

Perinatal Mood Disorders & Psychotropic Medications

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Overview

- 1 in 5 Adults in U.S. have a mental health problem
- 1 in 2 U.S. adults will develop a mental health condition sometime in their lifetime
- Current prevalence of any mental illness is 18.29%
- 8.5% of U.S. adults have substance abuse problem
- 4% of adults report serious suicidal thoughts
- 56.5% of adults with mental illness have received no care in the past year

Perinatal Mood Disorders

- Depression: Occurrence of any major or minor episodes during pregnancy or any time within 12 months of birth
 - Upwards of 20% incidence in pregnancy
 - Approximately 12-16% incidence after birth
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- J Am Diet Assoc.2009 Sep;109(9)1566-75

Perinatal Mood Disorders

Anxiety

Pregnancy—About 16% incidence

Postpartum—About 18% incidence

J Affect Disord.2016 Aug;2

2.6% to 39% for “any anxiety disorder”

Clinical Psychologist.2017 March, Vol 21(1), 4-19

Perinatal Mood Disorders

OCD

- Obsessive Compulsive Disorder
- Higher incidence in perinatal period compared to general population
- Incidence 2-2.5 % in pregnancy and Postpartum
- Incidence 1-1.25% in general population
- Up to Date, Dec, 2016

Perinatal Mood Disorders

- Attention Deficit Disorder
 - Actual incidence is unknown.
 - Prescriptions for ADHD medications in childbearing women have increased from 0.9% in 2003 to 4% in 2015
 - Most common drugs: amphetamine salts and lisdexamfetamine (Adderall and Vyvanse)
 - CDC

Perinatal Mood Disorders

- ## Bipolar Disorder
- Two main types: Bipolar I and Bipolar II
- Incidence ranges from 0.4-4.5%
- Misdiagnosis is frequent—50 to 75% (depending on who is making the diagnosis)
- Suicide attempts reach between 32 and 36%
- Neuropsychiatry (2014)4(1),95-107

Perinatal Mood Disorders

- Post Traumatic Stress Disorder
 - Prevalence rates 10-20% for lifetime and 5% for current PTSD
 - For high risk women, prevalence rates up to 24% during pregnancy
- *Depress Anxiety*, 2016 Jul;33(7):584-591

Perinatal Mood Disorders

- Substance Use Disorders
- Difference between drug use & drug abuse with lack of clear methods for distinguishing the difference.
- Substance use usually decreases in pregnancy
- Actual rates of abstinence and relapse not known
- Drug Alcohol Depend.2015 May 1;147-155

Perinatal Mood Disorders

- Tobacco Use
 - Approximately 10% of women reported smoking during last 3 months of pregnancy
 - About 55% of women quit smoking during pregnancy
 - Of women who quit, 40% started smoking within 6 months of birth
 - CDC: Tobacco Use & Pregnancy; Data from PRAMS (Pregnancy Risk Assessment Monitoring System)

Perinatal Mood Disorders

Alcohol Use

- 87% of women who drank ETOH before pregnancy quit drinking
 - 6.6% reduced the amount of ETOH intake
 - 6.4% reported no reduction in intake
 - 30% of women reported any ETOH use in pregnancy
 - 8% reported binge drinking on at least one occasion
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- Epidemiology of Alcohol Use: Up to Date, Feb 15, 2018

Perinatal Mood Disorders

- ## Illegal Drugs
- Roughly 6% of pregnant women use illegal drugs
- Women are at highest risk for developing a substance abuse disorder during reproductive years
- Most common substances (after tobacco and alcohol) are marijuana, cocaine, amphetamine type stimulants, and opiates
- Relapse common in postpartum period. Frequency of relapse depends on substance used.
- Substance Use During Pregnancy. Version 1.F1000Res.2016;5:F1000 Faculty Rev-887.

Pregnancy Adaptations

- Mother must cope with physical, physiologic, emotional, and social changes engendered by pregnancy.
- Each can affect the mother's mood and mental health.

