Psychiatric Disorders in Pregnancy and the Postpartum Period

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March 5, 2014
Learning Objectives

- Describe the epidemiology of depression in pregnancy and the postpartum period
- Learn and utilize special approaches to assess for depression in this population
- Counsel women about treatment of depression during pregnancy and breastfeeding, including risks and benefits
- Understand diagnosis and treatment options for other psychiatric illnesses in pregnancy, including bipolar disorder, OCD, and schizophrenia
Your patient...

- “Felicia”: 23 year old woman cared for by you since she was 19
- H/o major depressive d/o, including hospitalization for suicide attempt age 17
- Paroxetine (Paxil) for two years with good results
- Attending school to become medical assistant, working part-time
Your patient...

- Newly married for a year
- Interested in having a child soon
- Heard about some risks with antidepressants in pregnancy
- Very nervous about discontinuing medication
- During annual exam states she is considering stopping her oral contraceptives
What do we know about depression in pregnancy?

- Pregnancy once thought to decrease risk of depression—this is false
- In 2008, more than 7% of women took an antidepressant sometime during their pregnancy
- 500,000 U.S. pregnancies per year in women w/ psychiatric illness predating or emerging during pregnancy
How can we screen for depression in pregnancy?

- PHQ-2 and PHQ-9 are good tools to standardize screening
- Can screen with an interview
- Importance is to incorporate something you can sustain in practice
What type of mood disorders occur in the postpartum period?

- Postpartum/baby “blues”: ~80% of women affected
  - Feeling overwhelmed
  - Irritability
  - Tearfulness
  - Exhaustion
  - Trouble falling or staying asleep
  - Usually resolves by two weeks postpartum
What type of mood disorders occur in the postpartum period?

- Postpartum depression
  - 10-20% of women affected
  - Greatest risk is first 12 weeks after delivery, but risk persists for one year
  - Symptoms last more than 14 days
What type of mood disorders occur in the postpartum period?

- Postpartum depression symptoms
  - Tearfulness, sad or flat affect, irritability, mood instability
  - Feeling inadequate, guilty, overwhelmed
  - Sleep and appetite disturbance
  - Intense worries or obsessive thoughts re. harm to the baby
  - Difficulty concentrating or making decisions
  - Lack of interest in the baby, family or activities
  - Poor bonding
  - Thoughts of death or suicide
  - Somatic symptoms: HA, CP, palpitations, numbness, hyperventilation
What type of mood disorders occur in the postpartum period?

- Postpartum psychosis: 1-2 in 1000 women affected
  - Agitation and anger
  - Anxiety/Paranoia
  - Insomnia/Delirium/Confusion
  - Mania (hyperactivity, elated mood)
What type of mood disorders occur in the postpartum period?

- Postpartum psychosis
  - Suicidal or homicidal thoughts
  - Auditory hallucinations (about the baby, of a religious nature)
  - Visual hallucinations (seeing or feeling “a presence” or “darkness”)
  - Delusions and commands to harm the infant (not just an obsessive thought)

**EMERGENCY**: PSYCHIATRIC HOSPITALIZATION NECESSARY
“Suicides account for up to 20% of all postpartum deaths and represent one of the leading causes of peripartum mortality.” (2005 in Archives of Women’s Mental Health)
What is different about postpartum depression?

- Sleep deprivation the norm postpartum
- Strong societal expectations about maternal happiness postpartum
- 50% of postpartum depression goes undiagnosed
- Postpartum depression affects mothers, children, partners, and families
Dear Sleep,

I miss you. ☹

Molly
Back to your patient: What will you tell her about the risks of antidepressant use in pregnancy?

- Recent meta-analyses show somewhat increased risk of SAB
  - OR 1.45 – 1.87 depending on study
  - Confounding by other health factors
    - Women who take anti-depressants have other adverse health issues: smoking, etoh use, older age, other rx’d drugs, elevated BMI, DM, HTN
    - These are all significant pregnancy complication risk factors
Risks of antidepressant use in pregnancy....

