1

Perinatal Depression

- Anxiety and depressive disorders are the most common chronic disorders in women of childbearing age.
- Postpartum depression generally represents recurrent depressive illness that often has onset during pregnancy
- Women with mood disorders can enter pregnancy depressed and untreated, treated and euthymic or treated and ongoing depressive symptoms.

2

Rates of Depression during Pregnancy

Rates of depression in pregnant women screened in urban OB practices is about 20% versus 10% in suburban OB practices.

Half of the depressed women had stopped their ADs.

J Womens Health, Marcus, 2003;12

Minority women are twice as likely to meet criteria for depression during pregnancy and postpartum.

20% versus 9%.

J Consult Clin Psychology, Hobfall, 1995;63
Int Rev Psychiatry, O'Hara, 1996;8

Only about 15% of depressed women in these studies were receiving any form of treatment.

3

"Is it okay to take_____ during pregnancy?

4

"Is it okay to *not* take _____ during pregnancy?

5

Antenatal Depression and Pregnancy Outcomes

Increased rates of:

- Gestational hypertension
- Preeclampsia
- Preterm deliveries

More maternal use of cigarettes and alcohol during pregnancy.

Less attendance of prenatal care and less adherence to prenatal vitamins.

6

Risk of preterm delivery is 3X higher in depressed than in non-depressed women.

Risk of low birth weight infant is 4X higher in depressed women.

Risk of infant that is small for gestational age is 3X higher in depressed women

J of Clinical Epidemiology, Steer, Vol 45(10)1992

7

Postpartum Depression

PPD is the most common complication of childbirth, occurring in about 10% of women.

PPD onset is usually at about 4 weeks postpartum with help-seeking at about 8-weeks postpartum.

Unique clinical features of PPD:

- Very poor concentration, focus and memory.
- Extreme fatigue yet inability to fall sleep.
- High levels of anxiety and obsessiveness.

8

Postpartum Mortality

Psychiatric conditions are the leading cause of maternal death in the first year postpartum.

Overdose recently surpassed suicide as leading cause of postpartum maternal death.

Studies show that only 50% of postpartum women who die by overdose had a documented substance use screening during prenatal visits.

MMRC Illinois Data, 2021

9

Perinatal Mental Health Screening

U.S. Preventive Services Taskforce (USPSTF)

"Screen for depression in the general adult population, including pregnant and postpartum women."

American College of Obstetrics and Gynecology (ACOG)

Screen women at least once during the perinatal period using a validated tool. Postpartum visit should include a review of symptoms for clinically significant depression.

American Academy of Pediatrics (AAP)

Screening of maternal depression can be integrated into well-child visits.

10

State Medicaid Requirements and Recommendations

Maternal perinatal depression screening using a validated tool:

20 states require

22 states recommend

Nebraska does not have a policy

Maternal depression screening during well-child visits:

8 states require

27 states recommend

Nebraska does not have a policy

11

Screening Tools

Edinburgh Postnatal Depression Scale (EPDS)

Most widely used perinatal screening tool

Assesses depression and anxiety

10 questions

PHQ-9

Screens for depression

Rates and monitors depression severity

10 questions

PHQ-2

A “screen to screen” tool

Takes one minutes and can be used at every visit.

12

Screening for Depression alone is not enough

- Women who are positive on a depression screening tool need to be screened for bipolar disorder using the mood disorder questionnaire (MDQ.)
- Undiagnosed bipolar disorder is common in patients who present with depression.
- It is estimated that 20% of patient treated for depression in a primary care setting actually have bipolar diagnosis.

13

MDQ

- 15 question, self-administered questionnaire that screens for lifetime presence of manic symptoms.
- Patients who screen positive have a 70% of having a bipolar disorder.
- *Patients who screen negative have a 90% chance that they do not have a bipolar disorder.*

14

Screen for Substance Use

- Ask consistently and often in a non-judgemental manner.
- Ask about past history of substance use and current use.
- Don't make any assumptions about who is at "high risk" for substance use. Don't assume that pregnant women would not be using substances.

