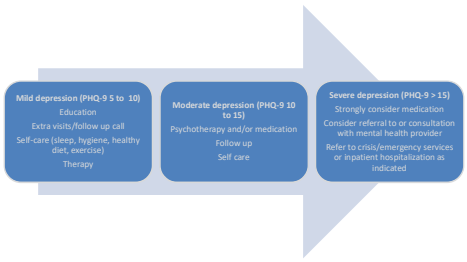
SCREENING

- Screening Tools
  - EPDS
  - PHQ-2, PHQ-9
  - GAD-7
- Screening Frequency
  - ACOG: at least once during perinatal period
  - AWHONN: screen in pregnancy and postpartum
  - AAP: well child visits at 1,2,4 and 6 months
  - USPSTF: at least once during and after pregnancy
  - NICE: up to 12 months postpartum

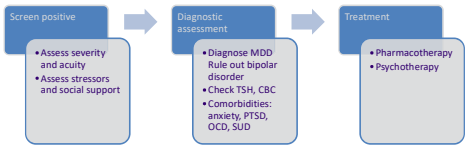
THE CONTINUUM OF PP MOOD CHANGES



TREATMENT OPTIONS



WHAT HAPPENS AFTER A POSITIVE SCREEN?



Prescribing in the Perinatal Period

COMMON QUESTIONS IN INFORMED CONSENT DISCUSSIONS

- Do I have to stop taking my psychiatric medication while pregnant? If I do what is the chance of my mental health getting worse?
- If I keep taking the medication, what are the risks to my baby?
- How might my condition and its treatment affect parenting?
- What are the chances of my mental health affecting my child's mental health?

RULES OF THUMB IN PRESCRIBING FOR PERINATAL MENTAL HEALTH DISORDERS

- Thorough diagnostic evaluation including an understanding of patients responses to previous treatments
- Understanding patient's treatment goals, concerns and constraints (financial, time)
- Prescribe only when clearly indicated and with a strong evidence base
- Changes to meds to be made before pregnancy if possible
- Ideally patient should be psychiatrically stable for at least three months before attempting to conceive
- Use medications with more safety information
- Minimize number of exposures
- Use a team approach
- Be supportive if the patient goes against your recommendations
- Recommend folic acid prenatally.
- Don't forget non – medication factors!

Chisolm et al 2016

PSYCHOTROPICS AND LACTATION

RISK – RISK ASSESSMENT

Risks of untreated depression

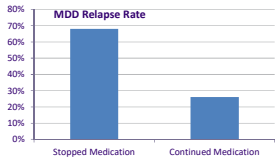
Parent:
Less engagement in prenatal care
Smoking & substance use
Suicide
Child:
LBW, PTB
Emotional and behavioral disorders
Higher rates of mortality in the first year
Increased depression risk through adolescence

Alternatives

Risks of antidepressants

PPH
PPHN
NAS
Unknown risks

RISK OF RELAPSE



Cohen et al, 2006; Bayrampour et al, 2020

Prescribing during pregnancy and breastfeeding

CASE 1

- 35 yo married female G1 at 16 weeks gestation presents with severe depression, PHQ-9 of 21, no suicidal ideation. She has had 5 depressive episodes in the past, one leading to psychiatric hospitalization for suicidal ideation. She tells you she did respond to sertraline and did not tolerate citalopram. What would you advise?

CASE 1 - CONTD

- 35 yo married female G1 at 16 weeks gestation presents with severe depression, PHQ-9 of 21, no suicidal ideation. She has had 5 depressive episodes in the past, one leading to psychiatric hospitalization for suicidal ideation. She tells you she did not respond to sertraline and did not tolerate citalopram. What would you advise?
  1. Psychotherapy
  2. Higher dose of sertraline
  3. Venlafaxine
  4. Vortioxetine

SSRIS IN PREGNANCY

- Sertraline – most safety data available
- No consistent evidence for increased risk of malformations (?paroxetine)

PERSISTENT PULMONARY HYPERTENSION

- Meta-analysis, 11 studies, 156,978 exposed women
- 1.8/1000 vs 2.9/1000
- NNH = 1000
- Lowest risk with sertraline

SSRI	Placental Passage	P Score
Sertraline	30%	0.83
Escitalopram	50%	0.69
Paroxetine	-	0.49
Citalopram	70%	0.21
Fluoxetine	65%	0.16