- Paroxetine (Paxil) in first trimester reported to increase risk of cardiac anomalies
  - 2/1000 births
- Criticism regarding inclusion of clinically insignificant defects
- 2013 meta-analysis showed no association w/ major malformations, but increase in total CV malformations: RR 1.63, CI 1.05-2.53
Back to your patient: What will you tell her about the risks of antidepressant use in pregnancy?

- 2013 meta-analysis of congenital malformations and cardiovascular defects of SSRIs
  - Quality evaluated: sample characteristics, exposure and outcome measurements, follow-up, control for potential confounders
  - No effect on major congenital malformations
  - Small statistically significant increased risk of CV malformations: RR 1.36, CI 1.08-1.71
  - Persistent effect after limiting inclusion to studies adjusted for confounding
Risks of antidepressant use in pregnancy….

- Can say that SSRIs are not major teratogens
- Possible exception is paroxetine
  - Should not be used in first trimester
  - Generally avoided in favor of other agents
Risks of antidepressant use in pregnancy....

- Many conflicting studies re. effect of SSRIs on preterm delivery risk
  - 2013 meta-analysis on studies published before June 2010 showed OR 1.55, CI 1.38-1.75
  - If causal, effect is mild, shortening pregnancy by 3-5 days
Risks of antidepressant use in pregnancy....

- Do SSRIs increase risk of persistent pulmonary hypertension of the newborn (PPHN)?
  - Failure of pulmonary vasculature to decrease resistance at birth
  - Causes hypoxia, may require intubation
  - 10-20% mortality
  - Thought to be associated with use after 20 wks
  - Rise in risk described as 0.5-2/1000 to 3-6/1000
  - Other risk factors: maternal smoking, maternal diabetes, neonatal sepsis, meconium aspiration, cesarean delivery
Risks of antidepressant use in pregnancy....

- Initial study in 2006 was case-control, OR 6.1, CI 2.2-16.8 of PPHN
- Six add’l studies have shown mixed results
- Large population-based cohort study in 5 Nordic countries of 30K women who used SSRIs in pregnancy
  - OR 2.1, CI 1.5-3.0
  - Controlled for confounders: smoking, obesity, c/s, IUGR, psychiatric illness
  - Women who had psych admission but not on antidepressants also had increased risk of infant w/ PPHN
- Conclusion is small or no association, and in 2012 FDA stated evidence is insufficient to determine
Risks of antidepressant use in pregnancy....

- All SSRIs can cause neonatal serotonin syndrome and withdrawal syndrome
- Together called “poor neonatal adaptation” or “neonatal behavioral syndrome”
- Difficult to distinguish from each other
  - Poor feeding and sleeping
  - Vomiting
  - Altered muscle tone
  - Tremors, jitteriness, seizures
  - Hypoglycemia
  - Respiratory problems
  - Constant crying
Risks of antidepressant use in pregnancy….

- Neonatal Behavioral Syndrome
  - Temporary--resolves by two weeks or sooner
  - Can require extended hospitalization
  - Possibly worse with paroxetine (Paxil) due to short half-life, no active metabolites
  - Current thought is more likely to be a withdrawal effect

- No data to support long term effects on neurodevelopment, based upon
  - IQ scores at 16 and 86 months
  - Parental and observer report of behavior at age 4 years
  - Confounded by residual maternal depression and/or multiple med exposures (e.g. antipsychotics, etc.)
A word about the FDA pregnancy category system....

- Confusing, falsely suggesting an increasing level of risk from category A to X
- e.g.: OCs are X because there is no reason to use in pregnancy, but no evidence of birth defects
- e.g.: RHO immune globulin (Rhogam) is C ???
- Meds in the same category have very different levels of actual risk and of evidence supporting their categorization
A word about the FDA pregnancy category system....