15

- No specific substance use screening tool is recommended.
- Ask about alcohol, opioids, prescription drug misuse, illicit drug use and cannabis use which is rising is pregnant women.

16

Medication Use During Pregnancy

80% of women take at least one dose of medication excluding vitamins during their pregnancies.

Eur J Clin Pharm, Headley, 2004;60.

Antidepressant-use has risen from about 2% in 1996 to about 7 to 8% at present.

Am J Obstet Gynecol, Cooper, 2007;196.

SRIs are the most studied class of medications used during pregnancy.

Enormous amount of data has been collected on SRI use during pregnancy over the last 20 years.

17

Exposure to Maternal Depression

Exposure to Antidepressant Medication

18

Recurrence of depression following antidepressant discontinuation during pregnancy

- Prospective study of pregnant women who either stopped or continued their antidepressant for pregnancy.
- Roughly 70% of the women who stopped their antidepressant relapsed during pregnancy. Relapse occurs quickly - generally within 4 weeks of discontinuation.

JAMA, Cohen, 2006(295)5

19

SRI-Use During Pregnancy: What Are the Controversies?

- Poor neonatal adaptation syndrome (neonatal abstinence syndrome)
- Cardiovascular malformations.
- Persistent pulmonary hypertension of the newborn.

20

Antidepressant Use in Pregnancy

What is exposure?

Exposure to SRI
+ illness (no remission or partial remission)
+ psychosocial risks (abuse, poverty, lack of access to healthcare)
+ environmental exposures (diet, pollution)
+ stress (cortisol HPA-axis dysregulation)
result in **outcome.**

21

Pregnant depressed women have may other risk factors affecting pregnancy outcomes:

- Tend to be older
- Less educated
- Lower SES status
- More obese
- More likely to have gestational diabetes
- More likely to have toxic environmental exposures

Women who take psychotropics during pregnancy are significantly different in their health and risk factors than women who do not take medications during pregnancy.

22

Poor Neonatal Adaptation Syndrome

- Jitteriness, tremors or shivering
- Increased or decreased muscle tone
- Feeding difficulties
- Irritability and inability to calm
- Tachypnea and/or respiratory distress

23

- Symptoms observed at birth in half the cases and between 12-hours and 5 days postpartum in the other half.
- Syndrome is generally mild and remits within several days to up to 2 weeks.

24

Early studies estimated that up to 30% of infants exposed to third trimester SRIs may exhibit these symptoms compared to about 9% of unexposed infants.

Subsequent studies that take into account other health risks for pregnant women taking SRIs as well as their severity of depression during pregnancy do not show a significantly increased risk of PNA in exposed infants.

25

Neonatal Outcomes After Prenatal Exposure to SRIs and Maternal Depression

Population data health and prescription records were evaluated for 119,547 women who delivered babies over a 3-year period.

- 14% of mothers had antenatal depression diagnosis.
- 3.7% took antidepressants during pregnancy.
- Compared neonatal outcomes in women diagnosed with depression who did not take SRIs during pregnancy with women diagnosed with depression who took SRIs during pregnancy and women with no depression and no SRI-use.

Oberlander, Arch Gen Psychiatry 2006:63(8)

26

Take-home message

After matching for confounding variables, the infants of depressed mothers who took SRIs during pregnancy did not differ significantly from unexposed infants for almost all birth outcome measure including rates of preterm deliveries, average birth weights, feeding problems and other adverse birth outcomes.

Only difference: exposed infants were more likely to experience transient respiratory distress compared to unexposed infants.

27

" . . . findings may suggest that previous studies failed to account for maternal illness severity, thereby attributing adverse neonatal outcomes to SRI exposure rather than to maternal depression" for most adverse neonatal outcomes.

Increased risk of transient respiratory distress did not disappear when confounding variables taken into account so it is likely a true effect of SRI-exposure.

28

Cardiovascular Malformations

- Cardiovascular malformation is the most common birth defect in newborns.
- Occur in about 1% of newborns.
- Small septal defects account for 80 to 90% of cardiovascular defects and half close spontaneously prior to age 4.

