Psychiatric Disorders in Pregnancy

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Education Learning Objectives

1. Become familiar with 1st line treatments for mood, anxiety, and psychotic d/o

1. Understand the latest developments from research

1. Understand that the majority of psychotropics are not major teratogens
Question #1

Which of the following antidepressants is Category D in pregnancy?

A) Duloxetine
B) Fluoxetine
C) Paroxetine
D) Desipramine
E) Mirtazapine
Question #2

Which of the following psychotropics is considered a major teratogen?

A) Lithium
B) Lamotrigine
C) Lurasidone
D) Valproate
E) Clozapine
Pregnancy and Mental Illness

Once thought to be a time of emotional well-being for women

Frequently present prior to conception for consultation

In non-puerperal populations, there is increasing evidence of high rates of relapse following discontinuation of psychotropic medications
Evaluation

(1) normative or pathological,

(2) manifestations of a new-onset psychiatric disorder

(3) an exacerbation of a previously diagnosed or undiagnosed psychiatric disorder.

Even when performed, definitive treatment frequently not delivered
Mood Disorders Diagnosis

Depression: More supportive features include anhedonia, guilt, hopelessness, thoughts of suicide

Normal features in pregnancy: changes in sleep and appetite, fatigue, and lower libido

Self-injurious or suicidal behaviors appears to be relatively low in women who develop depression during pregnancy.
Mood Disorders Treatment

Severity of the underlying disorder

Mild-Moderate: Non-pharmacological

IPT is ideally suited for the treatment of depressed pregnant women

No response or who have more severe symptoms, pharmacologic treatments must be considered.
AD use in Pregnancy

(1) risk of pregnancy loss or miscarriage
(2) risk of organ malformation or teratogenesis
(3) risk of neonatal toxicity or withdrawal syndromes during the acute neonatal period
(4) risk of long-term neurobehavioral sequelae.
Classification of psychotropics

Most psychotropic medications—category C

No psychotropic drugs are category A

Can be often ambiguous (e.g. TCAs) - retrospective/case reports

more rigorous prospective design or have relied on large administrative databases or multi-center birth defect surveillance programs.
SSRIs

Prospective data are available for all of the SSRIs.

Baseline incidence of major congenital malformations in newborns born in the US is between 2% and 4%.

All studies published have indicated the overall risk of malformations in SSRI-exposed infants does not exceed this baseline level.

Paroxetine: cardiac risk?
TCAs

Three prospective and more than 10 retrospective studies examined the risk of organ malformation in over 400 cases of first-trimester exposure. These studies do not indicate a significant association between fetal exposure to TCAs and risk for any major congenital anomaly.

Desipramine and nortriptyline preferred—less anticholinergic and least likely to exacerbate orthostatic hypotension.
Bupropion

May be an attractive option for women who have not responded well to SSRIs or TCAs.

The most recent information from the Bupropion Pregnancy Registry maintained by the manufacturer includes data from 517 pregnancies involving first-trimester exposure to bupropion.

-20 infants with major malformations (3.9%)
SNRIs and others

Venlafaxine (150 exposures),
Duloxetine (208 exposures), Mirtazapine (104 exposures),
Nefazodone (89 exposures), Trazodone (58 exposures)

Gold standard = 500-600 exposures showing 2 fold increase

Most commonly used: fluoxetine, citalopram, sertraline
MAOIs

- insufficient studies
- hypertensive crisis
  - tocolytics
SSRI safety

Some reports- decreased gestational age, low weight, poor neonatal adaptation.

Meta-analysis- in utero exposure may have statistical significance on certain outcomes

Observed effects- small (3 days shorter gestation age, 75g lower birth weight, less than half a point on 1 and 5min Apgar
SSRI safety

Recent studies- poor peri-natal outcomes with SSRI exposure close to delivery.

transient neonatal distress syndromes associated with exposure to or withdrawal from antidepressants in utero.

tremor, tachypnea, restlessness, increased muscle tone, and increased crying.

resolves in 1-4 days
SSRI safety-Persistent Pulmonary HTN of the newborn

Initial report 2006-SSRI after the 20th week of gestation was associated with a six-fold greater risk of PPHN (1% of infants)

Since 2006: 3 studies show no association

1 study showed much lower risk than 1%
Long term effects of prenatal AD exposure

Less studies available

No differences between the children exposed to fluoxetine or TCAs in terms of IQ, language, temperament, behavior, reactivity, mood, distractibility, and activity level.