- New model somewhere on the horizon...
  - Clinical considerations
  - Risk assessment
  - Specifics on fertility, pregnancy, and lactation
- In the meantime...
  - **Drugs in Pregnancy and Lactation** (Briggs, Freeman, & Yaffe)—accessible through library catalog as electronic book
  - **Medications and Mother’s Milk** (Hale)
  - **Reprotox**—library website under “databases”
What should you tell her about the risks of discontinuing medication in pregnancy?

- With hx recurrent major depression, 68% relapse rate w/ discontinuation of medication around the time of pregnancy
- Depression in pregnancy associated w/
  - Poor weight gain
  - Increased risk of preterm delivery
  - Low birth weight
  - Increased use of cigarettes, alcohol, other substances
What should you tell her about the risks of discontinuing medication in pregnancy?

- Mothers who are depressed show
  - Less affectionate behavior
  - Less response to infant cues
  - More hostile/intrusive interactions with their infants

- Children of mothers with untreated depression exhibit
  - Impaired emotional development
  - Poorer language development
  - Difficulties with attention
  - Decreased cognitive skills
  - Increased risk for long-term behavioral problems
What should you tell her about the risks of discontinuing medication in pregnancy?

- Children of mothers with untreated depression exhibit
  - More fussiness and colic
  - Impaired emotional development: fewer positive facial expressions
  - Poorer language development: less vocalization
  - Difficulties with attention
  - Decreased cognitive skills
  - Increased risk for long-term behavioral problems

- Remission of maternal depression improves children’s mental and behavioral disorders

*Consider depression during pregnancy and postpartum as an exposure with associated risks for the infant!*
To minimize risk, how might you manage her medication?

- In preparation for pregnancy
  - Gradually wean paroxetine (Paxil)
  - Weaning preferable to abrupt d/c due to risk for discontinuation syndrome in adults
- Consider beginning fluoxetine (Prozac)
  - Plan to continue it at least until the first missed period
  - Preferred during pregnancy due to theoretically more stable drug levels associated with longer half-life
To minimize risk, how might you manage her medication?

- Consider avoiding medication exposure during the first trimester
  - Valuable even if eventually restarts meds during pregnancy
  - Should only be done if you feel patient safe off medications (i.e. suicidality, etc).

- If treatment initiated in pregnancy, most women will need to continue postpartum
  - Sertraline (Zoloft) is considered preferable in breastfeeding due to short half-life
  - If stable on fluoxetine (Prozac) (or other agent), probably do not need to switch agents at delivery (vulnerable time for depression flare)
  - Switching a few weeks prior to delivery results in multiple exposures during pregnancy
What can you tell your patient about non-pharmacological treatment of depression?

- Cochrane Review: any psychosocial or psychological intervention, compared to usual postpartum care, is associated with reduction in risk of continued postpartum depression

- Breastfeeding may be somewhat protective against postpartum depression (oxytocin release?)
Non-pharmacological interventions...

- Cognitive Behavioral Therapy
  - Good results w/ group approach
  - 10-40% fail to complete full treatment (similar to pharmacotherapy)
  - May have enduring effects not seen w/ pharmacotherapy (up to two years)

- Six sessions of non-directive counseling w/ child health nurses was more effective than routine primary care in Sweden

- Telephone-based peer support out-performed care as usual (five 30-minute conversations)
Your patient...

- Elects to discontinue all medications prior to conception
- Responds well to Cognitive Behavioral Therapy during pregnancy
- Delivers a healthy term baby girl with no complications
What is the epidemiology of bipolar disorder in pregnancy?

- Usual age of onset in early 20s
- Delay in diagnosis on average
  - 9 yrs after first depressive episode
  - 6 yrs after first manic episode
- Discontinuation of medication associated w/ 85% recurrence of sx’s
What is the epidemiology of bipolar disorder in pregnancy?