Pregnancy Adaptations

Physical

- 1. Increased hormonal activity: estrogen, progesterone, oxytocin, prolactin, placenta
- 2. Increased blood volume
- 3. Changes in liver metabolic capacity
- 4. Increased renal glomerular filtration
- 5. Changes in maternal weight

Pregnancy Adaptations

- Physical
 - 6. Microchimerism (fetal cells circulating in maternal circulation and brain)
 - 7. Changes in brain structure
 - Hippocampus
 - Olfactory neurons
 - Brain's reward system
 - 8. Sleep Deprivation

Pregnancy Adaptations

- Five Common Symptoms
 - Weepiness
 - Mood Swings
 - Fear
 - Anxiety
 - Forgetfulness (pregnancy brain)

Pregnancy Adaptations

- Psychosocial
 - 1. Family Dynamics
 - 2. Past Trauma
 - 3. Insecurities
 - 4. Practical Concerns
 - 5. Dissonance between expectations & reality

Assessment

- 1. Thorough personal history
- 2. Family psychiatric history
- 3. Past or current use of psychotropic drugs
- 4. Past or current history of self harm behaviors
- 5. History of suicidal ideation or attempts
- 6. History of ER visits, hospitalizations, other types of treatment
- 7. Survey instruments: EPDS and GAD 7

Psychotropic Drugs

- Antidepressants
 - Selective serotonin reuptake inhibitors (SSRIs)
 - Serotonin-norepinephrine reuptake inhibitors (SNRIs)
 - Tricyclic Antidepressants (TCAs)
 - Monoamine oxidase inhibitors (MAOIs)
 - Atypical Agents

Psychotropic Drugs

- Anxiety & Panic Disorder
 - Benzodiazepines
 - SSRIs

Psychotropic Drugs

- Antipsychotic Agents
 - All antipsychotics reduce dopaminergic neurotransmission
 - First generation antipsychotics are D2 antagonists
 - They also block other receptors such as histamine-1, muscarinic-1 and alpha-1
 - Second generation antipsychotics are known as atypical or serotonin-dopamine antagonists and have less side effects

Psychotropic Drugs

● Mood Stabilizers

- Lithium
- Lamictal (lamotrigine)
- Depakote (divalproex)
- Tegretal; Trileptal (carbamazepine & oxcarbazapine)
- Some atypical antipsychotics (Seroquel, Zyprexa, Latuda)

Psychotropic Drugs

ADHD Medications

Methylphenidate--(Ritaline, Focalin, Concerta, Metadate)

Dextroamphetamine—(Dexedrine, Dextrostat)

Mixed Amphetamine—(Adderall)

Atomoxetine—(Strattera)

Bupropion—(Wellbutrin)

Alpha-2 Agonists (Clonidine, Catapres, Tenex (guanfacine))

Psychotropic Drugs

- Risks of Untreated Depression
 - Children can have poor growth, insecure attachment, elevated rates of illness, and emotional and behavioral problems.
 - Some research suggests increased symptoms of ADHD in offspring of mothers who had depression in pregnancy

Psychotropic Drugs

- Risks Associated with Antidepressants
 - No identified risks of birth defects EXCEPT for slightly increased risk of cardiac defects with use of paroxetine. Defects are usually mild.
 - Fetal echocardiogram should be done if mother has used paroxetine in early pregnancy.

Psychotropic Drugs

- Studies are mixed on whether or not use of SSRIs is associated with low birth weight or PTL. Since depression is associated with both, it is hard to tease out what confounding variables might be.
- Use of antidepressant meds in the 3rd trimester of pregnancy are associated with an increased risk of postpartum hemorrhage
- Studies are mixed about risks of autism in babies exposed to antidepressant drugs in utero

Psychotropic Drugs

- Neonatal Withdrawal Syndrome (NAS)
 - Mild symptoms occur in about 22% of newborns
 - Severe symptoms occur in 3% of newborns
 - May be more common if there is maternal use of fluoxetine (Prozac) or paroxetine (Paxil)
 - Withdrawal is not dependent on maternal dose
 - May be more likely with use in 3rd trimester