Masarwa et al, 2018

NEONATAL ADAPTATION SYNDROME

- 30% of SSRI-exposed babies
- High-pitched cry, sleep disturbance, tremor, hypertonicity/myoclonus, tachypnea, gastrointestinal symptoms, seizures
- Peaks within 2 days after birth, resolves in about 4 days
- Worse with SSRI + benzodiazepine
- Reducing dose in 3rd trimester does not prevent PNAS

Moses Kolko 2005, Warburton 2010

LONGER TERM EFFECTS ON CHILDREN

- Physical outcomes (5 studies - asthma, cancer, BMI, epilepsy): conflicting associations for BMI.
- Neurodevelopmental outcomes (18 studies - cognition, behavior, IQ, motor development, speech, language, and scholastic outcomes): no consistent associations
- Psychiatric outcomes (11 studies: ASD, ADHD, affective disorders): associations with affective disorder

Rommel et al 2020

OTHER ANTIDEPRESSANTS

Venlafaxine and Duloxetine

- Similar risks as SSRIs but fewer data
- No increased risk of major malformations
- Small but statistically significant increase in risk for postpartum hemorrhage
- PNAS similar to SSRIs

Mirtazapine

- No increase risk in major fetal malformations, limited data
- Conflicting reports of increase in spontaneous abortion, preterm birth and low birth weight
- Good choice for severe hyperemesis gravidarum

Huybrechts et al, 2020

CASE 2

- 37 yo G1P1 at 2 weeks PP, is breastfeeding, scored 20 on her EPDS, and reports smoking 10 cigs a day, wants to stop. She has no past history of depression but meets criteria for MDD currently. What would you recommend?

CASE 2 – CONTD

- 37 yo G1P1 at 2 weeks PP, is breastfeeding, scored 20 on her EPDS, and reports smoking 10 cigs a day, wants to stop. She has no past history of depression but meets criteria for MDD currently. What would you recommend?
  1. Sertraline
  2. Bupropion
  3. Sertraline + NRT
  4. Therapy + NRT

OTHER ANTIDEPRESSANTS - BUPROPION

- Limited published data
- During pregnancy:
  - No overall increase in risk of congenital malformations
  - Inconsistent results about association with heart defects (specifically left ventricular outflow tract obstruction
    - If real, 2 to 3 times higher than expected
    - Absolute risk small at 2.1-2.8 per 1,000 births
  - Lowers seizure threshold: possible risk in women with preeclampsia
- Postpartum:
  - One report of a possible seizure in a nursing infant whose mother was taking bupropion.
  - If bupropion is required by a nursing mother for either smoking cessation or depression treatment, no reason to avoid or discontinue

Turner et al, 2019

ANTIDEPRESSANTS IN LACTATION

- Most SSRIs RID < 10; Sertraline safest
- Isolated adverse events: uneasy sleep, colic, irritability, poor feeding, drowsiness
- Higher levels in breastmilk:
  - Citalopram, fluoxetine, venlafaxine
- Venlafaxine, duloxetine, mirtazapine
  - low to variable infant plasma levels, RID <10, no acute adverse effects
  - newborn and preterm infants: monitor for sedation and adequate weight gain

BREXANOLONE

- Approved by the FDA 3/19/19 for postpartum depression in adult women
- Allosteric modulator of GABAA receptors; Formulation of allopregnanolone
- 60-hour IV infusion
- Risk Evaluation and Mitigation Strategy (REMS)
  - Pulse oximetry
  - Certified health care facility
- Zuranolone in the works

CASE 3

- 35 yo married female G1 at 16 weeks gestation presents with severe depression, PHQ-9 of 21, no suicidal ideation. She has had 5 depressive episodes in the past, one leading to psychiatric hospitalization for suicidal ideation. She tells you she did not tolerate sertraline or citalopram. You started her on venlafaxine. On further questioning, she also reports that she has 2 – 3 panic attacks a day and asks for medication to control these as they are very impairing. What would you do?