- Postpartum is high-risk time for relapse
  - 50% occurrence
  - Study of 10,218 women showed bipolar disorder strongest predictor of hospitalization b/w days 10-19 postpartum (RR 37.22, CI 58.00-102.04)

- Prevalence of bipolar d/o is 4%
- Prevalence of GDM is 2-6% (higher in NM) and we screen everyone!
What is appropriate screening for bipolar d/o in pregnancy?

- Study of 150 women in Ontario referred for psychiatric assessment during pregnancy or postpartum
  - All completed Mood Disorder Questionnaire (MDQ) on first day of assessment
  - All were interviewed by psychiatrist
  - Traditional scoring gave sensitivity of 39%, specificity of 91%
  - Altering scoring to presence of 7 manic/hypomanic sx’s (without supplementary questions): sensitivity 88%, specificity 89%
Traditional Scoring of MDQ:
“Yes” to $\geq 7$ of 13 items in Question 1 AND
“Yes” to Question 2 AND
“Moderate Problem” or “Serious Problem” to Question 3

1. Has there ever been a period of time when you were not your usual self and...
   ...you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?
   ...you were so irritable that you shouted at people or started fights or arguments?
   ...you felt much more self-confident that usual?
   ...you got much less sleep than usual and found you didn’t really miss it?
   ...you were much more talkative or spoke much faster than usual?
   ...thoughts raced through your head or you couldn’t slow your mind down?
   ...you were so easily distracted by things around you that you had trouble concentrating or staying on track?
Traditional Scoring of MDQ:

“Yes” to ≥ 7 of 13 items in Question 1 AND
“Yes” to Question 2 AND
“Moderate Problem” or “Serious Problem” to Question 3

...you had much more energy than usual?
...you were much more active or did many more things than usual?
...you were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?
...you were much more interested in sex than usual?
...you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?
...spending money got you or your family into trouble?

2. If you checked YES to more than 1 of the above, have several of these every happened during the same period of time?

3. How much of a problem did any of these cause you—like being unable to work; having family, money, or legal troubles; getting into arguments or fights? No problem. Minor problem. Moderate problem. Serious problem.
What would be the treatment options for your patient if she had a hx of bipolar disorder?

- Lithium
  - 1st trimester exposure → 10X increase in incidence of Ebstein’s anomaly (right ventricle hypoplasia and abnormal tricuspid valve) (absolute risk with exposure is 1:1000 to 2:1000)
  - Reports of perinatal cyanosis and hypotonia (”floppy baby syndrome”)
  - Depending on disease severity could be d/c’d before conception and restarted after organogenesis
  - Not recommended for use in breastfeeding
What would be the treatment options for your patient if she had a hx of bipolar disorder?

- Valproic acid (Depakote, Depakene) and carbamazepine (Tegretol)
  - 1st trimester exposure → 10X increase in neural tube defects
  - Increase risk of oral clefts and other facial dysmorphisms
  - Both considered acceptable in breastfeeding
- Lamotrigine (Lamictal)
  - No clear increase in congenital malformations
  - Some possible increase in midline facial clefts
  - Metabolism is greatly increased in pregnancy, takes awhile to titrate, often needs to be decreased quickly at delivery to avoid toxicity
- Due to untx’d relapse risk of 50% postpartum, could start tx before delivery or in immediate postpartum period
What is the epidemiology of anxiety disorders in pregnancy?

- 1/3 of women experience anxiety d/o during lifetime
- Rates in pregnancy estimated at 12-39%
- Generalized anxiety d/o as high as 10.5% in pregnancy (formal diagnostic criteria)
- Among poor pregnant women, prevalence of PTSD is 7.7%
- Anxiety is common co-incident condition with depression
What is the epidemiology of anxiety disorders in pregnancy?

- Maternal anxiety assoc’d w/ adverse pregnancy consequences
  - More N/V
  - More tobacco and etoh use
  - More medical visits
  - Shorter gestation
  - Later child behavioral problems
  - Higher risk of postpartum depression
What are the options for treatment of anxiety disorders in pregnancy?

