

Depression Management and SSRI Use in Pregnancy

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No Disclosures

- I have no relevant financial relationships to disclose.



Objectives

- Definition and epidemiology of perinatal depression
- Adverse outcomes of depression
- Diagnostic criteria and screening strategies for perinatal depression
- Benefits and risks of treatment options



Perinatal Depression

- Depression that occurs during pregnancy or in the first 12 months postpartum
- 10-23% of pregnant women meet criteria
- Up to 70% of pregnant women report symptoms



Postpartum Depression

- Affects 1 in 7 women
- Only 20% of women report symptoms to providers.



Risk Factors for Depression During Pregnancy

- History of depression
- Anxiety
- Unplanned pregnancy
- Unmarried
- Lack of social support
- Domestic violence
- Low socioeconomic status
- Lower education
- Smoking



Risk Factors for Postpartum Depression

- Depression/anxiety during pregnancy
- Life stressors
- Traumatic birth experience
- Preterm birth
- NICU admission
- Lack of social support
- Breastfeeding difficulties



Outcomes of Untreated Depression

- Maternal:
 - ◆ Suicide
 - ◆ Alcohol, drug, tobacco abuse
 - ◆ Social isolation
 - ◆ Poor compliance with care



Outcomes of Untreated Depression

- Pregnancy:
 - ◆ Miscarriage
 - ◆ Premature birth
 - ◆ Growth restriction
 - ◆ Low birth weight



Outcomes of Untreated Depression

- Infant/Childhood:
 - ◆ Infanticide
 - ◆ Irritability
 - ◆ Conduct disorders
 - ◆ Other psychiatric illnesses
 - ◆ Suicide



Diagnostic Criteria

- Depressed mood and/or anhedonia X 2 wks
- ≥ 5 symptoms nearly every day:
 - ◆ Depressed mood
 - ◆ Anhedonia
 - ◆ Change in weight/appetite
 - ◆ Change in sleep
 - ◆ Fatigue
 - ◆ Guilt/worthlessness
 - ◆ Concentration
 - ◆ Suicidality



Screening Tools

Screening Tool	Number of Items	Time to Complete (Minutes)	Sensitivity and Specificity
Edinburgh Postnatal Depression Scale	10	Less than 5	Sensitivity 59-100% Specificity 49-100%
Postpartum Depression Screening Scale	35	5-10	Sensitivity 91-94% Specificity 72-98%
Patient Health Questionnaire 9	9	Less than 5	Sensitivity 75% Specificity 90%
Beck Depression Inventory	21	5-10	Sensitivity 47.6-82% Specificity 85.9-89%
Beck Depression Inventory-II	21	5-10	Sensitivity 56-57% Specificity 97-100%
Center for Epidemiologic Studies Depression Scale	20	5-10	Sensitivity 60% Specificity 92%
Zung Self-rating Depression Scale	20	5-10	Sensitivity 45-89% Specificity 77-88%



ACOG CO No. 630

Edinburgh Postnatal Depression Scale

- Includes anxiety symptoms
- Excludes some constitutional symptoms, such as changes in sleep



Edinburgh Postnatal Depression Scale

In the past 7 days:

- | | |
|---|--|
| <p>1. I have been able to laugh and see the funny side of things</p> <ul style="list-style-type: none"> <input type="checkbox"/> As much as I always could <input type="checkbox"/> Not quite so much now <input type="checkbox"/> Definitely not so much now <input type="checkbox"/> Not at all | <p>*6. Things have been getting on top of me</p> <ul style="list-style-type: none"> <input type="checkbox"/> Yes, most of the time I haven't been able to cope at all <input type="checkbox"/> Yes, sometimes I haven't been coping as well as usual <input type="checkbox"/> No, most of the time I have coped quite well <input type="checkbox"/> No, I have been coping as well as ever |
| <p>2. I have looked forward with enjoyment to things</p> <ul style="list-style-type: none"> <input type="checkbox"/> As much as I ever did <input type="checkbox"/> Rather less than I used to <input type="checkbox"/> Definitely less than I used to <input type="checkbox"/> Hardly at all | <p>*7. I have been so unhappy that I have had difficulty sleeping</p> <ul style="list-style-type: none"> <input type="checkbox"/> Yes, most of the time <input type="checkbox"/> Yes, sometimes <input type="checkbox"/> Not very often <input type="checkbox"/> No, not at all |
| <p>*3. I have blamed myself unnecessarily when things went wrong</p> <ul style="list-style-type: none"> <input type="checkbox"/> Yes, most of the time <input type="checkbox"/> Yes, some of the time <input type="checkbox"/> Not very often <input type="checkbox"/> No, never | <p>*8. I have felt sad or miserable</p> <ul style="list-style-type: none"> <input type="checkbox"/> Yes, most of the time <input type="checkbox"/> Yes, quite often <input type="checkbox"/> Not very often <input type="checkbox"/> No, not at all |
| <p>4. I have been anxious or worried for no good reason</p> <ul style="list-style-type: none"> <input type="checkbox"/> No, not at all <input type="checkbox"/> Hardly ever <input type="checkbox"/> Yes, sometimes <input type="checkbox"/> Yes, very often | <p>*9. I have been so unhappy that I have been crying</p> <ul style="list-style-type: none"> <input type="checkbox"/> Yes, most of the time <input type="checkbox"/> Yes, quite often <input type="checkbox"/> Only occasionally <input type="checkbox"/> No, never |
| <p>*5. I have felt scared or panicky for no very good reason</p> <ul style="list-style-type: none"> <input type="checkbox"/> Yes, quite a lot <input type="checkbox"/> Yes, sometimes <input type="checkbox"/> No, not much <input type="checkbox"/> No, not at all | <p>*10. The thought of harming myself has occurred to me</p> <ul style="list-style-type: none"> <input type="checkbox"/> Yes, quite often <input type="checkbox"/> Sometimes <input type="checkbox"/> Hardly ever <input type="checkbox"/> Never |

Edinburgh Postnatal Depression Scale

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, 5-10 (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)

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Beck Depression Inventory

- 0 I am not particularly discouraged about the future.
- 1 I feel discouraged about the future.
- 2 I feel I have nothing to look forward to.
- 3 I feel the future is hopeless and that things cannot improve.

1-10	These ups and downs are considered normal
11-16	Mild mood disturbance
17-20	Borderline clinical depression
21-30	Moderate depression
31-40	Severe depression
over 40	Extreme depression



Treatment

- Women on antidepressants prior to conception:
 - ♦ If treatment discontinued, 68% relapsed
 - ♦ If treatment continued, 25% relapsed



Cohen *et al.* 2006 JAMA

Treatment Options

- Behavioral and psychotherapy
- Electroconvulsive therapy
- Pharmacologic therapy



Behavioral and Psychotherapy

- Cognitive behavioral therapy is effective in pregnant women
 - ◆ Focuses on changing dysfunctional thought patterns
- Less evidence regarding the effectiveness of psychodynamic psychotherapy
 - ◆ Focuses on deeper, unconscious motivations.



Electroconvulsive Therapy

- Indicated for severe depression
 - ◆ Life-threatening
 - ◆ Fails to respond to medical therapy
- Safe and effective
- Requires close monitoring



Pharmacologic Therapy

- Tricyclic antidepressants
 - ◆ Neonatal withdrawal, rarely seizures
- Serotonin norepinephrine reuptake inhibitors (SNRIs)
 - ◆ Neonatal withdrawal, rarely seizures
- Selective serotonin reuptake inhibitors (SSRIs)



SSRIs and Birth Defects

- No consistent evidence linking most SSRIs with congenital anomalies
- One exception: paroxetine (Paxil®)
 - ◆ Major cardiac anomalies: OR 1.28 (1.11-1.47)
 - ◆ Septal defects and right outflow tract anomalies

UVA MEDICINE Berard *et al.* 2015 Br J Clin Pharmacol
 Knowledge that will change your world

SSRIs and PPHN

- Persistent pulmonary hypertension of the newborn
 - ◆ R-to-L shunting and profound hypoxia
 - ◆ Mortality of 10-20%
- FDA warning in 2006 following study showing 6-fold increase in risk associated with SSRIs

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SSRIs and PPHN

- FDA revised the warning in 2011 after conflicting evidence emerged
- Most recent study showed an OR of 1.28 (1.01-1.64).
 - ◆ Untreated: 25 per 10,000
 - ◆ SSRI: 34 per 10,000

UVA MEDICINE Huybrechts *et al.* 2015 JAMA
 Knowledge that will change your world

SSRIs and Neonatal Adaptation Syndrome

- Transient (< 2 weeks)
- Respiratory abnormalities
- Hypoglycemia
- Jitteriness
- Low Apgar scores
- OR 4.08 (1.2-19.93)
- Comparison groups = unaffected women
- Many women also taking benzodiazepines
- Lethargy
- Poor tone
- Weak/absent cry
- Feeding difficulties
- Convulsions