More research needed
Clinical Guidelines

Majority of women suffering from depression receive inadequate treatment

Management of depression guided by practical experience

Work with patient to arrive at safest decision

- Psychiatric history, current symptoms, attitude towards psychiatric meds during pregnancy
Discontinuation of AD during pregnancy

One study - women who discontinued their medications were 5X more likely to relapse

- risk/benefits should be discussed and treatment continued especially if recurrent/refractory depression

- reproductive safety profile of meds
Simplify and optimize medications

E.g. Patient has depressive symptoms with insomnia- consider a sedating TCA rather than an SSRI +benzo

Optimize: often dose decreased in pregnancy, but this may put mother at greater risk

changes in plasma volume, hepatic metabolism, and renal clearance may significantly reduce drug levels

-up to 65% reduction in TCA level shown
Bipolar Disorder

Pregnancy as protective factor - limited data

Risk for relapse and chronicity following discontinuation of mood stabilizers is high.
Lithium use in pregnancy - cardiovascular risk

Early reports of higher rates of cardiovascular malformations following pre-natal exposure to this drug.

Recent data suggest the risk following pre-natal exposure to lithium is smaller than previous estimates.

1 in 2,000 (0.05%) and 1 in 1,000 (0.1%).

Screening ultrasound and fetal echocardiography is recommended - 16 to 18 weeks.
Lamotrigine use in pregnancy

Good choice in bipolar patient in need of prophylaxis during pregnancy with mood stabilizer

Previous reports did not show an elevated risk of malformations

North American Anti-Epileptic Drug registry indicate an increased risk of oral clefts when exposed in 1st trimester

Prevalence: 9/1000 births
Far greater risk...

Anticonvulsants such as valproic acid and carbamazepine: increased risk of neural tube defects (3-8%) and spina bifida (1%).

- mid-face hypoplasia, congenital heart disease, cleft lip and/or palate, growth retardation, and microcephaly.

Increased risk: VPA above 1,000mg/day and greater than 1 anticonvulsant
Pre-natal screening-Anticonvulsants

Fetal U/S: 16-18 wks

Fetal neural tube defects: maternal serum alpha-fetoprotein levels and ultrasonography

4 mg a day of folic acid before conception and in the first trimester for women receiving anticonvulsants is frequently recommended

Use of folic acid to attenuate the risk of neural tube defects has not been systematically evaluated.
Cognitive development

Risk of neurodevelopmental disorders was about six times higher in children exposed to valproate monotherapy (12%) than in children with no anticonvulsant exposure (1.87%).

Higher risk in those exposed to polypharmacy with VPA (15%)

ASD was the most frequent diagnosis among VPA-exposed children
Psychotic Disorders in Pregnancy

- Typical high potency antipsychotics (haloperidol, thiothixene) are **low risk in first trimester**
- Low potency antipsychotics are associated with congenital malformations, but no absolute contraindication
- Atypical antipsychotics do not have much safety data; one study of 151 infants with prenatal exposure showed no increased risk
  - Many atypicals are used with other meds so difficult to isolate whether the


Managing pregnant women on antipsychotics

● Each case must be reviewed weighing risk/harm

● Can discontinue antipsychotic or change to typical antipsychotic
  ○ May not always be an option if meds do not control symptoms or women severely ill

● Can continue with antipsychotic with caveat that it is maintaining mother’s health but there may be an unknown associate risk for complication.
Anxiety Disorders

Anxiety symptoms may be associated with premature labor, lower birth weight, lower Apgars, and abruption.

Can attempt CBT and supportive psychotherapy.

Recommend slow tapering of anxiety meds prior to conception.

Abrupt discontinuation (esp benzos) can cause rebound panic or withdrawal symptoms.

Can use TCAs, SSRIs, SNRIs and benzos.
Benzodiazepines

Safety studies have had variable results; some older studies show increased risk of oral clefts while some newer studies refute this.

One meta-analysis showed increased risk of clefts after first trimester exposure (0.6%).

Benzos considered safe during 2nd and 3rd trimesters; can be used PRN unlike antidepressants.

Peripartum use of benzos associated with hypotonia, apnea, neonatal withdrawal syndrome and temperature instability.

Recommend taper and discontinue prior to delivery; however the peri-partum period can increase anxiety in women.
Electroconvulsive Therapy

Underused during pregnancy because of thoughts that it will harm fetus

Usually reserved for severe acute illness (e.g. acute mania, severely disorganized thoughts, impulsiveness and concern for self-harm)

Over 50 years of data supporting safe use

One report of possible associated placental abruption

Can be done safely with an obstetric OB and anesthesia
References