- Benzodiazepines
  - Possible 2X increased risk of clefts
  - Newborn hypotonia, apnea, hypothermia, feeding problems, withdrawal
  - Suggestion of developmental delay
- Buspirone (BuSpar) has almost no data on use in pregnancy
- Sedating antihistamines are often used: hydroxyzine
- SSRIs are often effective
What are the options for treatment of anxiety disorders in pregnancy?

- Mindfulness therapies have good data to support, including in pregnancy
- Traditionally 8-week intensive group training
  - Body scan
  - Formal sitting meditation
  - Mindful yoga
  - Taught to observe thoughts, feelings, and bodily sensations objectively w/o judging, clinging to, or pushing away experience
- Pilot study of 23 pregnant women showed statistically significant improvement in anxiety, worry, depression, increases in self-compassion
What is the epidemiology of obsessive compulsive disorder (OCD) in pregnancy?

- OCD: recurrent thoughts, impulses, or images that are intrusive and cause anxiety/distress and behaviors that attempt to reduce distress or prevent dreaded event
- Onset in women in early 20s
- Pregnancy/birth described as triggering event for many women
  - 1.2% of general population affected
  - 4-9% postpartum
What is the epidemiology of obsessive compulsive disorder in pregnancy?

- Fears of harming the baby
  - Worry about “contaminated hands” → excessive washing, avoiding contact w/ others, minimal child handling
  - Worry about “touching baby inappropriately” → avoidance of bathing and changing baby
- 80% of general population experience intrusive thoughts about deliberate or accidental harm to baby
  - Usually easily dismissed
  - Women w/ OCD give more meaning to the thoughts, which makes it more distressing to them
How is OCD diagnosed and treated?

- Barriers: shame, fear of being judged as potentially harmful parent, misdiagnosis as postpartum psychosis
- Psychiatric Diagnostic Screening Questionnaire can be used for screening
- Clinical interview is appropriate re. experience of and reaction to intrusive thoughts
- Cognitive Behavioral Therapy is effective
- SSRIs may be helpful
What is the epidemiology of schizophrenia in pregnancy?

- Onset typically age 25-35
- 50% of women w/ schizophrenia will become pregnant
- 50% are unplanned/undesired pregnancies
- Discontinuation of medication will lead to relapse in 50% during 2 years of follow-up, vs. 15% when meds continued
- 24% of postpartum women relapse in 3 months
- Abrupt discontinuation of meds is associated with increased risk of relapse
How is schizophrenia treated in pregnancy?

- Meta-analysis showed congenital malformation rate of 2-2.4% w/ typical antipsychotics, but no specific pattern
  - Thioridizine (Mellaril)
  - Fluphenazine (Prolixin)
  - Chlorpromazine (Thorazine)
  - Promethazine (Phenergan)
  - Trifluoperazine (Stelazine)
  - Haloperidol (Haldol)
How is schizophrenia treated in pregnancy?

- Low birth weight may be increased with typical antipsychotics, but hard to distinguish med effect from disease effect.
- Some have been associated with neonatal withdrawal/extrapyramidal signs.
- Long-term effects on behavior and intelligence are similarly difficult to assess due to underlying maternal disease.
How is schizophrenia treated in pregnancy?

- No conclusive evidence of increased risk of teratogenesis w/ atypicals
  - Clozapine (Clozaril)
  - Olanzapine (Zyprexa)
  - Quetiapine (Seroquel)
  - Risperidone (Risperdal)

- Weight gain assoc’d w/ atypicals can lead to increased risk
  - Neural tube defects
  - HTN d/o of pregnancy
  - GDM
  - LGA babies and neonatal hypoglycemia
You want to screen your patient for postpartum depression. When should you screen?