29

The FDA and Paxil

- 2005 FDA changed Paxil from C to D based on unpublished study of 527 women showing a 2-fold increase in CV malformations.
- 8 studies with >5400 women showed no increase risk of CV malformations with any individual SRI.
- Some other small studies of SRIs have shown association with CV malformations and others have not.

30

2 case cohort studies of approximately 14,000 infants born with major birth defects showed no association with SRIs, including any individual SRI, for any specific malformation including cardiac.

Alwin New England J Medicine 2007

Louick New England J Medicine 2007

Study 1170 women who took first trimester Paxil failed to find an association with cardiac defects.

Einarson Am J Psychiatry 2008; 165

31

Confounding Factors in Evaluating Cardiovascular Risk

Diagnostic bias as infants born to mothers taking SRIs get twice as many cardiac echocardiograms as non-exposed infants.

Records used in retrospective studies may not be an accurate reflection of actual exposure.

SRI-exposed infants are exposed to other risk factors including other medications and maternal illness.

Exposed infants have reduced gestational-age compared with infants born to non-depressed women.

32

Persistent Pulmonary Hypertension of the Newborn

PPHN estimated to occur in 1 - 2/1000 births.

6 studies examining association between SRIs and PPHN.

The first study (2006) showed risk 6X baseline rate. Study lacked statistical power.

2006 FDA warning regarding SRIs and PPHN.

Swedish Birth Registry Study (2008) examined about one million births and risk of PPHN.

Odds-ratio for development of PPHN with SRI-exposure in pregnancy resulted in a risk odds-ratio of 2.1 to 3.7 or an absolute risk of 3 to 6/1000.

Pharmacoepidemiology Drug Safety,Kallen, 2008;17(8)

33

Evaluating PPHN Risk

Risks for PPHN include: maternal obesity, C-section delivery, preterm delivery, maternal smoking and gestational diabetes which are associated with pregnant women who have psychiatric illness.

Women who filled SRI prescriptions in Swedish Study were older and more likely to smoke.

34

Absolute risk is low: 11,000 exposed infants in Nordic Study resulted in 33 cases of PPHN which is a rate of 3/1000.

FDA retracted warning regarding PPHN in 2011 based on studies published after 2006 showing decreased risk or no increased risk with SRI-use.

35

Pharmacokinetics of Antidepressants

- Metabolism and clearance of ADs increase during pregnancy due to increases in hepatic metabolism and renal blood flow.
- AD levels may fall, especially after week 20 of pregnancy.
- Worsening of symptoms may necessitate an increase in antidepressant dose during pregnancy.

36

Antidepressants and Lactation

- All antidepressants are acceptable for use during lactation.
- The best antidepressant to use during lactation is the one that has historically worked the best for that woman.
- Paroxetine and Sertraline are “favorites” for breastfeeding based on studies or infant serum levels but the study sizes are too small to fully discriminate between the differences in antidepressants during lactation.

37

Final Thoughts

- There is a false dichotomy between the interest of the infant and the interest of the mother.
- The best antidepressant to use during pregnancy and lactation is the antidepressant that has worked best for that woman.

38

- Reducing the dose of an antidepressant during pregnancy and potentially not treating depression to remission risks exposing the unborn infant to both the effects of the SRIs *and* the effects of depression which is the worst outcome.

39

- Low socioeconomic minority women are very difficult to engage in treatment. Intense intervention study could only engage 1/3.
- In the U.S., a drug can not be a teratogen but still be a “litagen.”

40

Resources for Clinicians

- **Medication use in pregnancy**
  Mother to Baby: mothertobaby.org
- **Medication use during lactation**
  elactanci: e-lactancia.org
  InfantRisk Center: infantrisk.com
- **To support patients and families and for referrals**
  Postpartum Support International
  Nebraska Chapter: psichapters.com/ne/
- **UNMC Reproductive Psychiatry Clinic Telehealth**:
  Patients may schedule by calling 402-552-6007

41

42