POSTPARTUM DEPRESSION (PPD)

FLAME LECTURE: 134

TOOHEY / BURNS 9.7.23

LEARNING OBJECTIVES

- Identify risk factors for postpartum blues and depression
- Differentiate between postpartum blues and depression
- Describe treatment options for postpartum blues and depression
- Recognize appropriate treatment options for mood disorders during lactation
- Prerequisites:
  - NONE
- See also – for closely related topics
  - FLAME LECTURE 39 – Depression in Pregnancy
  - FLAME LECTURE 235 – Depression in Women
  - FLAME LECTURE 135 – Postpartum Psychosis

POSTPARTUM PSYCHIATRIC DISEASE

- Postpartum Blues
  - 60-80% of all postpartum patients may feel depressed, anxious, or even angry in the days following delivery
  - Self-limiting
  - Supportive Care; no medication required
  - Typically regress within 2 weeks)
  - However, 20% will progress to major depression
  - Irrespective of whether postpartum blues progresses to depression, for how common this condition occurs, it is not discussed enough, normalized, and validated with our patients and in society at large

POSTPARTUM PSYCHIATRIC DISEASE

- Postpartum Depression (*formally called MDD with peripartum onset*)
  - The single most common complication of pregnancy and postpartum!
    - 10-15% of postpartum women
  - DSM V criteria
    - Symptoms present for most of the day almost every day for > 2 weeks which causes clinically significant distress or impairment in social, occupation, or other areas of functioning
    - Depressed mood, loss of interest or pleasure, AND 4 of the following:
      - Changes in appetite/weight, sleep and psychomotor activity, decreased energy, feelings of worthlessness/guilt, difficulty thinking, concentrating, or making decisions, recurrent thoughts of death or suicide, plans or attempts.
- Postpartum Psychosis (FLAME LECTURE 135)
  - Most commonly, an untreated bipolar disorder

RISK FACTORS[1,2]

MAJOR RISK FACTORS:

- History of prior psychiatric or psychological problems
  - The strongest predictor of PPD is the presence of depression and anxiety during pregnancy
- History of postpartum depression
  - Recurrence risk of 30%
- Life events
  - Death of a loved one, divorce, loss of job, moving
- History of physical or sexual abuse, or current IPV
- Teenagers – incidence of PP Depression can be as high as 26%

RISK FACTORS[1,2]

MODERATE RISK FACTORS

- Peripartum traumatic events
  - Emergent C/S, operative delivery, postpartum hemorrhage, AFE, etc.
- Personality characteristics – nervous, shy, self conscious, low self esteem, pessimistic, poor coping skills
- Relationship problems
- Family History of Depression or PPD

RISK FACTORS[1,2]

THYROID HORMONES AND DEPRESSION RISK

- Conflicting studies regarding relationship
- 4-10% of postpartum pts have transitory thyroid dysfunction
- However, Hypo-/Hyperthyroid states can mimic depression, mania, & psychosis
  - In individual cases, it is reasonable to screen for thyroid function

SCREENING – *Edinburgh Postnatal Depression Scale*

In the past 7 days:

1. I have been able to laugh and see the funny side of things	5. I have felt scared or panicky for no very good reason	*9. I have been so unhappy that I have been crying
☐ As much as I always could ☐ Not quite so much now ☐ Definitely not so much now ☐ Not at all	☐ Yes, quite a lot ☐ Yes, sometimes ☐ No, not much ☐ No, not at all	☐ Yes, most of the time ☐ Yes, quite often ☐ Only occasionally ☐ No, never
2. I have looked forward with enjoyment to things	*6. Things have been getting on top of me	*10 The thought of harming myself has occurred to me
☐ As much as I ever did ☐ Rather less than I used to ☐ Definitely less than I used to ☐ Hardly at all	☐ Yes, most of the time I haven't been able to cope at all ☐ Yes, sometimes I haven't been coping as well as usual ☐ No, most of the time I have coped quite well ☐ No, I have been coping as well as ever	☐ Yes, quite often ☐ Sometimes ☐ Hardly ever ☐ Never
*3. I have blamed myself unnecessarily when things went wrong	*7. I have been so unhappy that I have had difficulty sleeping	Scoring: QUESTIONS 1, 2, & 4 (without an *) Are scored 0, 1, 2 or 3 with top box scored as 0 and the bottom box scored as 3. QUESTIONS 3, 510 (marked with an *) Are reverse scored, with the top box scored as a 3 and the bottom box scored as 0. Maximum score: 30 **Possible Depression: 10 or greater** Always look at item 10 (suicidal thoughts)
☐ Yes, most of the time ☐ Yes, some of the time ☐ Not very often ☐ No, never	☐ Yes, most of the time ☐ Yes, sometimes ☐ Not very often ☐ No, not at all	
4. I have been anxious or worried for no good reason	*8. I have felt sad or miserable	
☐ No, not at all ☐ Hardly ever ☐ Yes, sometimes ☐ Yes, very often	☐ Yes, most of the time ☐ Yes, quite often ☐ Not very often ☐ No, not at all	

TREATMENT[1]

- Medications:
  - GABA-A receptor positive allosteric modulators (PAMs)
  - SSRI and SNRIs
  - Tricyclic Antidepressants
  - Monoamine Oxidase Inhibitors
- Interpersonal Psychotherapy / Cognitive Behavioral Therapy:
  - Currently thought to be one of the most effective models for PPD given the importance of interpersonal relationships and role transitions in the peripartum period
  - Based on the premise that there are 4 problem areas
    - Grief, Role transitions, Interpersonal disputes, Interpersonal deficits
- Support Groups

TREATMENT[1]

- ECT (Electroconvulsive Therapy)
  - Safety has been demonstrated for many years in pregnancy
- Inpatient hospitalization
- Duration of treatment:
  - Treat for at least 6-12 months
  - Continue maintenance therapy if:
    - Pt has a history of 3 or more episodes of major depression
    - Previous episodes have been severe or prolonged
    - There is a coexisting anxiety disorder
    - Depression has an early or late onset
- Remember to counsel regarding future fertility plans

TREATMENT - *MEDICATIONS*

- Physicians often hesitate to prescribe psychiatric medications during pregnancy & lactation because of unknown effects of the medication on the fetus/infant
- But what about the risk of not treating—the risk of uncontrolled depression?
  - 68% of pregnant women who stop meds during or just prior to pregnancy relapse[3]
    - Usually during the 1st trimester
    - Rate is higher than non-pregnant women
  - Depression itself carries a higher risk for abnormalities in neonatal development
    - ↑ Preterm delivery: Children of mothers with MDD born at 35 weeks vs. 39.4 weeks[4]
    - ↓ motor maturity[4], ↓ head circumference[5], ↓ Apgars[5], ↑ Maternal self-harm[5]
    - Children of mothers with PPD suffer from lower cognitive and language function
  - Increased stress and depression *during* pregnancy cause hormonal changes in fetus
    - Increased cortisol[4], catecholamines, alter uterine blood flow
    - Associated with neuronal cell death and abnormal development of brain structures as well as sustained HPA dysfunction in the neonate
  - Anti-depressants typically take 2-6 weeks to become effective

TREATMENT[1]

- Medications:
  - Oral Zuranolone
    - FDA-approved in 2023; GABA-A receptor positive allosteric modulator (PAM)
    - The GABA system is the major inhibitory signaling pathway of the brain and CNS and contributes to regulating brain function (i.e., mood, arousal, behavior, cognition)
    - In two studies performed cited by the FDA, participants received zuranolone or placebo once daily for 14 days if symptoms if symptoms of depression began with 30 days of pregnancy, and showed improved symptoms on the HAMD-17 depression scale on both day 15 after treatment as well as Day 42
  - IV Brexanolone
    - FDA-approved in 2019; PAM for both synaptic and extrasynaptic GABA-A
    - Available through a restricted program called the REMS (risk evaluation and mitigation strategy) program in certified health care facilities
    - The IV infusion is for 60 hours straight one time
    - Studies found that there was immediate improvement after the infusion as well as sustained improvement in depression symptoms upon 30-day follow up

