Depression in Pregnancy

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Why Perinatal Psychiatry?

Roadmap

The Myth of Pregnancy as Antidepressant

Depression in Pregnancy

Nosology and Nomenclature

DSM-V Criteria for Major Depressive Disorder (MDD) with Peripartum Onset

5 or more of the following during same 2 week period

- Depressed Mood
  - Diminished Interest or Pleasure
- Appetite/Weight
- Sleep
- Psychomotor
- Energy
- Concentration
- Guilt/Worthlessness
- Suicidal Ideation

But can we narrow that down?

1st Trimester Perinatal onset of MDD = anxious/melancholic subtype of depression:

- High anxiety
- Decreased Sleep
- Decreased Appetite
- Psychomotor agitation

Postpartum Onset of MDD more likely to be atypical subtype of depression:

- Anhedonia
- Increased Sleep
- Increased Appetite
- Psychomotor retardation

Who is at risk?

- History of depression
- Discontinuing antidepressants in pregnancy (5 fold increased risk)
- Family history
- Childhood maltreatment
- Single motherhood
- More than three children
- Cigarette smoking
- Low income
- Age <20
- Domestic violence
- Insufficient social support
- Pre-existing hypertension

Putnam et al 2017. The Lancet Psychiatry
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Obstetrical Associations with Perinatal Depression

- Planned C-Sections
- Increased Nausea and Vomiting
- Epidural Analgesia


Associated Risks of Perinatal Depression

- Pre-term Birth (<37 weeks) (RR 1.39; Grote et al 2010)
- Nerve Growth Factor (NGF) in placental tissue of untreated depression and controls
- Trophic Factors (e.g., NGF)

Kakkara et al (2013) PLOS ONE

Associated Risks of Perinatal Depression: Infants

- 6-fold increased risk of postpartum depression (Beck et al 2006)
- Low Birth Weight
- Intrauterine Growth Restriction
- Higher plasma cort and norepinephrine in infants, decreased dopamine and serotonin
- Right frontal EEG asymmetry early marker of negative affect
- Increased crying and fussing compared to infants of postpartum onset
- Anxiety levels and increased cortisol age 7 to 8
- Increased central adiposity at age 3 compared to children of postpartum onset

Depression in Pregnancy

Prevention, Screening, and Treatment

• Prevent – Identify at risk individuals
• Screen – Identify MDD in pregnancy
• Treat – Select appropriate strategy

Prevention

• US Preventive Task Force Recs:
  • Refer to counseling services for pregnant women with certain risk factors
  • History of depression
  • Current Subclinical depressive symptoms
  • Low income
  • Adolescents
  • Single parenthood
  • Intimate partner violence
  • History of Adverse Childhood Experiences

Cognitive Behavioral Therapy and Interpersonal Therapy: NNT 13.5

Screening

• ACDG Screening Recommendations
  • At least once during perinatal period
  • Patient Health Questionnaire-9
    • 0-5 (mild); 6-10 (moderate); 11-19 (moderate-severe); 20-27 (severe)
  • Edinburgh Postnatal Depression Screen (validated for pregnancy)
    • 0-7 (mild); 8-16 (mild-severe); 17-40 (severe)
### Basic Treatment Algorithm

- **Is depression in severe range?**
  - Yes: Antidepressant + Psychotherapy Referral
  - No: Inadequate response to medication?
    - Yes: Antidepressant
    - No: Psychiatric referral

### Caveats:
- Bipolar Disorder/Psychotic features
- Psychiatric emergencies

### Choosing an antidepressant: General Principles

- Monotherapy better than polypharmacy
- Use what’s worked
- Use what we have data on
- Use the Lowest **EFFECTIVE** dose
  - But be prepared to increase over course of pregnancy
- Avoid lowering dose/stopping prior to delivery
- Undertreated when entering postpartum
- No evidence of dose relationship to Neonatal Adaptation Syndrome

### Risks of antidepressants

- The limits of observational research
  - Data is confusing and conflicting
- Confounds
  - Confounding by indication
    - Comparing Antidepressant Exposed with unexposed VS. Antidepressant exposed vs untreated depression
- More frequent monitoring → more likely to find minor malformations
Risks of antidepressants

- No impact on fertility
- Does not increase rate of spontaneous abortion
- Pre-term birth – mean difference of 3 days (Ross et al 2013, JAMA Psych; Lindqvist et al 2014 J Thomb Haemost)
  - Possible dose effect (Ross et al 2011 J affect disorders)
- Low birth weight – mean difference 74g (Ross et al 2013)

Risks of Antidepressants: Congenital Malformations

- Sertraline
  - Traditionally the “safe” go to.
  - Recent meta-analysis 36% increased risk of cardiovascular related malformations and atrial/ventricular septal defects (Shen et al 2017 Br J Clin Pharm).
  - But 3 large meta-analyses negative
- Paroxetine
  - Traditionally the “no no”. Three large meta-analyses. Effect sizes noted to be small
  - Recent data on paroxetine of >8000 exposed in first trimester compared to depressed unexposed found no increase. (Huybrechts et al 2014, NEJM)

Huybrechts et al 2014 NEJM

- 1,000,000 million enrolled in Medicaid
- 64,000 on antidepressants in first trimester
- Outcomes any cardiac malformation, right ventricular outflow tract obstruction, and ventricular septal defect, other cardiac malformation
- Controlled for risk factors for malformation: maternal illness, other medications
- Controlled for depression and severity of depression using proxies (number of diagnoses, pain diagnoses, sleep disorders
Huybrects et al 2014 NEJM

- After adjustment for confounders:
  - No significant association for any antidepressant
    - SSRIs (Paroxetine, Sertraline, Fluoxetine)
    - SNRI (Venlafaxine, Duloxetine)
    - Tricyclic Antidepressant
    - Bupropion

Other risks

- Persistent Pulmonary Hypertension of the Newborn –
  - Either no association or small (additional 3 per 1000 infants)

- Postpartum Hemorrhage –
  - No increased risk or small risk (Number needed to harm 80-100)

- Poor Neonatal Abstinence Syndrome –
  - 5-85% of cases exposed
  - Resolves within days to two weeks.

Take home: antidepressants

- Data is difficult, conflicting and evolving
- Antidepressants are not major teratogens
- Additional risks (e.g. pre-term birth) may not be clinically significant
- Use a risk – risk model for informed consent
- Risks of antidepressants vs risks of untreated depression
Summing it all up

- Pregnancy doesn’t protect against Depression
- Depression has risks for mother and infant

Prevention
- Identify at risk individuals and refer to counselling

Treatment
- Psychotherapy is first line in mild-moderate depression
- Antidepressants + Psychotherapy in severe depression
  - Not without risk, but consider in context of untreated depression

Where to get help

- MGH Center for Women’s Mental Health
  - www.womensmentalhealth.org
  - Up to date information on medications in pregnancy and additional resources

- Colorado Center for Women’s Behavioral Health and Wellness
  - Referrals contact WBHW@ucdenver.edu
  - Questions? Want to talk over a case?
    - Andrew.M.Novick@cuansutho.edu