FLAME LECTURE: 40B

TOOHEY / BURNS 12.20.15

Learning Objectives

- Describe how certain medical conditions affect pregnancy
- Describe how pregnancy affects certain medical conditions
- Recognize appropriate treatment options for mood disorders during pregnancy
- Prerequisites:
  - NONE
- See also – for closely related topics
  - FLAME LECTURE 39 – Depression in Pregnancy
  - FLAME LECTURE 40A – Anxiety in Pregnancy
  - FLAME LECTURE 134 – Postpartum Depression
  - FLAME LECTURE 235 – Depression in Women
  - FLAME LECTURE 135 – Postpartum Psychosis

Bipolar Disorder - REVIEW

MANIA	HYPOMANIA
Lasts ≥7days	Symptoms for >4 days
Severe social/ occupational impairment	No social/occupational impairment
May require psych hospitalization	No hospitalization
May have psychotic features	No psychotic features

COMMON SYMPTOMS

DIGFAST
Distractibility
Insomnia
Grandiosity
Flight of ideas
Activity/agitation
Speech (pressured)
Thoughtlessness

Bipolar Disorder - Introduction

- Bipolar I = presence of manic episodes with or without depressive episodes
- Bipolar II = presence of hypomanic and depressive episodes *without* any mania
- Bipolar disorder cycles between depressive episodes and manic or hypomanic periods
  - Pregnancy tends to precipitate an increase in depressive episodes while postpartum can feature either an increase in episodes of depression or mania
  - There is also a higher risk of postpartum *psychosis* in patients with preexisting bipolar disorder
- Due to a significant overlap in symptoms, perinatal risks are similar between bipolar disorder and major depressive disorder in pregnancy **(see FLAME 39)**
  - Patients with bipolar disorder tend to have more severe disease comorbidities and complications than women with MDD, including substance abuse, psychiatric hospitalizations, and multiple psychiatric diagnoses
  - Likewise, they are more likely to have an psychiatric hospitalization during pregnancy

Risk factors for relapse:

- Short period of stability before conception
- Unplanned pregnancy
- Discontinuing medications from 6 months prior to pregnancy through the first trimester
- Current psychiatric symptoms
- Bipolar disorder diagnosis ≥ 5 yrs ago
- History of at least one mood episode/yr
- History of relapse during prior pregnancy

Relapse timing[1]:

- 1st trimester – 66.6%
- 2nd trimester – 23.8%
- 3rd trimester – 9.5%

Clinical Consequences - Maternal

- Non-adherence to prenatal care
- Increased usage of tobacco, alcohol, and drugs
- Poor appetite and poor weight gain
- Insomnia and Anxiety
- Worsening of depression (which may lead to development of psychotic symptoms)
- Suicidal ideation and behavior
- Not initiating breastfeeding
- Impaired maternal-infant bonding
- Postpartum depression or psychosis

Clinical Consequences - Neonatal

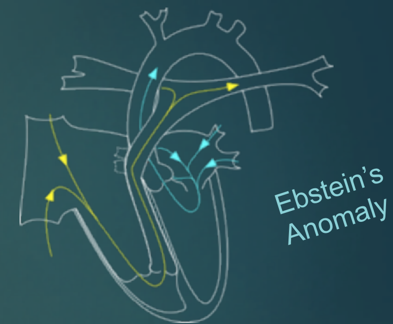
- Poses higher risk for abnormalities in neonatal development
  - Higher rate of preterm birth (similar risk with MDD)
  - BPD associated with large for gestational age fetuses where as MDD associated with small for gestational age
  - Higher cord blood cortisol levels[1], lower motor maturity[1], smaller head circumference[3], lower Apgars[3], maternal self harm[3]
- Increased stress and depression during pregnancy cause hormonal changes in fetus
  - Increased cortisol and catecholamines may alter uterine blood flow
  - Associated with dysregulation of the HPA axis, neuronal cell death, and abnormal development of fetal brain structures as well as sustained HPA dysfunction in the neonate
  - Increase in uterine irritability

BPD Treatment – *Medications*[1,4]

- Physicians often hesitate to prescribe or continue psychiatric medications during pregnancy because of unknown effects of the medication on fetal development. However, not treating poses serious risks as mentioned above—especially for relapse!
  - Relapse of bipolar disease is highest risk with abrupt discontinuation of medications

BPD Treatment – *medications*[1,4]

- Lithium:
  - The classic fetal anomaly risk is for Ebstein's Anomaly (cardiac anomaly with tricuspid valve leaflets displaced into right ventricle)
    - While lithium is known to increase the risk for Ebstein's anomaly, the overall risk is still very low (1/20,000 -> 1/1000) and this increased risk is significant only in the *first trimester*
  - Lithium has also been associated with: hypoglycemia, nephrogenic diabetes insipidus, polyhydramnios, reversible changes in thyroid function, premature delivery, and floppy infant syndrome
  - Recommendations:
    - Mild disease: taper lithium before conception
    - Severe episodes but low risk for relapse: taper lithium before conception and restart lithium after first trimester
    - Severe episodes with high risk for relapse: continue lithium through pregnancy with close fetal cardiac monitoring



Effective Dose:
Lithium: 0.8-1.2
Carbamazepine: 8-12
Valproate: 80-120

Lithium intoxication occurs ~1.5meq. Sx: diarrhea, vomiting, drowsiness, muscular weakness, ataxia

BPD Treatment - *Medications*

- Valproate: associated with neural tube defects through folic acid competition
  - Also associated with craniofacial anomalies, limb abnormalities, cardiac anomalies in fetus and hepatotoxcitiy, withdrawal and hypoglycemia in neonates
  - Not recommended for pregnancy
  - If must continue using, folate supplementation is necessary
- Carbamazepine: associated with facial anomalies including cleft lip/palate
  - Furthermore, reproductive age women taking carbamazepine should NOT be using COC's because carbamazepine increases the metabolism of these contraceptives
  - Not recommended for pregnancy
- Lamotrigine: especially effective in treating depressive episodes of bipolar disorder
  - Note: reproductive age women taking lamotrigine should NOT be using COC's because these contraceptives can increase the metabolism of lamotrigine
  - Possible risk of oral cleft defects but not established. Generally well tolerated by mother and fetus
  - Recommended during pregnancy

Treatment – *Medications*[4]

Bipolar Disorder Medications			
Generic Name	Brand Name	Pregnancy Risk Category	Lactation Risk Category
Mood Stabilizers			
Lithium	Lithium	**D**	**L4**
Valproic Acid	Depakote	**D**	**L2**
Carbamazepine	Tegretol	**D**	**L2**
Lamotrigine	Lamictal	**C**	**L3**

Though it's received L4 rating, Lithium use during breastfeeding is not generally discouraged. In small trials it has NOT been shown to have significant adverse effects, though not many long term studies have been done. It does concentrate in breast milk, however milk drug levels are ~10-60% (avg ~40%) of maternal serum levels. Most practitioners recommend continuing lithium with close follow up on infant BUN, Cr, and TSH levels.

1. UpToDate
2. Mei-Dan et al, *ObGyn, March* 2015
3. Kurki, et al, *ObGyn*, 2000
4. ACOG Practice Bulletin 92, April 2008 ("Use of Psychiatric Medications during Pregnancy and Lactation")