Psychotropic Drugs

- NAS (Neonatal Adaptation Syndrome)
Symptoms

- Cyanosis
- Respiratory Distress
- Constant Crying
- Feeding Difficulties
- Temperature Instability
- Hypo or hypertonia
- Apnea
- Irritability
- Tremor/Jitteriness
- Vomiting
- Seizures
- Hyper-reflexia

Psychotropic Drugs

- Other Newborn Risks/Symptoms
 - Hypoglycemia occurs in about 19-20%
 - Pulmonary Hypertension—Very rare
 - 2.1/1000 incidence in unexposed infants
 - 3.1/1000 incidence in exposed infants

SSRI Side Effects

- Nausea
- Stimulation
- Sedation
- Sexual Side Effects
- Apathy
- Weight Gain, 5-30#, usually late onset 3-12 months
- Cognitive dysfunction—short term memory deficits, word finding difficulties

SSRI Side Effects

- Elimination half-life correlates with likelihood of withdrawal symptoms after med is stopped. 5 week washout for fluoxetine; about 10-14 days for other SSRI's
- Withdrawal symptoms—include dizziness, irritability, insomnia, paresthesias, dysesthesias; least with fluoxetine (longest half-life), most with paroxetine (shortest half-life)
- Hyperprolactinemia (breast enlargement, irregular menses, amenorrhea, galactorrhea)

SSRI Side Effects

- Excess perspiration
- P450 Effects

Risks of Untreated Anxiety

Chronically elevated cortisol levels

- May impact birth weight, head circumference, height
- Higher incidence of preterm birth
- Increased risk of miscarriage
- Infant may have increased fussiness and temperamental problems
- Infant may have lower scores on measures of mental development

Risks of Untreated Anxiety

- Infant/child may have problems with attention, attention regulation, and emotional reactivity
- Association between hyperactivity and inattention in boys
- Emotional problems in girls and boys
- Conduct problems in girls
- Anxiety can impact/impair parenting behaviors

Anxiety Meds Side Effects

- SSRIs—see previous slide
- Benzodiazepines
 - Multiple meta-analysis studies suggest no or minimal risk/relationship between exposure and birth defects
 - A birth registry suggested increased risks of pyloric stenosis and alimentary tract atresia
 - May increase risk of cleft lip/palate from 6 in 10,000 to 11 in 10,000

Anxiety Meds Side Effects

- Increased risk of miscarriage
- Increased risk of preterm birth
- No association with low birth weight in some studies and slight association of low birth weight if fetus exposed early in pregnancy

Anxiety Med Side Effects

- Chronic use in pregnancy can impact infant:
- Low Apgar scores
- Hypothermia
- Hyperreflexia
- Hyper or hypotonia
- Irritability
- Lethargy
- Restlessness
- Tremor
- Diarrhea
- Poor Feeding
- Vomiting
- Sx can last up to 3 mo

Risks of Untreated Bipolar

- Increased risk of episodes of illness recurrence
- Increased risk of behaviors detrimental to pregnancy
- Increased risk for preterm birth and SGA infant
- Depressive symptoms occur more frequently than manic or hypomanic symptoms
- High risk of postpartum psychosis
- High risk of suicide

Risks of Mood Stabilizers

- Miscarriage
- Major and minor structural malformations
- Fetal growth restriction and low birth weight
- Preterm birth
- Neonatal toxicity and withdrawal
- Postnatal developmental effects upon behavior, cognition, and emotional regulation

Risks of Mood Stabilizers

- Medication effects vary according to gestational age
- Exposure between weeks 3-8 of gestation associated with birth defects
- Exposure in 3rd trimester associated with toxicity and withdrawal
- Highest risk for birth defects with Valproate
- Carbamazepine associated with severe skin disorder 1-6/10,000 (TEN & Stevens-Johnson)

Risks of Mood Stabilizers

- Carbamazepine associated with aplastic anemia and agranulocytosis
- There is a 5-8 times greater incidence of above if med is used compared to the general population not exposed to it.
- Overall risk is very low in general population:
 - 6/1,000,000 per year for agranulocytosis
 - 2/1,000,000 per year for aplastic anemia