TREATMENT - *MEDICATIONS*

TCAs

- Imipramine, nortyptyline, amytriptyline
- Relatively non-selective
- Until recently were 1st line
- Have many side effects due to affinity to histamine, muscarinic & a-adrenergic receptors
- High overdose toxicity
- No increased risk for birth defects
- Good for women with frequent headaches
- Some neonatal withdrawal

MOIs

- Parnate, Nardil, and Marplan
- Require restricting tyramine containing foods
  - No ETOH, aged cheese, liver, orange pulp, smoked fish, packaged soups amongst many other food limitations
  - If not followed, can result in hypertensive crisis OR intracranial bleed
- Dangerous to use with a TCA
- High overdose toxicity
- Concern about ↓ uterine blood flow
- Possible ↑ risk for birth defects
- AVOID IN PREGNANCY

SSRIs

- SSRIs are not a major risk factor for infant malformations
  - Only paroxetine found to have increased risk for cardiac malformations
- In 2006 Public Health Advisory warning released regarding SSRI's increasing risk for Persistent Pulmonary HTN, but since then there have been conflicting studies and FDA advises not to change practice in prescribing SRI's

TREATMENT[1]

- Neonatal Withdrawal Syndrome[6]:
  - Most often associated with TCA's, most commonly after 3rd trimester exposure
  - Symptoms: neonatal tachycardia, cyanosis, tachypnea, clonus, irritability, feeding difficulties, temperature instability
  - Usually self-limited, encourage breastfeeding

TREATMENT – *MEDICATIONS*[6]

ANTIDEPRESSANT MEDICATIONS			
Generic Name	Brand Name	Pregnancy Risk Category	Lactation Risk Category
TCA's			
Amitriptyline	Elavil, Endep	C	L2
Amoxapine	Asendin	C	L2
Clomipramine	Anafranil	C	L2
Desipramine	Norpramin	C	L2
Doxepin	Sinequan/Adaptin	C	L5
Imipramine	Tofranil	C	L2
Maprotiline	Ludiomil	B	L3
Nortriptyline	Pamelor/Aventyl	C	L2
Protriptyline	Vivactil	C	N/A
SSRI's			
Citalopram	Celexa	C	L3
Escitalopram	Lexapro	C	L3*
Fluoxetine	Prozac	C	L2*
Fluvoxamine	Luvox	C	L2
Paroxetine	Paxil	D	L2
Sertraline	Zoloft	C	L2

Remember, physiologic changes during pregnancy affect pharmacology:

- 50% increase in blood volume by 24-26 weeks
- Glomerular filtration rate increases by 50% in the second trimester
- Therefore, adjustments in doses of medications during pregnancy are often necessary

TREATMENT – *DURING LACTATION*

- Tricyclics or metabolites have not been detectable in breast milk
- Fluoxetine - low levels detected
- Sertraline - no levels detected, no data on metabolites
- Buproprion - no levels detected
- Dose infant is exposed to is much less than during pregnancy
  - An infant would need to breastfeed exclusively for 2 years to accrue the level of exposure during one month of pregnancy
  - Infants have comparable level of metabolic enzymes with adults
- Metoclopramide: often prescribed to ↑ milk production but has a risk of exacerbating depression in patients with a history of mental illness

IMPORTANT LINKS

- ACOG Practice Bulletin 92, April 2008 ("Use of Psychiatric Medications during Pregnancy and Lactation")

1. UpToDate.com
2. Robertson, et al, *Gen Hospital Psychiatry*, 2004
3. Cohen et al, *JAMA*, 2006
4. Marcus, et al, *Psychiatry*, 2006
5. Kurki, et al, *ObGyn*, 2000