BENZODIAZEPINES IN PREGNANCY AND LACTATION

- Withdrawal symptoms with rapid taper
  - Case reports of panic attacks, miscarriage
- All BZs independently associated with increased risk of SA (range of adjusted ORs, 1.13-3.43).
  - Dose-response relationship
- Concurrent use with antidepressants may be associated with an increased risk of malformations (OR 1.4, CI 1.09 to 1.8)
- Neonatal "floppy infant" – hypotonia, hypothermia, low APGAR scores, lethargy
- Breastfeeding
  - Concerns about sedation
  - Lorazepam – short-acting, lower transmission into breast milk

Grogoriadis et al, 2019; Sheehy et al, 2019

OTHER ANXIOLYTICS

Medication	Pregnancy	Lactation
Hydroxyzine	No major malformations	Higher doses may cause decreased milk supply or infant sedation
Propranolol	± IUGR; neonatal bradycardia and hypoglycemia	Few studies, no adverse events
Trazodone	Limited data; no evidence of congenital malformation	Limited data; low levels in milk; no adverse effects especially in infants>2 months old and maternal dose < 100 mg
Buspirone	Limited data; no evidence of cong malformations	Limited data; low levels in breastmilk
Prazosin	Limited data; use with caution especially in normotensive women	No data
Gabapentin	Limited data; no evidence of congenital malformations	Limited data, maternal doses of gabapentin up to 2.1 grams daily produce relatively low levels in infant serum.
Pregabalin	Limited data; ?congenital malformations	Limited data, but amounts in breastmilk are low

OTHER HYPNOTICS

Medication	Pregnancy	Lactation/development
Diphenhydramine	Inconsistent reports of malformations	Drowsiness, irritability in breastfed babies
Doxylamine	No increase in malformations	Sedation, irritability with lactation; no effects on development at 3-7 yo
Mirtazapine	Not expected to inc rate of malformations	Only 9 reports; small amounts in breast milk
Trazodone	Not expected to inc rate of malformations	Small amounts in breast milk; limited information
Zaleplon	Limited information; no reports of malformations	Limited information
Zolpidem	Not expected to inc rate of malformations. ? Inc rate of PTB and LBW	Limited information

CASE 4

- 30 yo female presents for preconception counseling on 40 mg citalopram and 5 mg aripiprazole. She has a history of recurrent MDD, most recent episode one year ago, with a suicide attempt. Her symptoms have been in remission for 6 months and she would like to conceive in the next few months. What would you advise?

CASE 4 – CONTD

- 30 yo female presents for preconception counseling on 40 mg citalopram and 5 mg aripiprazole. She has a history of recurrent MDD, most recent episode one year ago, with a suicide attempt. Her symptoms have been in remission for 6 months and she would like to conceive in the next few months. What would you advise?
  1. Taper and stop aripiprazole, continue citalopram
  2. Taper and stop both aripiprazole and citalopram; start sertraline
  3. Taper and stop both medications and recommend psychotherapy as she is in remission
  4. No changes to medication regimen

SECOND GENERATION ANTIPSYCHOTICS AND MALFORMATIONS

- No increased risk: Aripiprazole, Olanzapine, Quetiapine
- Minor increased risk: Risperidone, Paliperidone
- Insufficient data: Amisulpiride, Asenapine, Lurasidone, Sertindole

ANTIPSYCHOTICS AND BREASTFEEDING

- Most data available for olanzapine and quetiapine
- Low levels found in breastmilk for maternal dosages upto 40 mg / 400 mg
- Watch for sedation
- Ask about co sleeping

ANTIDEPRESSANTS IN PREGNANCY AND POSTPARTUM: TAKE HOME POINTS

- Consider the risk of untreated depression when making treatment decisions
- SSRIs are generally considered first-line in pregnancy
- Consider using an antidepressant which worked well in the past
- Avoid changing antidepressants once the woman is pregnant (to minimize the number of exposures for the baby and prevent relapse)
- Avoid tapering antidepressants in the third trimester

RESOURCES

- Patient information brochure https://www.nimh.nih.gov/health/publications/perinatal-depression/index.shtml
- Perinatal Support Washington: http://perinatalsupport.org/
- UW PAL for Moms Perinatal Psychiatry Consultation Line https://www.mcmh.uw.edu/ppcl
- UW PAL for Moms Care Guide https://www.mcmh.uw.edu/care-guide
- Reprotox: www.reprotox.org
- Lactmed: https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm
- MGH Center for Women's Mental Health: https://womensmentalhealth.org/

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