There may be transient decrease in platelets or WBCs

Risks of Mood Stabilizers

- Lamotrigine—first line for bipolar
- Main risk is serious skin rash (Stevens-Johnson)
- Drug must be started at low dose and dose increased VERY GRADUALLY
- Most cases of life threatening rash occur within 2 to 8 weeks of start of treatment

Risks of Mood Stabilizers

- Lithium
- Narrow therapeutic margin; toxicity can easily occur at doses close to therapeutic level
- May be some association with fetal cardiac defects. Fetus should have echocardiogram if exposed to Lithium in early pregnancy
- Has many side effects including possible hypothyroidism, hypercalcemia, renal effects, CNS depression and heart failure from myocardial toxicity

Risks of Mood Stabilizers

- Lithium toxicity can occur in newborns with late pregnancy exposure, especially with higher serum levels
- Use during 2nd and 3rd trimester can increase neonatal risks of:
 - Cardiomegaly
 - GI bleeding
 - Polyhydramnios
 - Nephrogenic diabetes insipidus
 - Hepatomegaly
 - Goiter & Hypothyroidism
 - Premature Labor

Risks of Antipsychotics

- Minimal evidence for risk of birth defects
- Neonatal toxicity and withdrawal, especially if used in 3rd trimester
- Placental passage varies with drug
- Patient is at risk for extrapyramidal symptoms, especially with first generation drugs and risperidone
- Preterm birth occurs more often if fetus exposed to first generation antipsychotics
- No evidence of adverse effects for behavioral, cognitive or emotional development

Risks of Antipsychotics

- Second generation antipsychotics may be associated with mild increase in birth defects, especially of the heart.
- Second generation antipsychotics include:
 - Aripiprazole (Abilify)
 - Clozapine
 - Olanzapine
 - Risperidone
 - Ziprasidone

Risks of Antipsychotics

- Aripiprazole (Abilify):
 - May evoke compulsive gambling behaviors
 - May cause increased risk of suicidal thoughts, especially if used with antidepressant meds
- Clozapine:
 - Severe neutropenia (infection/death as consequence)
 - Orthostatic hypotension, bradycardia, syncope
 - Seizures—Risk is dose related
 - Myocarditis, cardiomyopathy and mitral valve incompetence

Risks of Antipsychotics

- Olanzapine (Zyprexa):
 - Post injection delirium/sedation syndrome

Quetiapine (Seroquel):

Increased suicidal thoughts and behaviors

Risperidone (Risperdal, Risperdone):

Avoid use in patients > 65 years

Ziprasidone: No special warnings

Alternative Treatment Options

- Counseling
- Exercise, especially outdoors
- Acupuncture for Anxiety & Stress Relief
- Hypnosis
- Light Therapy
- Negative Ion Therapy
- Float Tanks
- Earthing
- Nutrition

Breastfeeding & Psychotropic Med Use

- 1. Meds with lower molecular weights pass into breastmilk more easily (i.e. 200 g/mol or less)
- 2. Drugs that are highly protein bound will have less active metabolites in the breast milk
- 3. Maternal weight adjusted dose ratios can be calculated in regard to breast milk

Lactation and Meds

- Citalopram (Celexa)—7.9%
- Escitalopram (Lexapro)—3.9%
- Fluoxetine (Prozac)—3-12% of maternal dose
- Fluvoxamine (Luvox)—0.98%
- Paroxetine (Paxil)—1.2%
- Sertraline (Zoloft)—0.5%bre

Lactation and Meds

- Antipsychotics: Limited info; exposure of infant appears to be low
- Stimulants: Only a few studies; Drug concentration in breast milk is often low, but can vary considerably depending on which drug
- Substance Abuse Meds: Probably okay for methadone and buprenorphine. Unknown in regard to Antabuse.
- Nicotine: Okay; less exposure with use of nicotine replacement than with use of cigarettes