UVA MEDICINE Lattimore *et al.* 2005 Am J Perinatology
 Knowledge that will change your world

SSRIs and Autism

Maternal exposure to anti-depressant SSRIs linked to autism in children

A New Study Raises Old Questions About Antidepressants And Autism

Reports Linking SSRIs With Autism Are Greatly Exaggerated

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SSRIs and Autism

Antidepressant Use During Pregnancy and the Risk of Autism Spectrum Disorder in Children

Takoua Boukhris, MSc; Odile Sheehy, MSc; Laurent Mottron, MD, PhD; Anick Bérand, PhD

JAMA Pediatr. 2016;170(2):117-124. doi:10.1001/jamapediatrics.2015.3356
 Published online December 14, 2015.

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Autism Study Details

- 145K patients in Canadian registry
- Risk of autism:
 - ♦ Any antidepressant: HR 1.87 (1.15-3.04)
 - ♦ SSRI: HR 2.17 (1.20-3.93)



Limitations

- Use in 1st trimester or before pregnancy was not associated with autism
- Only continued use in 2nd/3rd trimester was associated with autism
- Are these fundamentally different patient populations?



Limitations

- Autism was defined by diagnosis code
- When autism was confirmed by psychiatrist/neurologist, there was no significant association
- Several other studies have found no significant association



Use of SSRIs in Pregnancy

- Avoid paroxetine
- Discuss treatment benefits and potential risks
- Discuss risks of untreated maternal depression



SSRIs and Lactation

- Significant data indicate SSRIs are compatible with lactation
- Levels in milk are typically <3% of the maternal dose
- Most data support use of sertraline (Zoloft®), the preferred agent



The FDA Pregnancy Categories

- A, B, C, D, X
- Not a continuum of risk
- Removed from labeling as of 2015
- Alternatives?



InfantRisk

- Texas Tech University Healthsciences Center
- App for phone
- Hotline: 1-800-352-2519
- Website: <http://www.infantrisk.com>



InfantRisk

Safest
Human studies and extensive use in pregnant patients suggest there is little or no risk to the fetus. Thus, the possibility of harm is remote.

Safer
Studies in animals have not shown fetal risk. While studies in humans are limited, extensive use in humans suggests risk to the fetus is minimal.

Probably Safe
Studies in animals may show some risk. However no studies in humans are available. Use only if the risk is justified.

Possibly Hazardous
There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk.

Hazardous
Studies in animals or humans have demonstrated fetal abnormalities, or there is evidence of fetal risk based on human experience. Avoid if at all possible.

Unknown
There is no data or information available.



InfantRisk

PAROXETINE

DRUG NAME: PAROXETINE
 DRUG TYPE: Antidepressant, serotonin reuptake inhibitor
 TRADE NAMES: Amvox 20, Paxil, Serax
 USUAL DOSE: 20-60 mg daily
 LACTATION RISK: L2 - Significant Data-Comparable
 PREGNANCY RISK: P4 - Positive evidence of fetal risk
 RELATIVE INFANT DOSE: 1.2% - 2.8%
 SIDE EFFECTS: Sedation, insomnia, headache, dizziness, dry mouth, constipation. Use in children and adolescents.

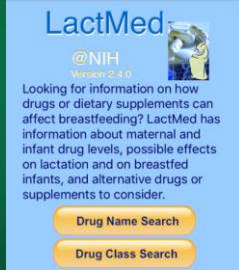
SERTRALINE

DRUG NAME: SERTRALINE
 DRUG TYPE: Antidepressant
 TRADE NAMES: Lunel, Zoloft
 USUAL DOSE: 50-200 mg daily
 LACTATION RISK: L1 - Extensive Data-Comparable
 PREGNANCY RISK: P3 - Unknown, risk to the fetus cannot be ruled out
 RELATIVE INFANT DOSE: 0.4% - 3.2%
 SIDE EFFECTS: Headache, dizziness, insomnia, nervousness, dry mouth, dyspepsia, nausea, diarrhea, anorexia, nervous, increased sweating, gait/ataxia in non-pregnant and non-



Other Resources

- Reprotox: www.reprotox.org
- LactMed



Summary

- Perinatal depression is a common and devastating condition, if left untreated
- The benefits of treatment typically outweigh the potential risks
- There are multiple resources available to evaluate the safety of medications during pregnancy and lactation