- Screening opportunities
  - Any routine infant or maternal postpartum visit
  - Special visits scheduled for following up on hx of depression
  - Example
    - First newborn check at 2 or 3 days after d/c
    - 2 weeks postpartum
    - 4-6 weeks postpartum
What method will you use to screen her?

- Postpartum Depression Screening Scale
  - 35-item Likert response scale ("Strongly Disagree" to "Strongly Agree")
  - Third grade reading level
  - Completed by patient in ~10 minutes
What method will you use to screen her?

- Postpartum Depression Screening Scale items address seven areas
  - Sleeping/Eating Disturbances
  - Anxiety/Insecurity
  - Emotional Lability
  - Cognitive Impairment
  - Loss of Self
  - Guilt/Shame
  - Contemplating Harming Oneself
What method will you use to screen her?

- Edinburgh Postnatal Depression Scale
  - 10-item self-report scale ("Yes, most of the time" to "No, not at all")
  - Available in several languages
  - Intended for use at 6-8 weeks postpartum
  - Completed by patient in ~5 minutes
What method will you use to screen her?

- Edinburgh Postnatal Depression Scale addresses symptoms of
  - Inability to laugh
  - Inability to look forward to things with enjoyment
  - Blaming oneself unnecessarily
  - Feeling anxious or worried
  - Feeling scared or panicky
  - Feeling that “things have been getting on top of me”
  - Difficulty sleeping because of unhappiness
  - Feeling sad or miserable
  - Crying
  - Thoughts of harming oneself
What method will you use to screen her?

- **Postpartum Depression Screening Scale**
  - For combined major and minor postpartum depression
    - Sensitivity 91%
    - Specificity 72%

- **Edinburgh Postnatal Depression Scale**
  - For combined major and minor postpartum depression
    - Sensitivity 68-80%
    - Specificity 77%
Your patient...

- Has positive screen for postpartum depression
- Would like to start a medication
- Is concerned due to breastfeeding her baby

What do you advise?
Antidepressants in Lactation

- Sertraline (Zoloft) currently favored SSRI during breastfeeding
  - Short half-life
  - Low or undetectable infant plasma levels
  - More follow-up data on infant development
- Paroxetine (Paxil) and fluvoxamine (Luvox) also show low infant plasma levels
- Could use in patients w/ prior good effect:
  - Fluoxetine (Prozac)--long half-life
  - Citalopram (Celexa)--high breast milk concentration
Antidepressants in Lactation

- Omega-3 fatty acids showed significant response rate in one open-label study.
- Medication exposure to fetus via placental transfer will almost always be greater than to the newborn via breastfeeding.
- Most national guidelines recommend six months of treatment once depression is in remission.
Back to your patient...

- Partner has been very involved, attending prenatal and well child check appointments
- Wants to know what he can do to help

What do you tell him?
How can her partner and family members help?

- Mothers without social support twice as likely to develop postpartum depression
- Among Latina women, those satisfied with marital/partner relationships showed lower risk of depressive sx’s postpartum
- Among high risk women, better social support → quicker improvement in depressive sx’s
- Educate partner about signs of mania/hypomania: can be uncovered w/ use of SSRI. Also educate about the importance of treatment!
Take-home points...

- For SSRI use in pregnancy, risks of medication exposure in pregnancy are overall low vs. 68% recurrence of maternal depression w/ discontinuation
- Neonatal behavioral syndrome is self-limited, but can cause prolonged hospitalization
- Prenatal visits provide multiple opportunities to assess for current depression and risk of developing postpartum depression
Take-home points...

- Assume that every woman of childbearing age will get pregnant
  - Folic acid, whether contracepting or not
  - Contraception, if desired
  - Consider antidepressant and other medication choices in light of possible future pregnancies
Take-home points...

- Screen early and often for postpartum depression
- Document risk/benefit counseling regarding medication use AND discontinuation
- Involve partner and family in treatment plans, as patient permits
mother's day rally for moms' mental health
References

References
